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Forum for Collaborative HIV Research

**Adherence to HIV Therapy:
Building a Bridge to Success**

Report from a Workshop Sponsored by:

DHHS Health Resource and Services
Administration (HRSA)
and
The Forum for Collaborative HIV Research

in collaboration with
NIH Office of AIDS Research

November 15-16, 1999
Washington, DC

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The Workshop was sponsored through a grant from the Health Resources and Services Administration. The Forum for Collaborative HIV Research would like to thank Joseph O'Neill, MD, Michael Johnson, MD, Jon Palinicek, MD, Joan Holloway, and Robert Soliz from HRSA for their support. Several people helped in the planning and implementation of this project including Bruce Agins, Carlos Arboleda, Judith Auerbach, Steve Chang, Henry Chang, Laura Cheever, Lisa Cox, Yvette Delph, Ruth Finkelstein, Linda Frank, Ruben Gamundi, Julia Hidalgo, Michael Joyner, Bonnie Lubin, William Strain, Ron Valdiserri, Phill Wilson. We want to thank all the speakers for their presentations. The background paper was written by David Barr and Robert Webster, who did a great job in a short time. The Forum administrative staff – Helen Nuamah, William Gist and Paul Oh made the Workshop possible. Much of the background investigation and thought behind this process was the work of Helen Schietinger, whom we deeply thank.

The Forum for Collaborative HIV Research, a project of the Center for Health Services Research and Policy at the George Washington University School of Public Health and Health Services, was founded in 1997. The goal of the Forum is to facilitate discussion regarding emerging issues in HIV clinical research and the transfer of research results into care. The Forum is a coalition of government agencies, clinical researchers, health care providers, pharmaceutical companies, and patient advocates. The Forum brings these constituencies together to identify gaps and impediments in the understanding of the medical management of HIV disease and develops recommendations to fill those gaps. June Bray is the Forum's Deputy Director. David Barr is the Executive Director.

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ADHERENCE TO HIV THERAPY— BUILDING A BRIDGE TO SUCCESS

**November 15–16, 1999
Washington, DC**

Introduction and Welcome

Goals and Background of the Workshop

Joseph F. O'Neill, MD, MPH – Health Resources and Services Administration (HRSA)

David Barr, JD – Forum for Collaborative HIV Research

Judith D. Auerbach, Ph.D – NIH Office of AIDS Research

In November 1997, the Forum for Collaborative HIV Research, the National Minority AIDS Council, and the NIH Office of AIDS Research sponsored a conference on research into adherence to HIV therapy. The conference brought together approximately 500 experts from government, academia, health care provision, and social service agencies, who are engaged in research on adherence issues, providing primary care, or are running educational and support programs with patients. The goal of that conference was to examine existing literature on adherence to medical treatment and to develop a research agenda to better understand the issues of adherence to HIV anti-retroviral therapy.

At that time, highly active anti-retroviral therapy (HAART) for HIV was relatively new. While adherence to treatment was presumed to be an important factor in the success of these new and promising therapies, little was known about adherence and HIV treatment. The 1997 conference examined literature in adherence research in other disease areas, and identified issues in HIV care into which adherence research should be conducted¹. We examined both the biomedical and behavioral aspects of three central questions:

- What are the factors that effect a patient's ability to adhere to therapy?
- What interventions can assist a patient's efforts to adhere to therapy?
- How can adherence to therapy be measured?

Several things have happened since that conference. First, it is clear that HAART can have a dramatic effect on HIV disease morbidity and mortality. Since the introduction of HAART, deaths from AIDS have dropped 44% in the United States. Rates of new AIDS cases show a similarly substantial decline. However, we also now know that HAART will not eradicate HIV. Patients must stay on complex treatment regimens for life. Good treatment compliance is difficult under any circumstance, and with HAART the complexity of the regimens and the unforgiving nature of HIV replication pose particularly difficult challenges for patients.

¹ The report from that conference can be found at the Forum's website at: www.gwumc.edu/chpr and then click on HIV Research.

The success of HAART is challenged by an HIV epidemic in the U.S. that is expanding to a population of patients who are more vulnerable, hard-to-reach and often have multiple crises in their lives. For most, HIV is now a disease of poverty. Today, people infected with HIV are 60% African-American or Latino; and of these, 70% of HIV-positive women are current and former drug users. This population is less likely to be on therapy or to have access to it. They see their physicians less often and are less likely to see a physician who is experienced in providing HIV care. An infrastructure to provide social services, medical care, housing, child care, mental health and substance abuse services, and education is essential if the promise of HAART is to be fully realized.

Two years since the conference on HIV treatment adherence research, it is also clear that without strict adherence to HIV therapy, HAART can not provide long-term suppression of HIV replication. Without adequate suppression, HIV is able to develop resistant mutations rendering HAART less or ineffective. Because of the complexity and duration of HAART regimens, adherence has emerged as a primary concern in quality and successful care. Therefore, it is important health care providers, social service providers, and patients have a good understanding of the need for and difficulties of adherence to treatment as they decide to start treatment and in order to be able to maintain good treatment adherence over the years.

To address these concerns, on November 15 – 16, 1999, the HRSA and the Forum for Collaborative HIV Research, in collaboration with the NIH Office of AIDS Research, held a workshop to see what has been learned since the 1997 conference. The workshop's primary focus was the examination of intervention efforts to educate health care providers and patients about HIV treatment adherence and to provide support to patients in their efforts to adhere to their HAART regimens. Workshop participants included academic researchers, government representatives, primary care providers, social service providers, pharmaceutical industry representatives, educators, and people with HIV and their advocates.

While two years is not enough time to develop, implement and evaluate research protocols that could determine which intervention approaches might best meet patient needs, much progress has been made to address these questions. In the last 2 years, the National Institutes of Health has funded 26 grants for research projects on adherence. HRSA has funded 12 programs to provide adherence support to underserved and vulnerable populations. Most of the HRSA-sponsored programs were represented at the 1999 workshop and many of those programs are described in this report.

For HRSA, the issue of adherence to HIV therapy is one that requires the expertise, collaboration, and coordination of services within primary care and social service settings, and ancillary treatment and support services. As HRSA performs a primary function in the provision and funding of these services, creating opportunities like this workshop to bring together the expertise, exchange information, and identify models for broader programs implementation is an important and valuable opportunity to address the challenge of treatment adherence and help to realize the promise of HAART therapy.

WHY IS ADHERENCE TO HIV THERAPY IMPORTANT?

Defining HAART Success and Failure: How Adherent Do You Have to Be?

Gerald Friedland, MD – Yale University School of Medicine

Dr. Friedland began his presentation with an overview of the goals of HAART. The biological goals include: (a) suppression of HIV replication to a level sufficient to prevent the development of drug resistant mutations and forestall the progression of HIV disease, and (b) the reconstitution of the immune system. Clinical goals are increased survival, reduced morbidity, and a better quality of life. The public health goal is to eliminate HIV transmission.

Several studies now show that patients who are able to suppress HIV replication below the level of detection of currently used assays (fewer than 20 to 50 copies/mL), have a substantially greater chance to achieve long-term viral suppression on HAART. It is also clear that even in successfully suppressed patients, HIV replication will rapidly rebound if HAART is discontinued. It is also necessary to obtain consistent and adequate drug levels in order to prevent the development of drug-resistant mutations. Therefore, to prevent progression of HIV disease, HAART must be taken regularly and continuously throughout a patient's lifetime.

The precise impact of various levels of non-adherence on antiretroviral therapy outcome has not been fully measured. While good adherence is a critical for success of HAART, a number of variables may modify the amount of adherence needed to achieve a such success. Dr. Friedland categorized and listed several factors that might modify the relationship of adherence and therapeutic outcome. These include specific features of the patient, his or her disease status, the infecting virus and, most importantly, the antiretroviral regimen. The patient's previous experience with antiretroviral agents may influence the amount of adherence needed. Antiretrovirals are usually of greatest potency in those individuals who have not received them previously. Similarly, the more advanced the state of disease, the more potent the required regimen and the more vulnerable the regimen's success may be to lapses in adherence. Close to seroconversion, with more limited viral species and resistance mutations and a more intact immune system, antiretrovirals may be more tolerant of incomplete adherence than late in HIV disease when the immune system is unable to control viral replication and multiple resistant species have emerged. Features of the predominant viral species, such as degree of resistance and fitness, may effect required levels of adherence, when stage of disease is constant. Finally, characteristics of the regimen may impact the needed levels of adherence. For example, potency and pharmacologic features such as absorption, metabolism and drug interactions may differ among regimens and, at a given level of adherence, result in differing therapeutic outcome. Emerging preliminary data from recent studies demonstrate that higher than anticipated levels of adherence are required in HIV therapeutics.

Measurement of adherence is still not precise and contributes to the difficulty of precisely relating levels of adherence to therapeutic outcome. In clinical care, adherence is usually measured by clinician's guess. This has been shown to be highly inaccurate and usually an overestimate. Other methods all have limitations including, pill counts, self-reporting, MEMS caps, pharmacy records, and metabolic drug levels. In recent studies with HIV therapies, MEMS cap measurements tend to show lower rates of adherence than self report, however, well collected self report data clearly correlates well virologic changes and is more practical in most settings. Regardless of measurement technique several fundamental questions include:

- What is the most appropriate time elapsed for adherence measurement? -. 1, 3, 7 days or a global percentage?
- Should all or individual drugs be measured?
- Should the units of measure be the percentage of doses missed, days missed, or intervals missed?

Emerging preliminary data from recent studies demonstrate that higher than anticipated levels of adherence are required in HIV therapeutics. Paterson et al, demonstrated that very high levels of adherence are necessary to achieve desired therapeutic effect, using MEMS caps in a population of 84 experienced patients at two HIV clinics. In this study, to achieve suppression of virus below 400 copies at 3 months in greater than 80% of patients, >95% adherence was necessary. A linear relationship between levels of adherence and viral load suppression was observed. A recently published report from 5 HIV clinics studied self-reported adherence among 173 antiretroviral experienced patients. Adherence to therapy during the previous four weeks at months two and six of the study was evaluated. At six months, none of the patients with adherence levels of less than 80 % were non detectable, 17% were non-detectable with 80-95% adherence levels, 41% with levels of 95-99% and 47 % of those who were 100% adherent were non-detectable (p=0.06). Viral load measures and CD4 cell counts were significantly correlated with adherence. Among those who were <80% adherent, at six months, there was a rise in viral load of .2 log and fall in CD4 count of 18 cells. In contrast, among those who were 100% adherent, viral load fell 1.1 logs and CD4 cell count rose 72 cells.

% adherence	% non-detectable viral load
>95	81
90 – 95	64
80 – 90	50
70 – 80	25
<70	6

Striking anecdotal examples of the effect of lapses in adherence, exist as well. In patients carefully followed by MEMS caps, even short drug holidays resulted in rapid rise in viral titer, which ultimately was associated with the disappearance of predominantly wild type virus and the appearance of resistant mutant virus. The fragility of current regimen potency is illustrated in clinical trials of induction/maintenance regimens. In these studies, reducing the intensity and potency of regimens after achieving non-detectable viral load



Forum for Collaborative HIV Research

**Center of Health Services Research and Policy
The George Washington University Medical Center**

March 22, 2000

Dear Colleague:

Enclosed please find the two most recent reports from the Forum for Collaborative HIV Research. The first is from a workshop entitled, *Adherence to HIV Therapy – Building a Bridge to Success*. This workshop, co-sponsored by the Health Resources Services Administration (HRSA), brought together experts from academia, health care provision, community-based organizations, pharmaceutical companies, and government to examine the latest findings about adherence to HIV therapy, with a special focus on intervention programs to assist patients in their adherence efforts. The workshop allowed us to look at what has been learned over the two years since the Forum co-sponsored the Adherence to HIV Therapy Conference. Also included is a background paper analyzing the literature on adherence to HIV therapy reported between November, 1997 to the present. To our knowledge, it is the first comprehensive literature review on this subject.

The Forum's Executive Committee, made up of representatives from each of the Forum's constituency groups – health care provision, research, government, industry, and patient advocacy – determines which projects the Forum will undertake and the scope of those projects. A list of Executive Committee members is attached. All Forum publications are available through our web site at www.gwumc.edu/chsrp then click on HIV research. In the coming year, the Forum will completely revise its website, providing easier access to publications, linkages to Forum member sites, and a name you can remember (HIVForum.edu).

In February, the Forum welcomed June Bray, Ph.D. as the Forum's Deputy Director. Dr. Bray has extensive experience in clinical research. She comes to the Forum from Social and Scientific Systems, where she served as the Director of the CPCRA Operations Center and was President of the Center for Health Information Management. Prior to her work with SSS, Dr. Bray was Associate Director of Clinical Research and Information at the American Foundation for AIDS Research and a consultant on AmFAR's international project in Nepal. Previously, she was the Principal Investigator of a national evaluation of alcohol and substance abuse prevention programs. As the Forum's Deputy Director, Dr. Bray will coordinate many of the Forum's projects.

As the Forum enters its fourth year of operation, I would like to take this opportunity to update you on the work of the Forum over the past year and describe some of our projects in the coming year. Descriptions of our work from the past year and our work plan for this year are attached.

Please contact me at ihodxb@gwumc.edu if you have any questions. Please feel free to distribute these reports to your colleagues. Additional copies can be obtained by contacting Paul Oh at 202-530-2334.

Yours truly,

A handwritten signature in black ink, appearing to read 'David Barr', written over a horizontal line.

David Barr
Executive Director

Forum for Collaborative HIV Research

Upcoming projects – 2000-2001

1. Meeting on Drug Interactions and HIV Antiretroviral Therapy - April 1, 2000, Noordwijk, the Netherlands

The goal of this meeting is to further coordination of research to obtain data on drug interactions in the use of HIV antiretroviral therapy. The meeting continues discussions began at the workshop on HIV salvage therapy last May. The Forum meeting would focus discussion on issues such as:

- Data-assay-, and drug-sharing mechanisms;
- Standards for drug interaction data in drug licensing.

The Forum's meeting will immediately follow the *1st International Workshop on Clinical Pharmacology of HIV Therapy*, March 30- April 1, 2000. That workshop will bring together leaders in the clinical pharmacology in HIV disease. Holding our meeting in conjunction with the Workshop will allow invited workshop participants the opportunity to first see and discuss the latest data before engaging in a discussion about methods to better exchange information and assays, as well as discuss future steps in research.

2. Evaluation of the feasibility of clinical studies examining the optimal time to begin antiretroviral therapy. Washington, DC, Spring- Summer 2000

As a follow-up to the January NIAID conference on "Long Term Clinical Studies in HIV-1 Infection", the Forum's proposed feasibility study is the next phase in looking at long-term clinical studies and will focus on issues relating to the question of "when to start" antiretroviral therapy. These issues include how to recruit and retain patients in such studies, the effects of different health care systems on study recruitment and design, the long-term applicability of such studies, and the effects of implementation of large studies on other research priorities. The Forum analysis will provide essential information to researchers and funders regarding issues that must be considered in designing long-term strategy studies for the use of antiviral therapy. The format for this study includes:

- Preparation of background research paper investigating recruitment and retention strategies developed in "early vs. deferred" protocols from other disease areas.
- Compilation and analysis of data examining at what stage of HIV disease people learn of their infection and when they access care.
- Development and implementation of a survey to better understand patient and provider attitudes towards participation in long-term clinical effectiveness studies, and the degree of uncertainty that exists regarding when to begin anti-viral treatment;
- Facilitation of one or two small meetings to develop expert opinion on the impact of these studies on other research priorities, and the relevance of long-term clinical studies in the rapidly changing AIDS treatment environment.

3. Pathogenesis of Metabolic Abnormalities in HIV Disease and Treatment April – September, 2000

In follow-up to the Forum's November 1999 meeting on the pathogenesis of metabolic abnormalities associated with HIV disease and treatment, the Forum will conduct three small workshop meetings covering the areas of bone metabolism, mitochondrial toxicity, and adipocyte biology. These small, intensive group meetings will allow for more specific and

in-depth discussion about further research needed to understand the pathogenesis of these abnormalities. We will propose that the results of these meetings be completed by July 2000, and be compiled and presented at the 2nd *International Workshop on HIV-related Lipodystrophy*, September 23, 2000 in Toronto.

**4. Development of a Strategic Plan for Treatment of HIV Disease in South Africa –
*Assessment of a Collaborative Dialogue Project - July, 2000***

The goal of this project is to assess the feasibility of, and most successful design for a collaborative process involving leaders from government, industry, health care delivery, and community to develop and implement a strategic plan for the treatment of HIV disease in South Africa. In collaboration with the National School of Public Health of South Africa, we will assess whether the Forum model would be appropriate and useful in the development of priorities for treatment HIV disease in South Africa. An assessment report will provide the basis for potentially moving forward with a collaborative project and would be announced during the XIII World AIDS Conference in Durban, South Africa. If successful, the project in South Africa can be seen as a pilot for similar undertakings in other areas.

5. Immune-based Therapies, October 2000

The development of effective immune-based therapies and therapeutic vaccines can play a valuable role in the long-term management of HIV disease. In April, the FDA will hold a meeting to discuss standards of efficacy for immune-based therapies. Hopefully, this meeting will provide guidance for industry in the development of such products. To follow on the momentum of the FDA's work, the Forum project will focus on identifying gaps in drug discovery and development efforts for immune-based therapies and develop recommendations to fill those gaps. Included in the discussion will be an investigation into the possible role that immune system rebound may have on metabolism.

6. Hepatitis C/HIV Co-infection, - January, 2001

This new project will focus on pathogenesis, prevalence, and treatment of Hepatitis C and HIV co-infection. We will begin with a background paper describing the prevalence and impact of co-infection and current research efforts. A workshop to discuss further research needs will then be held in January, 2001.

The following projects are also in development.

Patient Outcomes and HIV Medical Management

As follow up to last year's conference on patient outcomes research in HIV disease and treatment, the Forum will investigate how people learn of their HIV status and then enter into care. The project will begin with a Planning Group comprised of members from CDC, HRSA, HCFA, SAMHSA, NASTAD, and state government representatives and then be broadened to include representatives from health care provision, community organizations, and the pharmaceutical industry. Questions for examination will include:

- At what stage of HIV disease do people most often learn their HIV status?
- What motivates people to get tested for HIV?
- How can people be assisted to learn about their HIV infection earlier in the course of the disease and access care?

- What are the most efficient and effective methods to link HIV testing and care programs?

The Role of Cohort Studies in HIV Research

In conjunction with Glaxo Wellcome, the Forum will examine the role that cohort studies can play in furthering understanding of many of the issues in which the Forum is involved. Glaxo Wellcome has been working for many years bringing together investigators from cohort studies and observational data bases to share data and discuss future activities. When possible and appropriate, the Forum will work in conjunction with this process to determine the role that cohort studies can play in further research on metabolic abnormalities of HIV disease and treatment, long-term clinical effectiveness of HIV treatment, and the development of salvage therapy regimens for heavily pre-treated patients.

Forum for Collaborative HIV Research
Executive Committee

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Victoria Cargill, M.D.	- NIH Office of AIDS Research
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Richard Pollard, M.D.	- University of Texas – Galveston
William Strain	- ACTG Community Constituency Group

Forum for Collaborative HIV Research

Project Description 1999 - 2000

- ***The Challenge of Clinical Trial Design for the Use Antiretroviral Therapy in Heavily Pre-treated Patients*** – In May 1999, the Forum co-sponsored this workshop focusing on the need for and design of studies of anti-viral therapy in heavily pre-treated patients. A central focus of the discussion included issues regarding standards for obtaining licensed indications for HIV drugs used in salvage regimens. Both the FDA and EMEA participated in the workshop, along with patient advocacy groups, pharmaceutical industry and government representatives, and clinical researchers. This workshop was held in conjunction with the 2nd International Workshop on Salvage Therapy in HIV Disease, of which the Forum is a member of the Organizing Committee.
- ***Metabolic Abnormalities in HIV Disease and Treatment*** – The Forum continued its investigation of HIV-related metabolic abnormalities with a workshop examining the pathogenesis and treatment of the disorders. The workshop, held in November 1999, brought together leading researchers, physicians, government and industry representatives, and patient advocates to review research into the causes of HIV-related fat maldistribution, lipodistrophy, and mitochondrial toxicities. A report from that meeting is forthcoming. The Forum's previous meeting examining the prevalence of HIV-related metabolic abnormalities led to the development of the "FRAM" study, a state-of-the-art cross-sectional analysis of the prevalence of these symptoms in HIV-infected men and women in the United States. Carl Grunfeld, M.D. is the Principal Investigator of this 16 site, 1200 patient study funded by the National Institutes of Health.
- ***HHS Working Group on HIV Treatment Information Dissemination*** – At the request of the government Co-Convenors, Anthony Fauci, M.D. and Eric Goosby, M.D., of the PHS Guidelines Panel on Antiretroviral Therapy for Adults and Adolescents, the Forum facilitated this Working Group made up of representatives from the Office of HIV/AIDS Policy (OHAP), the National Institutes of Health, the National Library of Medicine, the Health Care Finance Administration (HCFA), the Health Resources Services Administration (HRSA), and the Centers for Disease Control and Prevention (CDC). The Working Group met on a regular basis to define the role of HHS in disseminating treatment information, identify the methods for fulfilling that role, identify the roles that each agency and program can play in implementing the efforts, and determine how to coordinate efforts between agencies. The work of the Group resulted in a report and work plan now being considered for implementation by the Office of the Secretary for Health and Human Services.
- ***Development of a Research Agenda Regarding the Effect of HIV Standards of Care on Patient Outcomes*** – This two-part project first produced a research paper examining the methodology of outcomes research and its possible application in the medical management of HIV disease. The paper was followed by a two-day workshop that brought together 100 experts from government, academia, health care delivery, managed care organizations, community-based organizations, and the pharmaceutical industry. It was the first time such a meeting was held on this topic. The workshop examined current outcomes research efforts in HIV disease and facilitated discussion amongst participants about the needs and opportunities for further research in this area.
- ***Adherence to HIV Therapy – Building a Bridge to Success*** – In follow-up to the November 1997 conference on HIV treatment adherence research, in November 1999, the Forum and the

Health Resources Services Administration (HRSA), sponsored this two-day workshop. The workshop brought together 100 experts in the field from health care delivery, academia, industry, government and community. The group heard reports about the need for strict adherence and the dangers of non-adherence to therapy, the factors that effect patient adherence, and methods to measure patient adherence. The primary focus of the workshop was a series of presentations of intervention programs. The group then developed recommendations for enhancing intervention programs. The report from the workshop is now available. The workshop resulted in a panel presentation at the HRSA Ryan White All-Titles Conference in January 2000.

Adherence to Highly Active Antiretroviral Therapy
(HAART) Among Individuals with HIV/AIDS: A
Compendium of HAART Adherence Research,
November 1997-November 1999

Robert D. Webster, M.P.H.

David Barr, J.D.

Adherence to HIV Therapy: Building a Bridge to Success

Forum for Collaborative HIV Research

Center for Health Policy Research

George Washington University Medical Center

November 15&16, 1999

Washington, D.C.

INTRODUCTION

The issue of adherence to highly active antiretroviral therapies (HAART) is multidimensional. HAARTs potential for long-term effectiveness is dependent upon maximum and durable suppression of viral replication. To meet such success requires near-perfect adherence to a complex regimen often including three or more drugs, consisting of 20 or more pills each day, taken two or three times daily at strict intervals, and with their own ingestion protocol such as fasting and high-fat or high-protein meals.¹⁻² Adherence is a central issue of concern in antiretroviral (AR) therapy, but a gold standard by which patients should be measured is lacking. This paper highlights relevant findings from an extensive, but not exhaustive review of peer-review journals and conference abstracts on adherence and compliance to HAART since November 1997.

In December 1995, the FDA licensed the first protease inhibitor for AIDS therapy.³ In July 1996, encouraging results from clinical trials of "drug cocktails" containing this new class of antiretroviral agent were reported at the 11th International Conference on AIDS.⁴⁻⁷ The three classes that make up HAART regimens are nucleoside analog reverse transcriptase (RT) inhibitors, non-nucleoside analog RT inhibitors, and protease inhibitors (PI). Since 1996, an overwhelming amount of scientific evidence has been published lending to the validity of combination therapies for HIV and AIDS patients. Substantial rates of decline in opportunistic infections⁸ and AIDS related mortality⁹⁻¹⁰ have been observed. A number of studies have consistently witnessed reductions in plasma HIV-1 RNA and increases in CD4 cell count, even among patients with initially very low counts.¹¹⁻¹³ Adherence to complex HAART regimens are complex and inconsistent adherence to a treatment regimen may lead to the development of drug

resistant mutations resulting in treatment failure¹⁴⁻¹⁶ This increases the probability of at-risk populations becoming infected with multiresistant HIV, thereby producing a potential public health consequence. Plasma HIV RNA levels have shown to quickly rebound in those with undetectable viral loads after stopping therapy, in some cases even exceeding pre-therapy levels within 21 days.¹⁷ Recent evidence has shown that patients on long-term HAART with undetectable levels of plasma viremia can harbor replication-competent HIV-1 DNA in resting memory CD4+ T cells.¹⁵⁻¹⁷ This new evidence sheds light on the realities of an indefinite reprieve from complex regimens even when undetectable levels of plasma viremia have been met; at best, with current medications HAART may be a life-long process. Because of this recent scientific revelation, there must be a convalescence of patients, clinician/health care workers, public health personal, the pharmaceutical industry, and other ancillary services to create meaningful answers to the myriad of questions surrounding HAART adherence.

BENEFITS OF ADHERENCE

Strict detailed adherence to physician-prescribed HAART regimens has been shown to be clinically beneficial. In a study of PI adherence in 84 subjects, who used an electronic pill monitoring device, 81% of subjects with > 95% adherence had complete viral suppression compared to only 64% with 90-95% adherence, 50% with 80-90% adherence, 25% with 70-80% adherence and 6% with < 70% adherence.²¹ In a prospective observational study of adherence, a linear trend of increasing adherence was seen for those with reduced HIV RNA and increased CD4 cells. After six months of treatment those reporting 100% adherence had a 1.1 log₁₀ copies/ml decrease in HIV RNA and an increase of 72 x 10⁶ CD4 cells/l compared to a 0.2 log

10 copies/ml increase in HIV RNA and a loss of 19×10^6 CD4 cells/l for those with less than 80% adherence.³¹ Other studies have also shown a relationship between adherence and undetectable plasma viremia.²²⁻²⁵ Adherent individuals have been shown to have reduced viral loads and increased CD4 counts, live longer, and have better quality-adjusted life years; these effects are even more pronounced for patients who were naive to treatment prior to starting a HAART regimen.²⁶⁻²⁷

DEVICES USED TO MEASURE ADHERENCE

Adherence to AR therapy has been measured by a variety of mechanisms. The most common modes seen in the literature are pill count, pharmacy records, and self-report.²⁸ Others include drug plasma concentration²⁹⁻³⁰, plasma HIV-1 RNA and CD4 cell count,³¹ medical appointment keeping, electronic medication monitoring/medication event monitoring system (MEMS),³²⁻³⁶ patient reporting track-screen PC,³⁷ and clinician/provider estimate of adherence.³⁸ Some modes of measurement appear to be more accurate than others and no one measure has been established as a gold standard. For example, in a six-month study, evaluating 195 adherence estimates, objective evaluations of clinicians' estimates of patients' adherence with PIs, using MEMS, found clinicians to be overestimating patients' adherence. In fact, 25% of patients whose providers estimated to have greater than 90% adherence actually had adherence of less than 80%.³⁸ The appropriate number of days used, prior to interview, to measure adherence varies greatly in the literature. Measurement of adherence the day before interview is predictive of one's previous month adherence behavior. Weidle and colleagues found that adherence the day before interview is consistent with adherence one month before interview. Those who reported non-adherence on the day prior to the adherence interview were 9.9 times more likely to

report non-adherence the prior month than those who reported adherence.³⁹

RATES OF ADHERENCE

Estimates for adherence rates differ considerably from study to study. The range for adherence to ARs in recent analyses was from 25%⁴⁰ to 85%⁴¹. By analyzing plasma samples for concentrations of assigned drug(s), researchers can estimate the levels of adherence among patients, in addition to their reliability of self-report. For example, seven hundred twenty-two plasma samples were analyzed from the AIDS Clinical Trials Group protocol 175, a large, double-blind, randomized study of monotherapy versus combination dideoxynucleoside therapy. Samples were analyzed for assigned drugs particular to each patient. Approximately 75% of the 722 analyzed samples had detectable concentrations of their assigned drugs.⁴²

FACTORS THAT INFLUENCE ADHERENCE

A multitude of variables has been investigated and shown to affect adherence to AR medications, some more than others. For example, The HIV Cost and Utilization Study, a national representative probability sample of 1910 persons taking ARs, found 57% of the subjects to be 100% adherent over the seven days prior to interview. Heavy alcohol and drug users were significantly less likely to adhere to ARs (45% vs. 59%, $p=0.003$). Being older ($p<0.0001$), male sex ($p=.008$), non-minority ($p=0.001$), and insured ($p=0.003$) were significantly related to better adherence to ARs. In addition, drug regimens that worked well with patients schedules ($p<0.0001$) and the perception that ARs are effective and that non-adherence leads to viral resistance ($p<0.0001$) were also predictive of good adherence.⁴³

FACTORS ASSOCIATED WITH POOR ADHERENCE

A number of variables have been shown to be related to poor adherence. Untoward

effects/toxicities, including nausea,^{29,39,44-51} forgetting to take dose,^{39,45-46,48,52-56} and drug (including IDU) and alcohol use^{29,31,43,45-46,53,55,57-58} were the most commonly seen predictors. In a study of 505 patients receiving PIs for 4 months, 35% (n=177) discontinued treatment. Thirty-two percent of those who discontinued treatment did so because of nausea to ritonavir, 26% and 24% because of failure of therapy for indinavir and saquinavir, respectively.⁴⁴ In a diverse sample of AR recipients, twenty-nine poorly adherent patients listed a total of 50 reasons for not adhering to their therapy. Over half were related to side effects/toxicity and forgetfulness, 28% and 24%, respectively.³⁹ In a diverse sample of 235 individuals from London, Oslo and San Francisco, 46% reported that they forgot to take their HIV medication.⁵⁶ In multi-center study with 151 patients receiving PIs a history of alcohol dependence or drug use predicted poorer adherence ($p < 0.05$).⁴⁵ Variables associated with access to care, including problems with getting medicines re-supplied or lack of medicines,^{39,59} lack of insurance or money for treatment,⁶⁰⁻⁶¹ government subsidized health insurance and health care from public/University clinics,⁶¹⁻⁶² long distances to travel and lengthy waiting times for physicians and at pharmacies,^{60,66} and lack of housing⁶¹ were predictive of decreased adherence. The facility from which one receives his or her health care may have an effect on adherence. Among an ethnically diverse sample of 463 men who have sex with men (MSM) from New York City and San Francisco, 48.9% of those currently taking ARs reported at least one day in which a dose of medication was missed. Those receiving health care at a public facility were more likely to miss doses than those receiving health care from a private physician ($X^2 = 11.74$, $p = .039$).⁶³

The burden of medication on lifestyle (finished drug-course before scheduled medical visit (not motivated to get refill),⁶⁷ too many different medications and pills,^{29,51,68} avoiding side-

effects in key situations/embarrassment (job interview, dating),⁶⁹ work-place related intake problems,⁶⁹ lack of interest in getting information on HIV,⁶⁶ and too busy to work medication schedule into daily routine,^{46,53,66} also affected adherence. Gregory and colleagues analyzed the charts of 273 PI-naïve patients at the Johns Hopkins University HIV Clinic. In logistic regression analysis, only adherence to clinical visits remained independently associated with HIV-1 RNA suppression.⁶⁵ Analysis of phone records from 179 counseling/psychological HIV therapy patients in Buenos Aires, Argentina, found a medication adherence rate of 43%. Quoted reasons for poor adherence included problems in getting medication re-supplied (24%), avoiding side-effects in key situations (20%), and work-place related intake problems (17%).⁵⁹

Patient health beliefs, attitudes, and psychosocial health also had an affect on adherence. For example, failure of therapy,^{44,70} no improvement in health status,^{29,62} belief about the effectiveness of ARs (medication causing harm),^{51,55,71} taking unconventional treatments with ARs,⁷² non-detectable plasma virus/asymptomatic state,^{46,67} and extreme levels of anxiety and psychosocial problems^{49,62} were all associated with poorer adherence. In addition, a small number of studies found demographic variables such as younger age,^{46,62,73} low education/literacy,^{68,74,75} female gender,^{29,57} minority status,⁵⁸ and increased age⁷⁶ to be additional factors associated with poor adherence.

FACTORS ASSOCIATED WITH BETTER ADHERENCE

Variables most predictive of better adherence in the literature were a strong relationship (support, trust, and a feeling of being well cared for) between the patient and the clinician/health care provider and/or system^{45,77-80} improved CD4 cell counts and a lowered viral load,^{34,78,81} and emotional support and continued interaction with peers,^{45,77,82-83} In a diverse sample of 727 HIV

positive individuals, 22.8% female and 56.8% non-white, those who reported the ability to maintain social interactions and rated their social support highly were more likely to be adherent to medication, follow advice and instruction, and keep appointments for visits.⁸²

The belief that PIs will extend life,⁴⁵ and that poorer adherence leads to viral resistance⁴³ were related to increased adherence. Demographic variables associated with good adherence included higher income,^{81,84} education,^{66,81} older age,⁴³ and Caucasian race.⁸⁵ Other factors included stable mental health and long-term plans/goals,⁸¹ having health insurance⁴³ and addiction care,⁶¹ improved sex drive⁸⁶ and, surprisingly, an increase in the amount of pills taken per day.⁴³ Adherence data for 1910 individuals, analyzed from The HIV Cost and Services Utilization Study found AR adherence strengthened with an increase in the number of drugs and pills prescribed per day (1-10 pills 53%, 11-20 pills 61%, > 20 pills 59%).⁴³ For well over half (62%) of those receiving PIs in a multicenter study of 248 patients, the belief that PIs will extend one's life was the leading motivating factor for adherence.⁴⁵ In a study of adherence to PIs, for 74 subjects over a six-month period, Kaplin and colleagues found that those who initially responded to therapy with a decreased viral load adhered better to PIs over the length of the study period compared to those subjects whose viral load did not decrease.³⁴

Adherence Among the Homeless

ARs are sometimes withheld from HIV-positive homeless and marginally housed persons (H/M) in fear of poor adherence to therapy. Bangsberg and colleagues investigated adherence among a representative sample of 154 HIV-positive H/M persons in San Francisco. Access to PIs in this sample was poor; at baseline only 7% were currently taking ARs. Cohort retention was high (82%). Adherence was good among H/Ms taking PIs; 80% of these subjects reported

missing less than 2 doses per week (n=23). Of adherent subjects, 88% had detectable AR medication in their plasma (n=18).⁸⁷ In a representative cohort of 132 HIV-infected H/M subjects, 22% had received PI and reverse transcriptase inhibitor (RTI) therapy. Cohort retention after nine months was 95%. Eighty percent of the H/M subjects reported taking greater than 90% of their prescribed doses, and plasma drug levels were consistent with self-reported adherence (88% detectable, n=17).⁸⁸

Adherence Among IV Drug Users

It has also been hypothesized that HIV-positive individuals who are currently using, or have a history of using drugs, may be less adherent to AR therapy than those without this behavior or history. In a large sample of 727 individuals, 56.8% reporting never using injection drugs and 39.3% reporting being a former or current user, injecting drug use was not related to keeping appointments or following healthcare advice and instruction. Active IDUs were more likely to report lower medication adherence scores, although the amount of variance explained (1.3%) in step-wise regression was modest.⁵³ Information from a sub-sample of 66 individuals from a sample of 314 HIV-infected IDUs enrolled in a cohort study in France was analyzed. All 66 individuals had received double or triple combination therapy. Active drug users were no more less compliant than ex-IDUs, but one-third of these patients did have problems with AR adherence. Among patients taking triple combination therapy, those who were enrolled in drug maintenance treatment programs tended to be more compliant than those who were not (85.7% vs. 56.4%).⁵² A qualitative study of factors related to adherence of AR among IDUs who were stabilized on methadone was carried out with twenty-three individuals. Having a positive attitude toward the future, a good relationship with one's medical team, a belief that ARs

improve survival and help compliance with a heroin free state, and being in prison were factors positively affecting continuance of therapy.⁵⁴

Adherence Among Women

As is the case with other demographic variables, studies have found both poor^{29,48,57} and good^{56,76,89} levels of AR adherence among women. In a study of 102 female prisoners, predictors of good medication adherence included trust in medications and the health care system, and interpersonal relationships with physicians and peers.⁷⁷ Factors relating to decreased adherence among woman in a number of studies included forgetting to refill medications and not understanding how to take them,^{48,90} older age,⁷⁶ and side effects.⁴⁸ Other studies have also addressed adherence among HIV-positive pregnant women and have found mixed results.^{55,58}

Adherence and Race

The majority of studies have not found race to be related to adherence rates. Though race overall may not be an indicator, there may be characteristics or confounding factors within different racial groups that affect levels of adherence. For example, in a cross-sectional study of 158 outpatient HIV clinic patients, African Americans were no less likely to adhere to ARs than Caucasians (race OR=1.06). Caucasians reported inconvenience of medications ($p=0.02$) and taking more medication as directed as barriers to adherence; whereas, African-Americans reported that no storage place for medications ($p=0.024$), ceasing medication use because of feeling better ($p=0.033$), not taking medication away from home ($p=0.014$), and being to embarrassed to get refills ($p=0.019$) were barriers.⁹⁰ In a study of 74 HIV-infected patients that investigated the association of literacy with AR adherence regimens among African-Americans and Caucasians. African-Americans were found to be significantly less adherent to ARs (31% vs.

11%, $p<0.05$), understood less the meaning of CD4 lymphocyte counts (56.3% vs. 77.1%, $p<0.0001$), and were less likely to understand the meaning of HIV-viral load measurement (87.5% vs. 28.6%, $p<0.0001$). Over three-quarters (83.3%) of Caucasian patients were always adherent to ARs compared to 66.7% of African-Americans with high literacy; only 34.1% of African-Americans with less than a 6th grade reading level adhered to ARs ($p<0.0001$). It should be noted, however, that this study did not compare groups with equal literacy levels.⁷⁴

Adherence to Prophylactics

Adherence to prophylactic medications for preventing opportunistic infections is also a concern for many clinicians. High rates of non-adherence to opportunistic infection prophylaxis among HIV-positive patients have been seen.⁹¹⁻⁹³ Data was analyzed for 419 subjects in order to predict adherence to mycobacterium avium complex (MAC) prophylaxis. Intentions to keep all medical appointments (OR 3.20, $p=0.008$) and having a higher level of education (OR 1.90, $p=0.026$) were associated with increased adherence. Not being interested in getting more information about HIV (OR 0.34, $p=0.026$), being too busy (OR 0.40, $p=0.026$), and being concerned about long clinic waiting times (OR 0.47, $p=0.034$) were also associated with decreased adherence.⁶⁶ In a Centers for Disease Control (CDC) study of 839 interviewed patients, prescribed prophylaxis for pneumocystis carinii pneumonia (PCP), 79% said they always took their medications as prescribed. Side effects (34%), forgetting to take medication (28%), and difficulty working medications into daily schedule (15%) were the most frequent reasons for not being 100% adherent. Non-adherence to PCP prophylaxis was greatest among younger persons (18-25) ($p=0.02$), IDUs ($p=0.02$), individuals with knowledge of their HIV status > 2 years ($p=0.02$), taking PCP prophylaxis > 6 months ($p=0.02$), a history of crack cocaine use ($p=0.05$),

and asymptomatic HIV infection status ($p=0.06$).⁴⁶

ADHERENCE INTERVENTIONS

A variety of interventions have been tested and implemented in order to increase adherence to ARs. One approach that seems to be having particular success is the pharmacist counseling intervention. Though the intervention components may differ slightly from study to study, the basic approach of the hospital/clinic pharmacy intervention or individually advised intervention is that of counseling patients individually. This approach consists of adapting treatment to the patient's lifestyle (writing out a medication schedule and setting up a pill box), explaining the clinical benefits of optimal adherence and identifying any risk factors for non-compliance, and providing telephone support. In a one year study testing the pharmacy intervention approach, 186 patients, 73% male and 48% IDU, were randomized (2/1) to conventional care (attending physician prescribed treatment) or hospital pharmacy intervention. Good adherence was defined as more than 90% of the drug regimen being taken. Those in the pharmacy intervention group were significantly more adherent than those under conventional care ($p=0.0005$). This adherence coincided with a decrease in viral load ($p=0.04$).⁹⁴ Knobel et al. studied a similar intervention on 170 patients who were assigned (2/1) to the conventional care or individually advised group. Correct adherence, defined as greater than 90% for prescribed drugs, was estimated at 52.7% for those receiving conventional care and 76.7% for those being individually advised ($p=0.002$). Reliability of adherence was strengthened with evidence of change in viral load at the 24-week follow-up from baseline. Undetectable viral load (<50 copies/ml) was found in 54.5% of those receiving conventional care compared with 65% of those being individually advised ($p=0.18$). Even more pronounced was the reduction in viral

load of $1.02 \pm 0.5 \log_{10}/\text{ml}$ for the conventional care group compared to $1.98 \pm 0.7 \log_{10}/\text{ml}$ for those being individually advised.⁹⁵

Interventions such as alarm devices and directly observed therapy have also been shown to increase adherence. Mannheimer and colleagues investigated adherence among 49 patients, 88% minority and 47% former IDUs, using an ALR (tm), a small, portable medication alarm programmed to sound daily at medication dosing times. The frequency of 100% pill, time and diet adherence was dramatically improved from baseline (N=49, 25% adherence) to month one (N=36, 67% adherence, $p < .005$) and month three (N=18, 89% adherence, $p < .001$) follow-up.⁹⁶ Modified directly observed therapy (MDOT) is a procedure in which an outreach worker meets with a patient Monday through Friday morning, at the patient's house or site of his or her choice, in order to observe a completed medication dose. The outreach worker asks about and records missed doses that are to be self-administered during the evenings and weekends. The number of meetings is tapered based on the participant's readiness. After 10 months of MDOT, for a very diverse group of 32 patients in a pilot program, of which 24 completed the study, 46% successfully had their number of visits reduced from 5 to 1-3 per week. Missing one or more doses in the preceding four days was decreased from 47% at baseline to 15% at 6 months for the thirteen patients for which 6 months of data was available.⁹⁷

Other adherence interventions which deserve further investigation based on preliminary findings include, but are not limited to mass media adherence campaigns;⁹⁸ "Medication Management" (labeled pill boxes for dosing and dosing instruction cards) and "Patient Support" (patient planner, newsletter, and graphs of HIV RNA and CD4 cell counts);⁹⁹ videos/booklets, devised by people with HIV, that have laymen explanations of the science of HIV disease in

addition to the importance of adherence and approaches to increase adherence;¹⁰⁰ a customized compliance check list which tracks the number of screenings completed each month, changes in self-reported adherence, viral load and CD4 counts, and completed interventions in order to evaluate the degree to which the adherence program is working;¹⁰¹ automated telephone communications technology mixed with live counselor calls in order to deliver counseling support for adherence enhancement;⁸⁵ a case-by-case triaged approach using nurse educators, social case management and mental health interventions, which includes psychosocial evaluation and treatment to improve adherence,¹⁰² and a newsletter with up-to-date research findings including aspects of HIV/AIDS therapies and adherence.¹⁰³

Interventions made for the purpose of fully guiding the clinician/health care worker in his or her treatment implementation have also been addressed. A good example of this is the "HIV Medication Guide," which includes over 350 drugs involved in the management of HIV and opportunistic infections, and can be used by clinicians/health care workers and community organizations. It assists in guiding the health care provider in designing individualized, optimal drug administration schedules, while simultaneously helping to detect drug interactions and giving the appropriate nutritional and pharmaceutical tips that will lead to reduced side effects and improved compliance.¹⁰⁴

DISCUSSION AND RECOMMENDATIONS

Original research on HAART adherence in peer-review journals is limited but growing. The majority of articles that have been published are often based on the application of adherence studies in other fields of medicine, and how such findings may be applicable to HIV. The bulk of the original research reported on here was found in books of abstracts from a variety of

conferences that specifically feature HIV research.

While there is a wide array of adherence measurements, there is no gold standard and a variety of measures may be best. Of the available measurements, MEMS caps, drug plasma concentrations, HIV-1 plasma RNA copies, and CD4 cell counts, though more expensive than conventional means (pill count, pharmacy records, and self-report), must continue to be used and improved on in order to obtain more accurate rates of adherence. Though ALR(tm) shows promise as a device to increase adherence, certain limitations must be addressed in order to improve upon attrition; 50% of the subjects, in the study by Mannheimer and colleagues, experienced malfunctioning with their devices. Since dramatic changes were seen for those without malfunctioning devices, technological advances in this area may have great potential in improving patient adherence.

AR adherence for those in hard to reach populations must be addressed. Preliminary data on adherence to ARs, though by use of small samples, among the homeless and marginally housed may be higher than hypothesized. Therefore, not only should ARs be made more available to this population, but also clinicians and outreach workers should not assume their patients' homelessness would result in poor adherence. Adherence rates for individuals currently using drugs is not favorable, but do not necessarily seem to differ from that of other groups in some studies.⁶³ Physicians should not make unwarranted assumptions about the ability of adhere to therapy because of a history of drug use. Factors influencing those who do comply with regimens seem to be similar to other populations. Those in drug maintenance treatment programs seem to have better rates of adherence. Research exploring the causes of adherence among IDUs in treatment setting warrants further research.

Most analyses of patient data in the literature and presented at conferences have not found any particular race to be more or less adherent than another. Though variables associated with adherence within race may differ from group to group.

Low literacy has been identified as a factor affecting adherence rates. Interventions that help to increase the understanding of HIV disease, including literature appropriate for the patient's level of reading, may go far toward increasing HIV adherence among those with lower literacy.

One untapped commodity of adherence intervention that may provide researchers with adherence questions may lie in the clinical trial setting. A retrospective chart review comparing adherence among individuals enrolled in an open label drug trial and those receiving antiretroviral drugs in the same clinical care setting found improved adherence for the former. Eighty-four percent (43/51) of patients in the clinical trial group had a plasma viral load of <400 copies/ml compared to 59% (15/36) of those in the clinical setting.⁶⁴ Other studies comparing clinical trials and outpatient clinics have yielded similar results.¹⁰⁵ Thus, the clinical trial setting may offer clues into variables associated with adherence and should be explored.

Quality adherence to AR therapy is an ongoing process in which the patient needs to be directly involved, it is not something an individual naturally possesses or lacks. Interventions to increase adherence must address cultural differences within race, gender, sexual orientation, and even religion. They must be tailored to meet culturally relevant barriers, including differences in language. Efforts must continue that help patients complete treatment, paying close attention to sociocultural circumstances as well as the psychological and economic factors that may impede upon adherence. Physicians should not automatically assume a future of poor adherence by their

patients on the basis of demographic and behavioral characteristics. These assumptions, on the part of the clinician, could stigmatize the clinician-patient relationship, thereby possibly introducing an additional impediment to adherence. An emphasis on language that stresses the inability of the patient to adhere to the devised medication regimen should be dropped and supplemented with language that stresses the role of the patient in devising and implementing an individualized treatment plan. Such language should be as elementary as possible with no reference to medical jargon.

Differences in access to health care are an important factor in adherence rates. Lack of insurance, dependence on public health care, and inability to fill prescriptions all effect adherence rates. Ensuring quality and consistent health care delivery is essential in promoting good adherence to therapy.

The current literature offers little information about the effect on adherence rates of pill burden, differences between drug regimens, stage of HIV disease, time on therapy, and mental health status. In other disease areas, these are cited as important factors in treatment adherence. Further study of these factors in HAART adherence is needed. Evaluations of adherence intervention tools, including counseling programs, DOT, methods to assist patients in deciding whether to start antiretroviral therapy, and educational materials are also needed. The success or failure of HAART, both as a treatment strategy for patients and a public health strategy to prevent the spread of multi-drug resistant HIV, is dependent upon the ability of patients to adhere to therapy. Support to assist patients in their adherence efforts should be comprehensive and considered a high priority in the delivery of HIV primary care and social services.

Bibliography

1. Deeks DG, Smith M, Holodniy M, Kahn JO. HIV-1 protease inhibitors: A review for clinicians. *JAMA*. 1997;277:145-153.
2. McDonald CK, Kuritzkes DR. Human immunodeficiency virus type 1 protease inhibitors. *Arch Intern Med*. 1997;157:951-959.
3. Fleming PL, Ward JW, Karon JM, Hanson DL, De Cock KM. Decline in AIDS incidence and deaths in the USA: A signal change in the epidemic. *AIDS*. 1998; 12(supplA):S55-S61.
4. Lalezari J, Haubrich R, Burger HV, et al. Improved survival and decreased progression of HIV in patients treated with saquinavir plus HIVID. *XI International Conference on AIDS. Vancouver, July 1996 [Abstract #LB.B6033]*.
5. Cameron DW, Heathciozzi M, Kravick S, Mills R, Potthoff A, Henry D, for the Advanced HIV Ritonavir Study Group. Prolongation of life and prevention of AIDS complications in advanced HIV immunodeficiency with ritonavir update. *XI International Conference on AIDS. Vancouver, July 1996 [Abstract #MOB411]*.
6. Berry P, Kahn J, Cooper R, et al. Antiretroviral activity and safety of indinavir alone and in combination with zidovudine in ZDV-naïve patient CD4 cell counts of 50-500 cells/mm³. *XI International Conference on AIDS. Vancouver, July 1996 [Abstract #Th.B.6019]*.
7. Markowitz M, Cao Y, Hurley A, et al. Triple therapy with AZT,3TC, and ritonavir in 12 subjects newly infected with HIV-1. *XI International Conference on AIDS. Vancouver, July 1996 [Abstract #Th.B.933]*.
8. Jones JL, Hanson DL, Dworkin MS, DeCock KM. HIV associated TB in the era of HAART. *1999 National HIV Prevention Conference. Atlanta, August 1999 [164]*.
9. Chiasson MA, Berenson L, Li W, Schwartz S, Singh T, Forlenza S, et al. Declining HIV/AIDS mortality in New York City. *J Acquir Immune Defic Syndr*. 1999;21:59-64.
10. Markan SE, Leonetti AM, Hopkins SG. Declines in AIDS-related mortality and factors associated with recent AIDS deaths in Seattle, King County, Washington. *1999 National HIV Prevention Conference. Atlanta, August 1999 [660]*.
11. Miller V, Staszewski S, Nisius G, Lepris AC, Sabin C, Phillips AN. Risk of new AIDS diseases in people on triple therapy [letter]. *Lancet*. 1999; 353:463.
12. Hammer SM, Squires Ke, Hughes, MD, Grimes JM, Demeter LM, et al. A controlled trial of two nucleoside analogues plus indinavir in persons with human immunodeficiency virus infection and CD4 cell counts of 200 per cubic millimeter or less. *New Engl J Med*. 1997;337:725-733.
13. Floridia M, Bucciardidni R, Ricciardulli D, Fragola V, PirilloMF, Weimer LE, et al. A randomized, double-blind trial on the use of a triple combination including nevirapine, a non-nucleoside reverse transcriptase HIV inhibitor, in antiretroviral-naïve patients with advanced disease. *J Acquir Immune Defic Syndr*. 1999;20:11-19.
14. Condra JH. Resistance to HIV protease inhibitors. *Haemophilia*. 1998;4:610-615.
15. Boden D, Hurley A, Zhang L, Cao Y, Guo Y, Jones E, et al. HIV-1 drug resistance in newly infected individuals. *JAMA*. 1999; 282:1335-1341.
16. Little SJ, Daar ES, D'Aquila RT, Keiser PH, Connick E, et al. Reduced antiretroviral drug

- susceptibility among patients with primary HIV infection. *JAMA*. 1999;282:1142-1149.
17. Harrigan PR, Whaley M, Montaner JS. Rate of HIV-1 RNA rebound upon stopping antiretroviral therapy. *1999 AIDS*; 13:F59-62.
 18. Wong JK, Hezareh M, Gunthard HF, Havlir DV, Ignacio CC, Spina CA, Richman DD. Recovery of replication-competent HIV despite prolonged suppression of plasma viremia. *Science*. 1997;278:1291-1294.
 19. Finzi D, Hermanova M, Pierson T, Carruth LM, Buck C, Chaisson RE, et al. Identification of a reservoir for HIV-1 in patients on highly active antiretroviral therapy. *Science*. 1997;278:1295-1300.
 20. Markowitz M, Vesanen M, Tenner-Rasz K, Cao Y, Binley JM, Talal A, et al. The effect of commencing combination antiretroviral therapy soon after human deficiency virus type 1 infection on viral replication and antiviral immune response. *J Infect Dis*. 1999;179:527-537.
 21. Paterson D, Swindells S, Mohr J, Brester M, Vergis E, et al. How much adherence is enough? A prospective study of adherence to protease inhibitor therapy using MEMS caps. 6th conference on Retroviruses and Opportunistic Infections. Chicago, January, 1999 [Abstract # 92].
 22. De Masi R, Tolson J, Pham S, Capuano G, Graham N, et al. Self-reported adherence to HAART and correlation with HIV RNA: Initial results with the patient medication adherence questionnaire. 6th conference on Retroviruses and Opportunistic Infections. Chicago, January, 1999 [Abstract# 94].
 23. Hecht FM, Colfax G, Swanson M, Chesney MA. Adherence and effectiveness of protease inhibitors in clinical practice. 6th Conference on Retroviruses and Opportunistic Infections. Chicago, January, 1999 [Abstract#151].
 24. Tebas P, Royal M, Fichtenbaum C, Blument M, Horsan W, Powderly W. Relationship between adherence to HAART and disease state.
 25. Barroso PF, Schechter M, Gupta D, Melo MF, Vieira M, et al. Adherence to antiretroviral therapy is associated with seminal viral load suppression. 39th Interscience Conference on Antimicrobial Agents and Chemotherapy. San Francisco, September 1999 [Abstract #597].
 26. Richter A, Simpson KN, Manskopf JA. Impact of drug non-compliance and the frequency of viral load testing on outcomes, costs and patterns of therapy. 12th World AIDS Conference. Geneva, June, 1998 [Abstract #42173].
 27. LeMoing V, Masquelier B, Moatti JP, Journot V, Sicard D, et al. To study predictors of immunologic response to PI therapy, along with virologic response, including adherence to therapy. 39th Interscience Conference on Antimicrobial Agents and Chemotherapy. San Francisco, September 1999 [Abstract #596].
 28. Watson DC, Farley JJ, Lovelace S, Vink P. Efficacy and adherence to highly active antiretroviral therapy in HIV-1 infected children. 5th Conference on Retroviruses and Opportunistic Infections. Chicago, January, 1998 [Abstract#230].
 29. Murri R, Ammassari A, Gallicano K, DeLuca A, Cingolani A, et al. Relationship of self-reported adherence to HAART with protease inhibitor plasma level and viral load. 39th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, September 1999 [Abstract #593].
 30. Tuldra A, Fumaz CR, Ferrer MJ, Bayes R, Arno A, et al. A specific intervention improves

- long-term adherence to HAART and ensuing virological outcome. *39th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, September 1999 [Abstract #595]*.
31. Haubrich RH, Little JS, Forthal DN, Kemper CA, Beall GN, et al. The value of patient-reported adherence to antiretroviral therapy in predicting virologic and immunologic response. California Collaboration Treatment Group. *AIDS*. 1999;13:1099-1107.
 32. Bangsberg DR, Hecht FM, Charlesbois EC, Zolopa AR, Holodnig M, et al. Spontaneous adherence audits predict viral suppression in the REACH cohort. *6th Conference on Retroviruses and Opportunistic Infections. Chicago, January, 1999 [Abstract#93]*.
 33. Golin C, Liu, Hays R, Ickovics J, Beck K, et al. Self-reported adherence to protease inhibitors substantially overestimates an objective measure. *6th Conference on Retroviruses and Opportunistic Infections. Chicago, January, 1999 [Abstract#95]*.
 34. Kaplin A, Golin C, Beck K, Lui H, Hays R, et al. Adherence to protease inhibitor therapy and viral load. *6th Conference on Retroviruses and Opportunistic Infections. Chicago, January, 1999 [Abstract#96]*.
 35. Vanhore GF, Schapiro JM, Winters MA, Merigan TC, Blaschke TF. Patient compliance and drug failure in protease inhibitor monotherapy [Letter]. *1996 JAMA*; 276:1955-1956.
 36. Vanhore GF, Schapiro JM, Winters MA, Merigan TC, Blaschke TF. Patient compliance and drug failure in protease inhibitor monotherapy [Letter]. *1996 JAMA*; 276:1955-1956.
 37. Wu A, Yu-Isenberg K, McGrath M, Jacobson D. Reliability, validity, and usefulness of touch-screen administration of QOL and adherence instruments in an outpatient clinic. *6th Conference on Retroviruses and Opportunistic Infections. Chicago, January, 1999 [Abstract#99]*.
 38. Miller L, Lui H, Beck K, Golin C, Hays R, et al. Providers estimates of adherence overestimate reports from medication event monitoring system (MEMS) for patients on protease inhibitors. *6th Conference on Retroviruses and Opportunistic Infections. Chicago, January, 1999 [Abstract#97]*.
 39. Weidle PJ, Ganea CE, Ernst J, McGowan J, Irwin KL, Holmberg SD. Multiple reasons for non-adherence to antiretroviral medications in an inner-city minority population: Need for a multi-faceted approach to improve adherence. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32375]*.
 40. Ford PM, Carson R, Pepperell S. Drug compliance in patients starting saquinavir. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #60151]*.
 41. Bachiller P, Arrando FR, Liceaga G, Iribarren JA, Olloquiegui E, et al. Adherence to antiretroviral therapy in HIV-infected persons. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32392]*.
 42. Kastrissios H, Suarez JR, Hammer S, Katzenstein D, Blaschke TF. The extent of non-adherence in a large AIDS clinical trial using plasma dideoxynucleoside concentrations as a marker. *1998 AIDS*; 12:2305-2311.
 43. Wenger N, Gifford A, Liu H, Chesney M, Golin C, et al. Patient characteristics and attitudes associated with antiretroviral adherence. *6th Conference on Retroviruses and Opportunistic Infections. Chicago, January, 1999 [Abstract#98]*.
 44. Youle M. Reasons for discontinuation of protease inhibitor treatment: A clinical survey. *12th*

- World AIDS Conference. Geneva, June, 1998 [Abstract #32353].*
45. Stone VE, Adelson-Mitty J, Duefield CA, Steger KA, Stein MD, Mayer KH. Adherence to protease inhibitor therapy in clinical practice: Usefulness of demographics, attitudes, and knowledge as predictors. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32337].*
 46. Jones JL, Nakashima AK, Kaplan JE. Adherence to primary prophylaxis for pneumocystis carinii pneumonia: Results from a multi-state interview project. *39th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, September 1999 [Abstract #586].*
 47. Nakashima AK, Jones JL, Burgess DA, Ward JW. Adherence to currently prescribed antiretroviral therapies: Results from a multi-site interview project. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #392/32326].*
 48. Paiva V, Santos N, Venturn-Filipe EM, Hearst N, Reingold A. Compliance with reverse transcriptase inhibitors or combination therapy among HIV+ women in Sao Paulo, Brazil. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32399].*
 49. Hirschhorn L, Quinones J, Goldin S, Metras L. Highly active antiretroviral therapy in the "real world": Experiences in an inner-city community health center. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32334].*
 50. Bonafanti P, Pusteria L, Fácetti O, Visona R, Faggion I, et al. Adverse reactions during protease inhibitors therapy. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #60658].*
 51. Johnston BE, Ahmad K, Smith C, Rose DN. Adherence to HAART among HIV-infected patients of the inner city. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32389].*
 52. Patrizia M, Carrieri C, Reynaud-Maurupt C, Pradier JP, et al. Compliance to multiple combination therapy with protease inhibitors among HIV-infected IDUs in France (cohort Manif 2000). *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32359].*
 53. Turner JG, Nokes KM, Corless IB, Holzemer WL, Inouye J, et al. History of drug use and adherence in HIV+ persons. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #391/32366].*
 54. Jones AM, Thaker H, Foley B, Barry C, Pronty G, et al. A qualitative study on retroviral therapy: Drug compliance in IVUD patients. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32361].*
 55. Brigido LF, Veiga AP, d'Ambrosio AC, Bueno A, Casseb J, Galbitti FF. Low adherence in antiretroviral users at Sao Paulo, Brazil. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32370].*
 56. Gir E, Pratt R, Bunch EH, Holzemer WL. Adherence to antiretroviral therapy: A four country comparison. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #60129].*
 57. Cheever LW, Kervly JC, Moore RD. Antiretroviral use and adherence predicted by active illicit drug use. *39th Interscience Conference on Antimicrobial Agents and Chemotherapy. San Francisco, September 1999 [Abstract #596].*
 58. Ohmit S, Schuman P, Schoenbaum E, Rompalo A, Cohen M, et al. Adherence to antiretroviral therapy among women in the HIV Epidemiology Research Study (HERS) and

- Women's Inter-Agency HIV Study (WIHS). *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32347].*
59. Burgos M, Revsin NS, Vilas A, Fontan L. Obstacles in treatment adherence: Patient reasons. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32400].*
 60. Nemecheck P, Tritle D. A survey evaluating pharmacy-related resources and their relation to drug adherence. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32398].*
 61. Schilder AJ, Hogg RS, Goldstone I, Stathdee S, Schechter MT, O'Shaughnessy MV. Adult social identity is part of culturally competent HIV care for sexual minorities and affects care-seeking behaviors and therapeutic adherence. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32355].*
 62. Klosinski LE, Brooks RN. Predictors of non-adherence to HIV combination therapies. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32375].*
 63. Halkitis PN, the Seropositive Urban Drug Injectors' Study Team. Access to antiretroviral treatment and adherence to treatment in injecting drug users and men who have sex with men. *1999 National HIV Prevention Conference. Atlanta, August, 1999 [Abstract #336].*
 64. Bergeron K, Gormley J, Sousa H, Tashima K, Flanigan TP, Merriman NA. Adherence to HAART in clinical trials vs. clinical care setting. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #60356].*
 65. Lucas GM, Chaisson RE, Moore RD. Highly active antiretroviral therapy in a large urban clinic: Risk factors for virologic failure and adverse drug reactions. *Ann Intern Med. 1999;131:81-87.*
 66. Kammann E, Williams P, Chesney MA, Currier J. Predictors of adherence to arithromycin prophylaxis for prevention of mycobacterium avium complex (MAC) disease. *6th Conference on Retroviruses and Opportunistic Infections. Chicago, January, 1999 [Abstract #444].*
 67. Murri R, Ammassari A, DeLuca A, Cingolani A, Antinori A. Definition and measurement of adherence to antiretroviral drugs in HIV-infected patients. *Lancet. 1999;353:1974*
 68. Moralez R, Figueiredo VM, Sinkoc MCB, Gallani C, Tomazin SM, et al. Adherence of patients with AIDS to treatment with antiretroviral medications: Difficulties related and proposition of attenuating measures. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #42442].*
 69. Burgos M, Revsin NS, Vilas A, Fontan L. Obstacles in treatment adherence: Patient reasons. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32400].*
 70. Woodward J, Wareham PS, Grohskopf L, Madigan D, Hooton TM. Protease inhibitor adherence and HIV-1 RNA response. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #60363].*
 71. Home R, Pearson S, Leake H, Fisher M, Weinman J. Patients' belief about HAART influence adherence to antiretroviral therapy. *39th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, September 1999 [Abstract #588]*
 72. Malafronte B, Perbost I, Dunais B, Rahelinirina V, Keita-Perse O, et al. Unconventional medicine and AIDS: Trends in behavior among patients receiving protease inhibitors. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #14119].*
 73. Catz S, McClure JB. HIV outpatient adherence: Relation of disease status to appointment-keeping. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #42453].*

74. Sipler AM, Cross JT, Lane DR, Davis, TC, Williams LM, et al. The relationship between literacy race, and adherence to patient antiretroviral therapies. *6th Conference on Retroviruses and Opportunistic Infections. Chicago, January, 1999 [Abstract#108]*
75. Kalichman SC, Ramachandran B, Catz S, Adherence to combination antiretroviral therapies in HIV patients of low health literacy. *J Gen Intern Med. 1999;14:267-273.*
76. Gardner L, Smith D, Stone V, Howard A, Schuman P, Rompalo M, et al. Adherence to antiretroviral medications in the HERS study. *39th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, September 1999 [Abstract #592].*
77. Mostashari F, Riley E, Selwyn PA, Altice RL. Acceptance and adherence with antiretroviral therapy among HIV-infected women in a correctional facility. *1998 J Acquir Immune Defic Syndr Hum Retroviral; 18:341-348*
78. Stone VE, Clark J, Lovell J, Steger KA, Hirschhorn LR, et al. HIV/AIDS patients' perspectives on adhering to regimens containing protease inhibitors. *J Gen Intern Med. 1998;13:586-593.*
79. Powell-Cope GM, Brown MA, Holzemer WL, Corless IB, Turner JG, et al. Perceived health care providers support and HIV adherence. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32354].*
80. Holzemer WL, Inouye J, Brown MA, Powell GM, Corless IB, et al. Psychological well-being and HIV adherence. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32368].*
81. Pratt R, Robinson N, Loveday HP, Pellowe CM, Franks PJ, et al. Improvement in sexual drive and a falling viral load are associated with adherence to antiretroviral therapy. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32343].*
82. Brown MA, Inouye J, Powell-Cope GM, Holzemer WL, Nokes KM, et al. Social support and adherence in HIV+ persons. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32346].*
83. Kunches L, Mazzullo JM, Miller-Mack E, Russell M, Ortega Z. Educational and support needs of people living with HIV to improve adherence to HAART. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32333].*
84. Martinez M, Marques A, Valdes J, Santana J. Factors associated in a Hispanic cohort with effective adherence and desired clinical results in patients with triple antiretroviral therapy (including one PI). *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32403].*
85. Byrd R, Fisher AE, Melbourne KM, Willey-Lessne C, Healy E, Morrill AC. Support intervention to enhance medication adherence. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #323349].*
86. Pratt R, Robinson N, Loveday HP, Pellowe CM, Franks PJ, et al. Improvement in sexual drive and a falling viral load are associated with adherence to anti-viral therapy. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32343].*
87. Bangsberg D, Robertson M, Charlesbois E, Tulskey J, Hecht FM, et al. Protease inhibitors in the HIV+ homeless and marginally housed: Good adherence but rarely prescribed. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #389/32406].*
88. Bangsberg DR, Zolopa AR, Charlesbois E, Tulskey J, Hecht FM, et al. HIV-infected homeless and marginally housed patients adhere to and receive early virologic benefits from

- protease inhibitors. *5th Conference on Retroviruses and Opportunistic Infections, Chicago, February 1 – 5, 1999 [Abstract #152]*.
89. Williams A, Wolf H, Yu C, Singh M. Adherence to antiretroviral therapy among HIV-positive women. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32374]*.
 90. Freeman TL, Stewart KE, DeMasi R, Sang MS. Adherence in the age of highly active antiretroviral therapy: Racial and gender differences. *1999 National HIV Prevention Conference. Atlanta, August, 1999 [Abstract #649]*
 91. Settle J, Wong M, Watson VM, Goolsby MR, Kaplowitz LG. Poor medication adherence extends to opportunistic infection prophylaxis. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32376]*.
 92. Lundberg B, Davidson A, Burman WJ. Patient and provider noncompliance with prophylaxis for pneumocystis carinii pneumonia. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #13234]*.
 93. Tupinambas U, Greco DB, Moll SS, Diniz LM, Xavier LF, et al. Profile of HIV patients and compliance to primary prophylaxis therapy to tuberculosis in an outpatient clinic in Belo Horizonte, Brazil, June '95 – July '97. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #22156]*.
 94. Knobel H, Carmona A, Grau S, Saballs P, Gimeno JL, Lopez-Colomes JL. Strategies to optimize adherence to HAART. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32322]*.
 95. Knobel H, Carmona A, Lopez JL, Gimeno JL, Saballs P, et al. Adherence to very active antiretroviral treatment: Impact of individualized assessment. *Enfermedades Infecciosas y Microbiologia Clinica. 1999;17:78-81*.
 96. Mannheimer S, Hirsch Y, El-Sadr W. The impact of the ALR™ alarm device on antiretroviral adherence among HIV-infected outpatients in Harlem. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32325]*.
 97. Stenzel M, McKenzie M, Flanagan T, Adelson Mity J. A pilot program of modified directly observed therapy to enhance adherence to highly active antiretroviral therapy: 6-month follow-up. *39th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, September 1999 [Abstract #589]*.
 98. Ward P, Grimshaw PJ. The development of effective media campaigns to encourage compliance with anti-HIV treatment. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32394]*.
 99. Farnsworth A, Milan L, Dumestre J, Allison S, Johnson D, et al. Use of medication management tools to increase adherence in a controlled trial of quadruple-drug therapy in HIV+ female patients. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32364]*.
 100. Lamp R, Babakhanian R, Houyez F, Hollander N, Broekhuizen A, Sousa Passos A. HIV treatment compliance and drug resistance. A model for cross-cultural treatment education to enable HIV-positive people to make effective treatment decisions. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32363]*.
 101. Nissen JC, Gajewski L, Grimone AJ, Vanscoy GJ. Nationwide protease inhibitor adherence program. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32327]*.
 102. Loor R, Amberg M, Moore P. Interventions to support patient adherence to HAART.

- 1999 National HIV Prevention Conference, Atlanta, August 1999 [Abstract #]*
103. Rohr M. "Bridging the gap" between the world of medicine and people living with HIV/AIDS as prerequisite for good compliance. *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32332].*
 104. Therrien R, Gagnon A, Mailhot M. Increasing patient adherence: Experience with the "HIV Medication Guide." *12th World AIDS Conference. Geneva, June, 1998 [Abstract #32369].*
 105. Heinasmaki T, Shi Q, Creagh T, Mather-Wagh V, Marshak A, et al. Adherence and antiretroviral responses to highly active antiretroviral therapy in patients infected with human immunodeficiency virus: Comparison between an outpatient clinic and a clinical trials unit. *12th World AIDS Conference. Geneva, June, 1998*

measures has resulted in rapid viral rebound in a substantial proportion of patients, providing additional, indirect support for the need for perfect or near-perfect adherence to maintain regimen potency.

Who Is on HIV Antiretroviral Therapy?

Julia Hidalgo, Sc.D. – Center for Health Services Research and Policy at the George Washington University School of Public Health and Health Services

Dr. Hidalgo provided background information about the demographics of people with HIV in the U.S., including where they live, information about their age, race, gender, and education levels. She discussed where people with HIV receive their health care, at what point in the course of HIV disease they come into care, and the quality of the care received.

At first the treatment population was composed largely of older white gay men who sought timely treatment. They were generally more educated, had higher incomes, had commercial insurance, and tended not to come from the South. After about 2 years of treatment, patients progress to HAART.

Now the epidemic is changing and concerns focus on:

- access to care
- source of primary care
- continuity of services
- continuity of health care coverage
- mental illness, substance abuse, or other co-morbidity
- incarceration
- personal, economic, and legal crises
- family and social support system
- infected family members

Systemic barriers to adherence services include:

- The HIV care system across the country is fragmented. About 40% of clinics offer on-site mental health care and two-thirds offer substance abuse treatment; on-site child care is rare. Even these clinical and support services are poorly integrated and coordinated.
- For both clinic and support services, capacity is inadequate to meet the demand.
- Support service providers are inadequately trained regarding HAART and adherence strategies.
- Formal adherence programs are limited in number and scope.
- Programs are often not culturally and linguistically competent.
- Insurance coverage varies and tends to be inconsistent.
- Treatment for substance abuse and mental health is inadequately funded.

The rise of managed care and other federal and state health care financing policies present particular barriers, including:

- HIV treatment has not been integrated into the services offered.
- HIV care providers do not generally participate in managed care.
- Some existing service strategies are deleterious to adherence, e.g. the failure of mental health services to be integrated or coordinated with primary care services.
- There is strict application of disability criteria for SSI and SSDI benefits.
- Welfare and Medicaid reform has led to loss of coverage.

How can the HIV/AIDS care system support adherence? First, adherence services must be defined - a funding agency cannot support something if they do not know what it is. In defining the services, we should:

- Integrate adherence into HIV services.
- Identify structural barriers.
- Expand programs.
- Among traditional and well-organized specialist and primary care providers, expand the multidisciplinary team approaches (e.g., CBOs, MCOs, care managers, schools, jails) to the patient, family, and informal support systems.
- Involve the whole team from the beginning.
- Expand case conferencing.
- Do not create a proliferation of small under-funded adherence programs.

Adherence services cannot be added to existing services without adding money. As for payment for providers of adherence services, the Care Act is important, but resource decisions are often made at the local level. Adherence services must be clearly articulated, measurable, and cost effective. In underwriting these services there is a clear role for sustained outside grant-giving and for industry.

FACTORS THAT AFFECT ADHERENCE: **WHAT HAVE WE LEARNED SINCE NOVEMBER 1997?**

Simplification of Therapy: Fewer Pills, Fewer Doses per Day

Renslow Sherer, MD – The CORE Center, Cook County Hospital

One of the major challenges to good adherence to HAART has been the complexity of the regimens. Many drugs need to be taken three times a day (TID), and the pill burden can be overwhelming, i.e. 15-20 pills daily. Some drugs should be taken with food, some without food, and still others with high fat meals. Simplification of treatment regimens to the greatest extent possible is essential if adherence efforts are to be successful. Fortunately, in the past three years, the convenience and tolerability of regimens have improved. There are now several available twice a day (BID) regimens, and several drugs are now being tested for once-daily dosing (QD). In addition, the pill burden can now be as low as a few pills twice daily.

Table I below shows the recent alterations in dosing of common antiretroviral therapies. For a complete description of the goals of HIV therapy, recommendations for initial and subsequent antiretroviral therapies, alternate dosing strategies, common toxicities, drug interactions, and strategies and references for adherence, the reader is referred to the HHS/KFF Guidelines for the Treatment of HIV Infection in Adults and Adolescents of February, 2000 at www.hivatis.org.

Table I: Altered Dosing of Antiretroviral Agents, 2000

<u>Class</u>	<u>Agent</u>	<u>Initially recommended dose (mg)</u>	<u>Amended dose (mg)</u>
<u>NRTIS</u>	ddl	200 BID	400 QAM
	AZT	200 TID	300 BID
	3TC	150 BID	300 QD
	Combivir	AZT+3TC BID	-----
	ABC	300 BID	-----
<u>NNRTIs</u>	NVP	200 BID	400 QD
	EFV	600 QD	QHS -----
<u>PIs</u>	NFV	750 TID	1,250 BID
	RTV*	600 BID*	400 RTV + 400 SQV BID
	SQV-SGC*	1,200 TID*	1,600 mg BID
	AMP	1,200 BID	-----

Thus rational sequencing of HAART regimens in the year 2000 implies that the initial and subsequent regimens best fit the patient with regard to potency, food restrictions, lifestyle, drug interactions, dosing schedule, and number of doses per day. The clinician should determine what matters most to the patient—e.g., the simplest possible regimen, fewest possible side effects, or avoidance of certain side effects—while ensuring optimal potency and durability of antiviral effect. When the first regimen has been selected, the clinician should anticipate and prepare the patient for the side effects likely with that specific regimen. Nausea, vomiting, headache, and fatigue are the most common side effects that cause patients to miss a dose.

In the past three years, new and unexpected toxicities have been associated with antiretroviral agents. A syndrome of fat redistribution, hyperlipidemia, and glucose intolerance has been observed and termed “lipodystrophy (LD)”. LD may affect half or more of patients on HAART with protease inhibitors, though severe manifestations are less common, i.e. 15-30%. 5-15% of patients on NRTIs alone may have the syndrome, and it has also rarely been described on patients with HIV who have never been treated. It appears less common among patients on the NNRTI class of drugs. For this reason, and for reasons of simplicity and tolerability of the regimens, an increase in the use of so-called “protease-sparing” regimens has occurred in the past year. Several clinical trials are now testing the relative merits of regimens with protease inhibitors compared to

regimens with three NRTI agents or with two NRTIs and an NNRTI, i.e. protease-sparing regimens.

For patients who have this toxicity on a protease-containing regimen in the setting of optimal virologic control, switching to a simpler regimen appears to result in continuous maximal viral suppression in the majority of patients. In addition, the simpler regimens are associated with modest improvements in adherence and quality of life.

Table II notes the updated goals of therapy for 2000. Note that the major tenets of maximal durable viral suppression remain the highest priority; it should be remembered that these goals led to the dramatic reductions in HIV mortality and morbidity in 1996-1999. At the same time, it is known that immune reconstitution with sustained rises in CD4+ T lymphocyte counts is also associated with improved HIV outcomes, even in the presence of low level viremia of 50 – 5,000 copies/ml.

In addition, for durable virologic control and immunologic restoration to occur, additional therapeutic goals have been recognized to be essential. In addition to optimal adherence, as described in this monograph, preservation of future treatment options is an important goal of therapy. Because treatment failure rates of 30-50% or more in numerous trials and cohort studies, planning for second and third line therapy with high probabilities of success is essential. Preserving future options increases the chances of success with these regimens. There is growing evidence that genotypic and phenotypic resistance testing can improve the likelihood of success with second line agents; thus an additional goal of therapy is the use of agents to which a patient's virus is susceptible.

Table II: Update Goals of Therapy, 2000

Clinical

Reduction of mortality and morbidity

Improved quality of life

Virologic

Maximal durable suppression of viral replication

Immunologic

Immune reconstitution

Therapeutic

Rational sequencing of HAART regimens

- Preservation of future treatment options
- Optimal adherence: simplification of Rx, reduction of side effects
- Use of *optimal* and *proven* effective doses of drugs
- Selection of drugs to which a pt's virus is likely to be susceptible
- Avoidance of drugs to which a pt's virus is likely to be resistant

Finally, a note of caution for clinicians and persons living with HIV alike regarding alternative dosing strategies is warranted. Some efforts to reduce pill burden and frequency have been unsuccessful. It is important to be conservative about the use of alternate dosing strategies until there is sufficient pharmacological and clinical evidence supporting the safety and efficacy of their use.

What Do We Know about Adherence Levels in Different Populations?

Laura Cheever, MD – HRSA

Dr. Cheever discussed recent data on how various demographic variables affect adherence to HIV treatment. She cautioned that much of this data is preliminary and in abstract form. Much of the data has only been subjected to a univariate analysis, which does not account for confounding variables, of which there could be many. Further, the sample sizes of the studies are often too small to detect differences that could exist.

In the literature on adherence to treatment of chronic diseases, demographic variables generally do not predict adherence. However, the AIDS epidemic has a unique demographic profile. Also, the legacy of Tuskegee may have an impact on the attitudes of African-Americans towards the acceptance and use of HIV anti-retroviral therapy. This remains to be studied.

Citing several studies², age, race, stage of disease, and sex were shown to be inconsistent adherence predictors. Depression, literacy levels, active drug and alcohol abuse predict poorer adherence. In one study, women were more likely to be less adherent than men. Insurance status, education and income levels, a physician's experience with HIV, and attitudes regarding the efficacy of medication were not predictors of adherence. Health beliefs and attitudes which correlated with better adherence included:

- Medications will often fit into daily routine;
- Poor adherence leads to drug resistance;
- Taking all doses is important;
- Feeling comfortable taking medications in front of people.

In conclusion, Dr. Cheever stated that the data provides epidemiologic predictors. The data does not provide any information about particular patients. Each patient needs to be assessed and treated individually. The data may be important, however, in exploring barriers in different populations and in designing adherence interventions in different populations.

HIV Treatment and the Rest of Our Lives: How Does It Affect Adherence?

Margaret Chesney, Ph.D. – UCSF Prevention Sciences Group

Dr. Chesney, a leader in the field of HIV treatment adherence research, spent much of her time talking about the dangers of over-emphasis on poor adherence as a cause of treatment failure. She stressed the need for physicians to be better informed about the appropriate use of anti-viral therapy. Stressing adherence to a sub-optimal regimen is harmful and, unfortunately, not uncommon. She cited an analysis of ACTG studies where 25% of patients did not understand the instructions regarding when to take which medicines. Non-adherence can undermine clinical trials and treatment. Conversely, adherence is necessary, but not sufficient, for successful treatment.

² HCSUS Survey. Wegner, 6th CROI, Chicago 1999, Abs. 98; Cheever, 39th ICAAC 1999, Abs. 591; Patterson, 6th CROI 1999, Abs. 92; Kaplan, 6th CROI 1999, Abs. 96

Dr. Chesney discussed a recent study in San Francisco, which screened people who had experienced symptoms of HIV infection (fever, sore throat, night sweats, diarrhea within 3 weeks of exposure). Of 390 persons screened for primary HIV infection (the first 12 months), 137 were found to be infected. The average patient was a 34-year-old white man, college-educated, whose annual income was about \$30,000. Adherence in this population (determined by self-reporting) declined with time.

People with symptoms adhere better, whereas drug toxicity and concomitant side effects become more important later in treatment. The UCSF Prevention Sciences Group found that during 1 to 12 weeks of treatment, adherence was at 80%; by 24 to 48 weeks of treatment, adherence had declined to 61%. Reasons for missing a dose early in treatment were forgetting, sleeping, being away, changing routine, being too busy, feeling sick, being depressed. In the UCSF group, the number of pills per day did not predict adherence.

Urban poor women are already stigmatized. They often have psychiatric disorders, such as post-traumatic stress disorder (many live in virtual combat zones). Substance abuse, demoralization, and parenting demands beyond their competence are also characteristic. How do they prioritize adherence to treatment in the context of these other, often more critical, crises?

Providers tend to focus on how much adherence is enough, and the relation between disease state and viral load. Often they fail to see the challenge of adherence in the broader context of people's lives. While it is true that non-adherence is linked to increases in viral load, it is not always true. For some people, as adherence decreases, viral load increases, but for others, as adherence decreases, viral load remains unchanged. Therefore, assumptions based on stable viral loads can be deceptive. Conversely, there are many reasons for treatment failure other than poor adherence. Assumptions that patients are non-adherent because of increases in viral load may also be wrong.

Providers may inadvertently enforce skipped doses (e.g., "Just keep doing whatever you're doing"). They must stress the importance of sustaining adherence and to do this we need to teach self-management skills.

We need to know more about the impact of side effects and co-morbidities on adherence efforts. Some side effects and symptoms—such as fat redistribution, lipid changes—have serious consequences. But, in clinical trials, side effects are reported only if the patient complains and patients are encouraged not to complain; therefore side effects are underreported.

Dynamics of Patient Adherence

-Predicting an Individual's Ability to Adhere to Treatment;

-Provider Attitudes toward Patients and Their Adherence Abilities

Ruth Finkelstein, ScD – New York Academy of Medicine

Predicting the ability of a patient to adhere to treatment can be an important component to determine whether or not that person should start antiretroviral therapy. Dr. Finkelstein discussed the difficulties that physicians face in trying to predict adherence, the assumptions that are often made about how adherence can be predicted, and the implications such assumptions can have on patient's live and public health policy.

The ability of physicians to accurately report on the treatment adherence of their patients is limited and often inaccurate. Dr. Finkelstein cited three studies. In the Miller study, of patients identified by their physician as adherent, 30% were taking <80% of their medication, while 22% of so-called non-adherent patients were taking >80% of medication. Patterson, et al, found that 1/3 fewer patients identified by physicians as >80% were so. Of patients identified by physicians as <80% adherent, 1/5 were actually 95% adherent and 1/3 were 80 – 90% adherent.

Multiple studies indicate variations in how treatment gets prescribed. The HCSUS study showed yearly increases in prescribing HAART for all patients from 1996 – 1998. But, despite lessening differences between sub-populations, in 1998, patients who were Black, Latino, women, uninsured, or Medicaid-insured were less likely to be on HAART. Also, differential decline in AIDS-related mortality by race, gender and transmission indicate that not all groups are being provided access to HAART, even when they are receiving medical care. Much of this difference is due to provider assumptions about the ability of different groups to adhere to therapy.

Several factors have been identified as affecting adherence, including:

- complexity of the treatment regimen, including number of pills/drugs, frequency, duration of therapy;
- patient's knowledge and beliefs about disease and medicine;
- access to social support;
- co-morbidities, esp. substance abuse and depression;
- stigma associated with illness;
- coping style;
- missed clinic appointments;
- meaningful life
- feeling comfortable with and trusting the physician;
- level of medication supervision;
- side effects management.

Dr. Finkelstein cited three major factors that effect treatment decision-making. First is the belief system of the physician. If the physician believes the best antiretroviral approach is to “hit hard, hit early”, then she is more likely to be aggressive in prescribing

therapy. If she believes that crack addicts cannot adhere to treatment, she is less likely prescribe therapy to patients she perceives to be crack addicts. The second factor is an individualized assessment of adherence risk/readiness. The third factor is an assessment using evidence about adherence.

Evidence can be assessed taking multiple factors into account. These include:

- Environmental factors: What is the patient's living situation? Does he have a telephone, a refrigerator, adequate water supply? Who does the patient live with and can they provide support?
- Mental/emotional health: Is the patient depressed? Are they undergoing treatment for depression or other problems?
- Substance use: Is the patient addicted to drugs or alcohol? What is the severity of the addiction? Does the patient use drugs/alcohol recreationally? If so, how often and how does this use affect his daily schedule? Is substance abuse treatment available?
- Knowledge about HIV and HIV treatment: Does the patient understand the need for good adherence? Does he understand the consequences of poor adherence? Does he know which pills to take, how many to take, how often and when to take them? Does he understand about any dietary restrictions? Does he understand about possible side effects? Can the patient read/understand basic health words and concepts?
- Attitudes and beliefs: Does the patient believe that she has the ability to follow through on the treatment decision? Does she believe in the efficacy of HIV medication? Is she open about her HIV status? Is she scared of people seeing her medication? What are her goals and expectations for treatment?
- Social support: Is the patient isolated? Who can assist the patient in taking medication regularly? What other responsibilities does the patient have which may affect the ability to adhere to HIV medication?
- Past experiences: What is the patient's previous history adhering to medication? Does the patient miss appointments, fill prescriptions, etc.?

Health care providers should also take the patient's payor source and the stability of that source into account. Finally, the provider should then engage the patient in a decision-making process where the advantages and disadvantages of starting therapy are weighed.

How Do We Define "Effective" Adherence Interventions?

Sheryl Catz, Ph.D. – Medical College of Wisconsin

Measuring adherence to treatment is one important aspect of measuring treatment effectiveness. In measuring adherence, it is important to examine the role of the patient, the health care provider, and the system through which health care is provided. No one form of measurement is complete or adequate. The ideal evaluation standard—unobtrusive, objective, practical—is lacking; therefore we must use a multi-method approach.

Methods for Measuring Adherence Outcomes:

Direct Measures

- directly observed therapy – is accurate, but may not be practical when pills must be taken several times a day for long periods of time;
- biomedical assay of blood and urine analysis – are objective and do not rely on patient reports, but are not always an accurate method due to pharmacokinetic factors, difficulties with timing tests with ingestion times, and susceptibility to “white coat effects.” They are also expensive and not always available;

Indirect Measures

- pill counts – are inexpensive and relatively easy to do, but do not provide information about whether the pills are actually taken and if taken according to schedule. Pill “dumping” can occur, and assessments can be impractical if the assessment period does not coincide with prescription refills or if there are too many pills to fit into containers;
- pharmacy refill records – are unobtrusive and do not rely on patient report, but have limitations similar to pill counts;
- service utilization records – can be used to calculate the percentage of appointments kept (a direct measure of appointment adherence and an indirect measure of medication adherence), but are only as accurate as the record-keeping system and the record review can be time-consuming and expensive;
- MEMS caps - these devices electronically record when a pill bottle is opened. Benefits of electronic monitoring include objectivity, the identification of specific patterns of medication-taking over time, higher rates of missed doses detected as compared to other measures, they are not easily tampered with; and graphs of MEMS data can provide behavioral feedback useful for motivating patients. However, the system is expensive and cumbersome when multiple medications are used. Accuracy is compromised by how often the patient opens the bottle and removes a pill (or not) but does not take the medication. We need MEMS technology in dosette boxes and technology that can accommodate liquids.
- patient reporting - self-reporting in the form of diaries, questionnaires, or interviews are an inexpensive and necessary component of adherence assessment. But, reports of poor adherence tend to be more accurate than reports of good adherence and there are problems with recall and comprehension. Reporting may be more accurate if you “give the patient permission” to admit skipping a dose, use the patient’s language, and provide recall cues over a brief time period.
- provider reporting - provider ratings tend to overestimate good adherence, but can be useful supplements to other adherence measures;
- collateral reports – can be most useful with children’s caretakers;
- clinical outcomes – should not be conceptualized as a measure of adherence. Viral load is not perfectly correlated with adherence. Some people with excellent adherence don’t achieve reduced viral load; some with reduced viral load are not consistently adherent. However, the idea of validating adherence measures against clinical outcomes makes sense given the end goal of taking medications consistently is to achieve medical benefit from them.

Process Evaluation of Adherence Interventions

To examine how different kinds of adherence interventions work or don't work we need to evaluate interventions which target changes at the level of the individual, provider, and system. Several process evaluation questions can be asked, including:

Individual level: Does the intervention effectively -

- Identify adherence barriers;
- Build problem-solving skills;
- Increase integration into daily life;
- Increase adherence self-efficacy;
- Increase knowledge;
- Increase motivation;

Provider Level: Does the intervention effectively –

- Increase provider communication skills;
- Build trust and rapport;
- Increase provider assessment skills;
- Match medical management to changing needs;
- Meet “best practice” goals ;
- Provide tailored feedback and educational materials;

System Level: Does the intervention effectively –

- Increase access to care;
- Provide continuous access to medications;
- Meet appropriate service utilization guidelines;
- Provide consistent environmental supports;
- Protect confidentiality

To define an effective intervention we need to address three issues. How much will adherence increase? What kind of adherence is being measured? Which components of individual, provider, and systemic interventions are the “active ingredients” necessary to increase adherence over time?

INTERVENTIONS TO ASSIST ADHERENCE

The majority of time at the workshop was devoted to presentations of various interventions to assist adherence efforts. These efforts included ways to educate providers and patients about the need for good adherence and the proper use of treatment regimens, as well as provide support and assistance for patients on therapy. The presentations were meant to provide representations of the types of programs being implemented. Many of them are still in fairly early stages of development. There are

several other programs in operation. Time prevented us from providing a more comprehensive review of adherence intervention programs.

ARMAP: Antiretroviral Medication Adherence Projects

Diana Antoniskis, MD – Kaiser Permanente

Kaiser Permanente, a managed care organization with a large HIV-infected patient population, and Group Health Cooperative, a primary-care based organization, collaborated in an effort to maximize the cost-effectiveness of ART. Their premise is that the adherence team should provide intensive educational and psychosocial evaluation before initiating antiretroviral therapy and that the team should include a pharmacist and a social worker.

The pre-therapy visit is the most important aspect of their program; it lasts 1-1/2 to 2 hours. The pharmacist reviews medications. The social worker reviews the patient's routine, perceptions, previous therapeutic experience, access to therapy, treatment for substance abuse, mental health issues, and self-advocacy, and offers a placebo (jellybean) regimen and support group. To aid adherence, team members use phone calls, follow-up visits (at 1 and 3 months), and a monthly support group.

The average clients were 38-year-old white men. During treatment, their quality of life improved, especially in mental health and overall health. Controls receive treatment but not the social interventions of the program. The program was well-received by both patients and providers. A continuation study with longer follow-up (9 months) is being planned.

TREAT — a Clinical Management Tool with Adolescents

Audrey Rogers, PhD – NICHHD

TREAT is an adherence intervention that focuses primarily on assessing patient's readiness to participate in treatment. The program relies on Prochaska's Trans-Theoretical Model of Change (TMC), which consists of the following four stages (relapse is a reversion to a previous stage):

1. Pre-contemplation—no intention of changing behavior
2. Contemplation—aware of the problem, but not committed to action
3. Preparation—intend to take action within 30 days
4. Action and maintenance—committed to change; has devised strategies to prevent relapse

TREAT is one arm of a program that includes REACH (observational) and ACCESS (social marketing). TREAT is offered in 15 cities to REACH subjects in whom HAART is indicated. Each is referred to a social worker to overcome barriers to treatment.

Clients are mostly minority girls, a third of whom are high school dropouts, and a fourth of whom have no health care coverage. Most were infected through sex. Few exhibited AIDS-defining conditions. For this group, disclosure is critically important; it is the first step out of denial.

The TREAT program is stage specific; at each stage, each client is given the following:

1. a binder with a videotape, an audiotape, and an illustrated booklet
2. counseling and an audiotape
3. counseling, an audiotape, a choice of drug regimen, a surrogate pill trial
4. audiotape

At relapse, each is given an audiotape.

The program has been in the field only a couple of months and implementation is not complete. The goal of 15 cities is an organizational problem, and the program hasn't been implemented as planned. A considerable proportion of the patients are in the pre-contemplation or contemplation stages of whom 57% are receiving no treatment. Evaluation is nested case-control. Acceptability ranges are good—more than 75% have accepted the program.

Harlem Adherence to Treatment Study (HATS)
Sharon Manheimer, MD – Harlem Hospital Center

The Harlem Hospital Infectious Disease Clinic, a primary care clinic, undertook HATS, a randomized clinical trial, in an attempt to change peer-centered social support intervention for promotion of adherence to ART. The study's three components are: peer support, concrete services, and education.

- Peer support comes from trained HIV-infected peers who are successfully taking HAART. These peers address mistrust of the system and lack of support. They show the client how to navigate the system and communicate with providers, serve as role models and educators, and give feedback.
- Concrete services include HIV primary care, nutrition, and gynecological and psychological services.
- Education is directed to clients as well as clinical and non-clinical staff members and peers.

For this study, data were collected through detailed interviews. The client population was half men; average age 44 years; 75% African American, 20% Latino; 58% heterosexual; 78% unemployed; 75% on Medicaid; 20% in unstable housing; 60% didn't discuss their condition with friends, 35% felt ashamed, 30% would stop taking ART if they were using street drugs. Self-reported adherence was 64%; provider-reported adherence was 69%. The most common reason for non-adherence (50%) was forgetting.

Barriers to adherence were:

- low confidence in taking HIV medications alone and no one to help
- depression
- active substance abuse

Health Care Provider Adherence Training Curriculum (HCPATC)

Linda Frank, PhD – University of Pittsburgh

AETCs train clinicians (including dentists), and offer clinical consultation and technical assistance to build clinic capacity. HCPATC is a national AETC.

The training is targeted for low-, medium-, and high-volume providers. For low-volume providers (fewer than 10 cases a year), the question is when to refer. For medium-volume providers (fewer than 50 cases a year), the focus is on co-management. High-volume providers (more than 50 cases a year) are AETC faculty members and serve as experts.

Adherence must be addressed at every level. Strategies are intertwined with case conservation, mini-residencies, and on-site and distance consultation. The curriculum was devised to circulate guidelines, both of which must be continually updated. The curriculum refers the reader to the Web site.

Adherence is placed in the context of the client-provider relationship and the individual client. The curriculum, implemented by all 14 AETCs, is driven by the premise that the patient is the decision-maker. New modules will be developed to address changing trends in the epidemic. Current components of instruction are:

- introduction
- pathogenesis and viral dynamics
- principles of HAART
- adherence principles and strategies
- psychosocial issues of adherence
- cultural issues of adherence
- slide set
- experiential exercises
- process evaluation and outcome evaluation

For researchers a fundamental question is how to get information from a study into the field. The answer is to work with the AETC.

Action Point—San Francisco

Josh Bomberger, MD – San Francisco Department of Health

Action Point is a store-front clinic, which is street-based and geographically appropriate. The program stores and dispenses medications for 100 to 150 homeless people and offers whatever other services they need to succeed with an individual adherence plan. The patient decides how much medicine to take away.

The clinic offers monetary incentives and needle exchange three days a week. Adherence must be integrated into the patient's drug life. Such a clinic must offer flexible hours (6 days/week, 12:00 to 6:00 pm), adequate staff support (including a nurse, a case manager, a pharmacist, an acupuncturist), and supervision by flexible and imaginative people. Action Point offers love, respect, and social support. The clinic forms a sense of

community. It is a link to primary health care, and drug and mental health treatment. Referrals come from providers, self, friends, CBO staff, and jail.

Their goals are:

- reduce harm
- reduce viral load
- increase immune response
- refer clients to drug and mental health treatment
- improve stability of housing and access to food
- reduce multi-drug resistance
- reduce drug use and dependency
- raise the standard of care among the HIV-infected urban poor
- reduce costs of health care to the public sector
- improve clients' self-esteem

To be enrolled, clients must be documented HIV positive with a CD4 of less than 500 or a viral load greater than 10,000, and TB negative. Within six weeks of enrollment, they must have established a relationship with a primary care provider.

Clients tend to be over 40 years of age; 29% are white, 25% African American, 13% Latino; 98% use illicit drugs; some are women and transsexuals; 60% started HAART within a month. Most come in once a week. The most common regimen is D4T, 3TC, NLF.

Action Point offers its clients:

- individual adherence plans with frequent reassessment (which is time-consuming and intense)
- medication storage and dispensing
- medi-set filling and management
- case management, including finding housing, food, mental health care, etc
- a pager reminder system
- referrals for drug and mental health treatment
- \$10 weekly incentive pay
- acupuncture
- treatment advocacy
- referral to primary care
- “hang out” space

The program costs about \$4200 per year per active clients. Sustainability of staff may become a problem—it's staff-draining work.

Structured Training and Monetary Reinforcement
Marc Rosen, MD – VA Connecticut Healthcare System

Contingency management in the VA Connecticut Healthcare System involves paying the patient to take medication at the right time. Intervention involves detailed review and discussion. Patient and provider meet once a week for counseling for 4 weeks; then again at week 8 and week 12. All patients get MEMS caps, but counseling is given only for the drug of poorest compliance. Review of MEMS-generated printouts gives the patient feedback. In addition to MEMS feedback, patients are paid \$2 to \$10.

The average age of clients was 48 years; 93% were male; 75% African American; many use illicit drugs.

Contingency management produced a significant effect. Adherence began at 95 to 100%. This level decreased but still remained higher than in the control group. The same interventions in a non-VA population showed that contingency management with MEMS caps still gave better results than the control.

However, the study is limited by its small size and cannot be generalized as done because clinics will not pay patients \$10/day indefinitely. Nevertheless, some findings are generally useful. MEMS compliance reports are helpful for patients and providers. Self-reports differ from MEMS-generated reports, probably because patients want to please providers. Although it is hard to estimate the percentage of compliance, details of the MEMS reports reveal patterns, which can then be addressed, e.g., are doses missed on weekends, mornings, or afternoons? Cost—\$80 per cap—is a drawback to MEMS.

***ADHERE—Adherence to Drugs for HIV,
an Experimental Randomized Enhancement***
Jeffrey Samet, MD – Boston University Medical Center

ADHERE is a 24-month prospective study of 240 HIV-infected people with different levels of problems with alcohol use. The study focuses on the relationship between alcohol use and outcomes of HIV infection with regard to testing an intervention to enhance adherence to ART.

Program components are:

- brief clinical intervention for the alcohol problem
- medication timer
- counseling on efficacy of ART and the importance of adherence
- nurse's home visit to tailor an individual approach of adherence assessment
- self-reporting for each ART medication
- MEMS caps

Intervention adds nurse's visits to the baseline of a visit and a home visit at 1 month and 3 months.

Of 106 subjects enrolled so far: 19% are women; 40% are African American, 23% Latino, 31% white; 22% are homeless; and 59% are injected-drug users.

Challenges are:

- adherence measures—MEMS or self-report
- recruitment
- follow-up—at 6 months, 71 of 81 were captured
- selection of outcome variables

The Role of Social Service Providers in HIV Treatment Education

Carlos Arboleda – Gay Mens’ Health Crisis

Social service providers have important opportunities to provide treatment education and support to their clients. Clients are often more comfortable talking with case managers than with physicians and are usually given more time to do so. In order for social service providers to provide treatment information, adherence support, and advocate for better care for their clients, they need education and training on HIV treatment issues.

To meet this need, Gay Mens’ Health Crisis, a large social service provider and educator in New York City, offers a workshop entitled “The Role of Treatment Education in Client Services.” Workshop participants solve problems in scenarios based on fact. The problem-solving scenarios provide participants with background information about HIV disease and treatment, along with opportunities for them to understand how HIV treatment issues impact their work in social services. All participants are given background materials on treatment issues, including clinical practice guidelines, fact sheets, and GMHC’s treatment newsletter. The participants are then placed on a mailing list and are sent regular information about treatment forums. GMHC also runs a treatment library that provides providers and people with HIV comprehensive treatment and medical information.

The most important aspect of the workshop is its attempt to help social service providers understand how treatment issues directly impact their work, even though they do not provide medical care. The scenarios are designed to show how a knowledge of HIV pathogenesis, disease manifestations, and treatment impact primary prevention programs, case management, housing services, nutrition services, drug treatment services, etc.

More than 400 people have completed the workshop. Participants come from social service organizations throughout the New York metropolitan area including drug treatment centers, housing services, child services, HIV primary prevention programs, and case management services. GMHC staff are often asked to bring the workshop to a particular agency and the workshop has been performed in all boroughs since its inception. The majority of participants are people of color. Evaluation of the workshop includes a survey asking participants what they thought of the event, what they learned, what aspects of the workshop were most useful. Responses are very positive. Most important, participants frequently refer their co-workers to the workshop.

Directly Observed Therapy (DOT)

Tim Flanigan, MD – Brown University

Dr. Flanigan described a program of directly observed therapy (DOT), where workers watch patients take medication on a regular basis. At Miriam Hospital, 80% of the HIV-infected are poor and on Medicare. They tend to be co-impacted by substance abuse including alcohol, depression, and violence, and have spent time in jail. There is also an ongoing epidemic of TB, but TB is curable with daily or twice-per-week medication. Adherence to HAART competes with the client's other priorities and crises.

Directly observed therapy is a time-consuming way to encourage adherence, but it does not have to be continued forever. In some circumstances, such as incarceration, DOT works well, but is difficult to sustain after release. At Miriam Hospital, a pilot program of modified DOT, using community health education workers, enrolled the hardest to reach patients. DOT is best done by people from the community. This program employs near-peers. They are high school graduates who get salary plus fringe benefits totaling about \$20,000/year. The goal is to teach patients strict and sustained adherence and then to gradually move them off the program. Each patient is met by a near-peer outreach worker every weekday morning in a location selected by the patient. At each visit the worker delivers the day's prepackaged doses of medications chosen by the primary care physician. The morning dose is observed; the others are self-administered and self-recorded.

Clients enrolled in this study were: an average age of 38 years; 65% are women; 68% have been in jail; 84% are HAART-experienced; 46% are substance abusers. Of the 37 patients enrolled, 24 have completed 6 months on the program and 2 have completed 12 months on the program and now take medications entirely on their own. All believe the outreach worker helps, and 87% feel they are better able to take their medications.

Adherence Support for HAART: A Multi-Site Evaluation

Mark Waters, RN, MPH – New York State AIDS Institute

The New York State AIDS Institute, in conjunction with the New York Academy of Medicine, is conducting a multi-site evaluation of adherence support programs in New York State. The project goals are to increase adherence, empower clients to make informed treatment decisions, and to identify effective adherence interventions. The project objectives are to provide consumers with access to adherence services, integrate adherence services into the continuum of HIV care, and develop a collaborative infrastructure across provider organizations.

The project involves 10 organizations that provide both clinical and non-clinical support for persons at greatest risk for non-adherence. The New York Academy of Medicine is conducting the program evaluations to assess the effectiveness of the interventions. Adherence is measured using self-reports, MEMS caps, pill counts, viral load, clinic attendance, prescription refills, patient diaries, and CD4 cell counts. The multi-site evaluation collects data on program characteristics, client characteristics, intermediate outcomes, adherence rates, and health outcomes.

Project services include:

- individualized treatment plans
- HIV treatment education
- Treatment readiness
- Medication reminders
- Medication delivery
- Modified DOT
- Adherence monitoring
- Home visits
- Skills-building
- Counseling
- Phone support
- Peer support
- Case management

Of the 406 clients included in the evaluation, 58% are male, 37% are Latino, 36.7% are African American, 27.5% have a history of mental illness, and 83% have a history of drug or alcohol use. 50.2% report having previous adherence difficulties. 18.7% are new to HAART. Self-reported adherence rates from 213 clients show that 59.1% missed a dose in the last two weeks, and 36.4% missed a dose in the last three days. The mean adherence rate in the last three days was 81%. Most common reasons for missing doses were:

- simply forgot
- slept through dose
- didn't fit daily routine
- too hard
- depressed/overwhelmed

Bienestar

Rafael Landa – Los Angeles, California

Bienestar, a nonprofit founded in 1989, serves about 1500 clients at six locations in Los Angeles. It has filled a linguistic and cultural gap by serving the Latino community (97% of their patients). HIV infection has increased among minorities, women, and children. 87% of Bienestar's clients are between the ages of 20 and 37.

Complicating treatment of HIV and other infections among immigrants is distrust of authority engendered by the political chaos that often characterizes undeveloped countries. Bienestar has had to break down fear and guilt among those HIV-positive immigrants arriving from Central and South America, where they are regarded as sexual criminals. (Such attitudes are addressed with mental health interventions.)

Bienestar began connecting with other agencies and health care providers to increase the patients' network of services. A combination of all services, including education and social service, is required to attain adherence. They support a peer program in which the client is connected to another person, which encourages communication. The patient can choose services from the whole HIV program. Health care providers are bilingual foreign doctors who are waiting to qualify for US medical license.

Services include:

- education services
- pre- and post-HIV test counseling
- counseling and services for patients and their loved ones
- social services
- medication seminars and workshops
- exercise
- meditation
- peers who visit the client once or twice a week to follow up

Peer Education and Adherence to HIV Therapy in Children
John Farley, MD – University of Maryland–Baltimore (UMB)

This program will enroll 160 HIV-infected children. Most of the mothers discovered their HIV-positive diagnosis when they were pregnant. This program provides support and guidance in child development and parenting, disclosure, and coping. Adherence in the pediatric population is challenged by the dual illness of parent and child. There is often active illicit drug use within the family structure. Disclosure of HIV status and secrecy is an important issue, with the child often not knowing that either he or the parent have HIV. Secrecy about one's HIV status also makes obtaining social support difficult, if not impossible. Other significant problems include unstable living conditions, the need to plan for multigenerational care, and low literacy. Treatment is long-term, many patients have no symptoms, and palatability problems are significant. The situation is further complicated in adolescence by developmental issues.

The UMB Compliance Critical Path involves:

- psychological assessment
- caregiver/family assessment
- determine whether backup exists
- determine need for case management
- environmental assessment (home, school)
- medications-specific issues (dosage form)
- family education and training
- tools and reminders
- child/caregiver reinforcement (token economy, e.g., McDonalds coupons)

A study to measure adherence levels is underway using MEMS caps. The study focuses on caregivers of HIV-positive children who were younger than 13 at enrollment and who

are taking three or more antivirals. It excluded people who don't use pill boxes or do not set out pills in advance (which implies secrecy) or who use liquids. The remainder were given MEMS caps for one of their medications. Pharmacy re-fill information is collected for all medications.

To this was added a peer-educator and home visits for the test group. The peer-educator's visits changed from weekly to monthly, and they encouraged visits with a child psychologist.

Family support was determined by adding to the survey the question: "How many in your network know you have HIV?" To address the distrust issue, African-American psychologists embedded true-or-false questions including:

- "HIV medications work better for white people."
- "HIV was devised to infect minority groups."
- "Doctors give patients medications without telling them."

To date 40 subjects aged 2 to 11 have been enrolled. Most don't know their diagnosis. Most are African American. The caregivers include biological mother, biological father, biological grandmother, aunt, adopted parent, or foster parent.

Preliminary results revealed very high parenting stress scores, but neither health beliefs, nor distrust are major issues. The peer educator's home visitor was popular, however there's a significant disconnect in social support; that is, firm support networks exist, but few people in those networks know the patient is HIV-positive.

About 20% of the client's using HAART were in pre-contemplation and contemplation stages of Prochaska's model. A unique problem to the pediatric population is that children must be taught how to swallow pills.

As determined by MEMS and self-reporting, about 75% had missed at least one pill in the last 2 weeks. Overall adherence 3 months after intervention was 75% (before the intervention, it was 58%). A related issue is that non-administration of medication becomes Child Protective Services issue under the law.

AIDS Action Committee

Michael Immel – Boston, Massachusetts

This adherence program establishes different levels of education and support for clients with varying needs and understanding about their treatment. The program is one of 12 funded by the Department of Public Health in Massachusetts.

Acceptance and understanding of the issue within the social service agency is a challenge. Adherence must be incorporated into a broad range of issues; it's too narrow a specialty to be independent from related programs. And it must be integrated among staff and every aspect of their daily routine.

Counseling or social support was added to the existing treatment educational program. The social support is a buddy system—one volunteer per client. Buddies telephone their assigned client regularly. Forgetting (the convenience factor) was the primary reason for missed doses.

Readiness measures and techniques are extremely important to avoid the “intuition trap.” Another component is social services education regarding financial, legal, and housing issues; care providers must be taught to listen for indicators of problems in these areas. In addition, social marketing on a broader scale is needed. The public and the community needs to know and acknowledge that adherence goes on.

Among the education tools they produce are bilingual brochures written to be readable for various literacy levels. More detailed packet are given to more literate clients. Social services providers are given a poster intended for office use to stimulate discussion.

AIDS Project Los Angeles (APLA)

Nancy Wongvipat, M.P.H. & Janelle L’Heureux, M.S., R.D.

APLA, founded in 1983, serves about 8000 clients and is one of the largest AIDS social service organization in the United States with a staff of 170. Their services include mental health, nutrition, education, a dental clinic, food, housing, transportation, benefits management, legal services, a women’s program, and a health education and advocacy program. Their clients’ demographics--10% women, 90% men; 40% Caucasian, 22% African American, 32% Latino/a, 2% Asian Pacific Islander, 1% Native American, 3% other/unknown--represent the epidemic of Los Angeles County.

APLA has a Health Education and Advocacy (HEA) department comprised of five treatment advocates (TAs), two nutrition advocates (R.D.’s), an HIV resource center assistant, program manager, and a health education specialist (M.P.H.). APLA’s Treatment and Nutrition Advocacy components are unique in its adherence support in that support is provided in a community-based setting, consultations are not time-limited, and is provided within a one-stop shop setting, with the exception of primary medical care provisions. Treatment education consists of one-on-one consultation, community education forums (e.g. Treatment 101, on dealing with medication side effects), educational materials (e.g. fact sheets, newsletter with a monthly “Adherence Matters” column providing practical adherence tips) and intensive Treatment Advocacy Trainings. The Treatment Advocacy Training provides a comprehensive overview of adherence and practical case study exercises.

To better understand the adherence needs of our client, a survey was conducted in 1997, which resulted in 1322 responses. Results of the survey found the following: About 60% reported good adherence; 43% reported side effects from medication; 30% had problems with the number of pills; 27% forgot to take medication; 25% were unable to eat at the necessary times; 21% had difficulty taking pills as prescribed; and 11% had difficulty or were unable to take their medications at work.

To support adherence efforts, APLA employed a staff person devoted to the issue. A standardized assessment tool was developed and used by TAs to assess demographic and medical information, reasons for intake, and adherence concerns. The adherence section served three purposes: as an assessment instrument, an educational and skills intervention, and a follow-up evaluation tool. Adherence tools, including an illustrated medication schedule with pill stickers, daily routine and activities reminders, and food facts and suggestions, and pill boxes were provided to clients. Practical tips and support from TAs that were reported to be helpful with clients' adherence included identifying regular activities to serve as cues to taking doses, creating a personalized meal/medication schedule, utilizing pillboxes, and providing strategies to deal with side effects. Since TAs are not time-limited in their consultations with clients and given clients' comfort levels in a community-based peer setting, clients open up and disclose to TAs more so than they would to their clinicians. This openness and flexibility of the interaction help TAs find clues to assessing whether the client truly has an adherence concern and allow TAs to become more specific in their adherence assessment. Adherence data collected from the intake forms showed a 16% increase in overall reported adherence.

APLA has a centralized case management database, which aids in follow-ups and process monitoring, and in working with other staff and departments to achieve a more integrated adherence effort. They would like to see more reinforcement of adherence and integration of adherence support such as through case management and mental health staff, which is the direction they are heading in their adherence efforts.

Nutrition Support

Diet is part of adherence as well as to the overall well being of persons living with HIV/AIDS, but often overlooked in primary care settings, research studies and other settings. Whether we are dealing with body's response to medication, drug regimens, whether the client is experiencing weight loss or gain, or the development of opportunistic infections, all are issues involving nutrition. Registered dietitians at APLA offer nutrition education classes and meet with clients on a 1:1 basis to build self-management skills. Classes include; basic nutrition and HIV, food & water safety, meals and medication, dealing with side effects, measuring lean body mass, managing high blood sugars/diabetes, high cholesterol and triglyceride levels and a fitness class. Nutrition must be constantly reinforced, especially with complicated medication regimens. A dietitian can assist the client in interpreting in terms of food, the food requirements of specific medications.

Recognizing that there have been early and ongoing indications that nutritional issues are closely linked to progression of disease and treatment outcomes, an expert panel is being formed to develop national HIV nutrition guidelines. The goal of this document is to provide guidance about medical nutrition therapy as part of HIV healthcare management. The intent of these national guidelines would be to raise awareness of the important role of nutrition in HIV health care, guide physicians in their recommendations to patients, and provide guidance for patients themselves.

The project has been spearheaded by collaboration of government and non-government agencies. These are the Office of HIV/AIDS Policy at Department of Health and Human

Services, the HIV/AIDS Bureau at the Health Resources and Services Administration, the Office of Special Health Issues at the Food and Drug Administration and the Nutrition & HIV Program of AIDS Project Los Angeles. It is anticipated that the document will become a companion to the US Public Health Service Treatment Guidelines, and expected to be available in approximately a year. Nutrition fact sheets for each protease inhibitor can be found on the APLA website: www.apla.org

Project TEACH (Treatment, Education, and Access, Central Harlem)
Bradley Walrond – Minority Task Force on AIDS, New York, NY

Project TEACH is a peer-based project in which each peer is responsible for a constituency and for recruitment. Peers work less than 10 hours per wk at \$10 per hour; usually the peer is HIV-positive. Once a week peers have access to insurance people, health care professionals, and pharmacists to keep abreast of trends. Peers reflect the constituency; they are true advocates for the client base.

HIV-positive people live with an illness that will probably take their life. Nevertheless, treatment should be the client's informed choice, made with consciousness and responsibility. Because the person is not adherent does not mean the person is not responsible, and providers and caregivers must respect how clients choose to live and die with their disease, and not become "pill-pushers."

HIV/AIDS is not the only chronic disease, and the HIV/AIDS community can learn from other long-term chronic diseases, such as terminal cancer.

HIV University
Rebecca Dennison – WORLD, Oakland, California

Nine years ago, when Dennison was diagnosed HIV-positive, women and non-addicts had no place to turn, so Dennison started a monthly newsletter, which is now sent to over 12,000 women. Confidentiality is a huge problem. They send the newsletter in a security envelope and they don't sell their mailing list. More than 300 women have shared their experiences in the newsletter, some anonymously, some not. They have a monthly pot-luck dinner. In 1992 they had their first women's retreat; now they offer a retreat twice a year and there's a waiting list. Most of the women are low-income and get health care at under-funded clinics.

To enable these women to understand and combat their condition, Dennison and a group of women designed and developed a curriculum for their own "university." Courses include: anatomy and physiology, HIV and cellular infection, HIV disease, gynecology, sexually transmitted diseases, pregnancy, and perinatal transmission. Education sessions are now given in African American churches.

The support program began with volunteer AIDS activists, but now, through Ryan White Title IV funding, some of the volunteers can be paid. A new issue is arising as experienced volunteers age and die. Besides education, HIV University also offers

alternative and complementary therapy (acupuncture), clinical trials, and addiction recovery and relapse prevention.

Spirituality is important. They all know there's no cure, but they maintain hope day to day—hope that treatment will get better, hope for supportive relationships. What does it mean to take medication if you believe life and death are God's decision? We must figure out how to treat without being arrogant and pushy. Not everyone wants treatment; not everyone wants longer life at any expense.

Many research questions remain to be addressed, and a large meeting of patients talking about their problems and solutions they need would be helpful. For instance:

- About half of the women are co-infected with hepatitis C. What will medications do to the liver?
- People are very concerned about side effects. What can be done?
- Which medications may contribute to depression?
- Are scheduled interruptions harmful; is so, how so?
- What are drug effects peculiar to women and African-Americans?
- Are people not on medication because they're not informed and not getting good care, or because it's an informed choice?
- What is each drug's metabolism in pregnant women?
- What are the drug effects on the fetus and on children?
- Is a natural low viral load the same as a drug-induced low viral load?
- How do medications work with the immune system?
- What sequencing strategies should be used for people who want to have a baby one day?

Quality of life and the will to live are involved with adherence issues. Looking for assessment tools without considering the individual's desire to live is useless.

T.H.E. Course[®]

Valerie Scott & Maddy Rice – Glaxo Wellcome

Learning to live with HIV/AIDS requires behavior change and the ability to maintain that change. Can HIV self-management skills be learned? Adherence is a by-product of improved self-management skills. T.H.E. Course[®] is (T.H.E. stands for “Tools for Health and Empowerment”) a program that teaches life skills, premised on the idea that self-empowerment is the active participation in one's health care. It stresses that an HIV-infected person:

- needs to actively participate in their health care decisions with a trusted health care team
- understands the importance of a personal support system and learns how to put one in place
- understands the rationale for strict adherence and if he/she decides to initiate therapy, is fully committed to taking their medications as prescribed
- knows the effects and side effects of those medications

T.H.E. Course[®] provides tools for the HIV-positive person and caregivers (friends, family members, partners), tools for trainers. These tools are designed to reinforce behavior change.

T.H.E. Course[®] is delivered in an interactive, small-group setting and facilitated by a health care professional or peer educator (the “trainer”). Trainers attend a two-day Train-the-Trainer Program focused on the principles of adult learning, as well as procedures for organizing and delivering T.H.E. Course[®] curriculum. T.H.E. Course[®] uses participant-centered skills-building activities and discussions, aimed at improved HIV self-management behavior organized into 12 two-hour modules.

The modules focus on:

- patient self-empowerment and the importance of working collaboratively with one’s health care team
- medication self-management planning, adherence strategies, pharmacology and nutrition
- HIV pathogenesis
- recognizing signs and symptoms of HIV specific to women
- accessing medical and emotional care and paying attention to self-needs
- parenting, pregnancy, and contraception
- prevention of transmission: sexual, household, and maternal-fetal HIV transmission
- assessing risk behaviors and harm reduction strategies for alcohol and drug use
- principles, benefits and risks of combination antiretroviral therapy
- symptom management
- preventing opportunistic infections
- employment issues
- death and dying, wills, and advance directives

Participants are awarded an Empowerment Message Button for completing each module.

A clinical trial of the education modules was conducted in 11 different treatment sites: Immediate and delayed intervention groups served as active and control populations. Only participants who completed at least 7 of a possible 11 sessions were included in the analysis. Trial participants included 69 patients—28% were women; 33% were African American, 46% white, 17% Latino; average age was 43. Results of the trial showed statistically significant improvement in adherence lasting 12 months. A trend toward reduced viral load was also seen, however there was no change in CD4 cell count.

Even though medication adherence was good prior to T.H.E. Course[®] intervention it still improved and yielded improved sustained behavior changes in knowledge and empowerment as well. Program participants would like to have had T.H.E. Course[®] earlier in their disease. Trainers saw changes in the clients, as clients took a more active role in treatment. The trainer’s ability to motivate was crucial. They used incentives, maintained the materials current, and made learning fun. Participants need to be actively involved in the program and the curriculum should be flexible.

Medicaid Managed Care Contract Specifications

Jeff Levi, PhD – Center for Health Services Research and Policy (CHSRP) at the George Washington University School of Public Health and Health Services

Dr. Levi discussed the systemic approaches to the incorporation of adherence support into health care and social services. Adherence services need to be seen as an essential element of the continuum of care for people with HIV. To achieve this goal, adherence services must be part of the payment system through an expanded definition of case management and as a separately defined service. The impact will be greatest on the public sector, which pays for over half of HIV care costs.

Nearly half of HIV-positive persons receive health benefits from Medicaid, and more than half of the states (54%) use managed care for their Medicaid programs. Therefore, providers must learn to deal with managed care. State's contract with managed care organizations to provide services for their Medicaid recipients. That contract describes the services that the managed care company is expected to provide to patients. The negotiation of the contract specifications offers an important opportunity to assure that high quality care is available to patients. Furthermore, contract specifications offer an opportunity to define a broader set of services than normally provided by Medicaid. In this context, purchasers of health care services can more clearly define their expectations of contractors and can better determine appropriate reimbursement rates; providers can better understand purchaser's expectations and can better determine costs; and consumers can more clearly understand what services to expect.

CHSRP's purchasing specifications project has devised effective language to be used in such contracts. Three elements are critical:

- screening for HIV and sexually transmitted diseases
- following treatment and prevention guidelines
- ensuring access to an experienced provider

The specifications specify the need for an interrelationship between support services and primary care services and call for adequate reimbursement in a capitated setting. Adherence support services are included as an essential element of care. Specifications for adherence services describe the services and include counseling as a necessary part of treatment to initiate and sustain the course.

Purchasing specifications and other information are posted on the Web site (www.gwu.edu/~chsrp).

Correctional Institutions

Ellen Rappaport, MPH – Correctional Medical Services for Massachusetts Department of Correction

Of the 11,000 inmates in the Massachusetts state correctional system, 4% are HIV-positive. Our HIV Case Management program was developed to clinically manage HIV+ inmates and is very comprehensive. The program was implemented based on

recommendations from a local AIDS Task Force. This task force was made up of Department of Public Health officials, community resources, prison advocates, Department of Correction, contracted medical providers, and the local public health hospital. The program includes Nurse Case Managers (the mainstay of the program), on-site Infectious Disease specialists (physicians that have been “leant” by our public health hospital who provide care behind the prison walls), dietitians, HIV test counselors, and a discharge planner for inmates being released from custody.

Of the HIV patients, 77% of the population are taking some type of HIV medication. 84% of the patients on medications are taking triple therapy (usually includes a protease inhibitor). Most inmates participate in the Keep-on-Person (KOP) medication program. The program gives the inmate responsibility to self medicate and more control for their own health. Medication is packaged in “blister cards”. When there are peculiarities with various medications, e.g. need for ritonavir in the refrigerator or dry storage of Crixivan in original container, custody staff is educated about storing medication in containers other than the blister packs. The KOP program resorts to Directly Observed Therapy (DOT) if the patient is in segregation, and unable to participate in the KOP program or if the patient is not adherent with his/her medication.

A large amount of the Nurse Case managers’ time is spent on educating the inmates about when and how to take their medication. Case managers provide a very supportive environment and for the most part, the inmates are highly educated about HIV disease and HIV medication. There is close monitoring on how adherent the inmate is. In prison the way to monitor adherence may be different than is usually seen. Some ways we monitor adherence is to see if the inmate comes to pick up their medication on time or if they re-order their medication on time.

Medical providers in the prison setting have a unique opportunity to provide health care. For some, prison is the first place many inmates are introduced to health care. In a structured environment the inmates do well. The struggle for us as care givers, as well as, for some inmates, is when they transition into the community. Inmates must get help applying for benefits and services while they are still inside the prison. They are currently unable to apply for public benefits (e.g. Medicaid) while they are incarcerated. This makes it difficult in ensuring continuity of care for the inmate. Many of our inmates have other chronic diseases and on medications for those diseases. We discharge inmates who’s HIV medications are paid for through AIDS Drug Assistance Program (ADAP) but the non-HIV medications are not covered.

The incarcerated patient population is getting sicker; currently 57% of our HIV+ patients are co-infected with hepatitis C; and they are aging. The case management model, as an intervention, is effective in the correctional setting. The challenge before us as a society is to provide the incarcerated patients the tools to acquire a sense of self worth, the capacity to be a self advocate and ultimately feel empowered.

WORK GROUPS

After hearing the presentations on background information and the various types of interventions in development around the country, participants were assigned to one of four work groups: Hospital-based Clinics, Community-based Organizations (Free-standing Clinics), Social Service Agencies, Behavioral Health Service Agencies. The function of the groups was to identify the kinds of services needed within each of these settings to provide adherence support and education to/with people with HIV. Each group was to consider the same six questions for 2 hours and report the results of their discussion to the group. Below is a summary of those workgroup discussions. These summaries can be useful in planning broader implementation of adherence support services.

Questions posed to Work Groups

1. What are the components necessary to develop comprehensive adherence interventions within your respective setting?
2. Identify opportunities during the provision of care where adherence support/education could be provided.
3. Which adherence interventions seem most appropriate and promising for this care setting?
4. What are the opportunities for and potential risks and benefits of directly-observed therapy (DOT) within the care setting?
5. How do adherence support programs coordinate efforts and strategies and exchange information?
6. What are appropriate and feasible methods to evaluate the effectiveness of the interventions?

Summary of Work Group Discussions

- **Need for a Team Approach:** Underlying any components must be agency commitment. There should be vertical as well as horizontal “buy-in.” Consensus favors a team approach, albeit expertise-focused, which takes more time, money, and resources. Ideally the team should be composed of a primary care physician, a research director, a pharmacist, nurses, social workers, case managers, peer educators, and someone who is responsible for coordination and communication. All team members should be “on the same page”; that is, they should share the principles, values, mission, and philosophy of the program, and should use the core protocol and receive the same training.
- **Coordination of services:** Services must be integrated and linked with other services. Collaboration among and within agencies with providers and with clients would include referrals for mental health, substance use, and social services (often episodic over time); and sharing client information, but information sharing is risky—clients must consent, informed consent forms must be released, and the information must be protected.

- Adherence support requires looking at a patient's life, not just their HIV treatment. Issues such as child care, housing, mental health, pregnancy, drug use, access to social support, disclosure of HIV-status, and economic security must be addressed as they will drastically effect a patient's ability to adhere to therapy.
- Treatment should be client-centered with individualized care plans that address the client's concerns, in her or his chosen order. Time should be allowed to develop and address issues of adherence and to reinforce desired behavior over time. Adherence should be kept on the agenda, and the program's success and progress reevaluated from time to time. Input from clients should be sought. Care provision should be seen as on-going process, not a series of individual encounters. If better adherence depends, in part, in the development of a trusting doctor-patient relationship, then consistent interaction between those parties is essential.
- To enable access to services, clinics should focus on a specific population in a geographically limited area. Hours of operation should be flexible and should accommodate the clients' schedules.
- Coordination of care and services is an important and efficient means of providing adherence services. Assuming appropriate training is available, any service where an client interacts with a professional or peer is an opportunity to provide adherence support. Programs such as home health visits, meal delivery, adult day care, drug treatment, transportation, support groups, and peer-based education can incorporate adherence support services. Conduct case conferences with primary care provider, case manager, and other service providers to strengthen coordination and eliminate duplicative services.
- Making a detailed assessment with the client before starting therapy is perhaps the most important opportunity to intervene and ensure better adherence. Clients should be assessed to determine their readiness to accept a complicated and demanding treatment regimen. To encourage personal responsibility, the choice to accept treatment must be the client's. Continued follow-up and re-assessment is also necessary, as adherence and the relationship to treatment will change over time.
- Community organizing, community awareness, and client advocacy are important parts of the social program. The communities affected by HIV need to understand the difficulties people with HIV trying to adhere to these treatment regimens. In this way, the community can offer support, and not stigmatize people if and when adherence difficulties arise.
- Life transitions are particularly stressful times and need close attention to ensure that adherence to medication is maintained. These include release from prison, changing residency and/or jobs, having children, etc. The crises that these transitions can create are both emotional and logistical. Ensuring continuity of care is an essential component of transition management.
- Training and education should be available for staff members, people with HIV, social workers, volunteers, peers, and providers. Training is important in areas such as needs assessment, readiness evaluation, collaboration with other agencies, patient education, and leadership development. Social service providers need training into the pathogenesis of HIV, its disease manifestations, and therapeutic regimens. Cross-training would be useful for staff members of medical and behavioral health agencies in HIV/AIDS, mental health, and substance use.

- Treatment information is an important component of adherence services. Patients need to understand why they are being given these drugs, why adherence is essential, have information about side effects, understand the various components of their treatment regimens and that they have choices to make. Treatment information should be culturally appropriate, easy to read, and accessible.
- Adherence services require space, staffing, and materials.
- Funding for adherence services should be incorporated in care plans and health delivery specifications.
- Assist clients in setting up a support system by identifying who they trust and depend on for care and support. Provide those persons with information about drug regimens and the need for adherence to therapy.
- Bring pharmacists into the team; they can alert the team regarding prescription refills. Work with pharmacies to ensure delivery of medications. Increase pharmacy services—longer hours and perhaps follow-up.
- DOT is an option for some people if it is included in a larger picture. It can provide positive reinforcement if an appropriate provider is available once a day to observe. It is helpful if DOT can be done on-site—perhaps a hospital-based clinic—which offers a chance for daily check-in and regular contact. The contact that comes with DOT allows providers to deal with issues of diversity, culture, and language and possible complications.
- DOT can work for diseases like TB, which require finite treatment for cure. However, with a chronic illness like HIV, the effectiveness and practicality of DOT is unclear. DOT is labor intensive and expensive. If resources to provide treatment are limited, then the use of DOT can lessen the availability of treatment. How long should DOT last? Can/should it be provided for a patient indefinitely? Will DOT be effective in helping patients with treatment adherence after DOT stops? Does DOT teach patients skills for adherence? Geographic limitations can make DOT untenable in many areas, particularly rural ones. The use of monetary and other incentives may be effective in getting people to take their drugs, but is it coercive? Do monetary incentive impact of patients' decisions to start therapy?
- There is no gold standard for evaluation of adherence intervention. But, evaluation is essential. Evaluations should utilize both as to process and outcome measures, including biologic outcomes, clinical outcomes, virologic effects, and adherence measures.
- Partnerships between CBOs and the research community are an important and underutilized avenue for program evaluation.

International Therapeutic Solidarity Initiative

**Increasing access to care for people living with
HIV/Aids in developing countries**

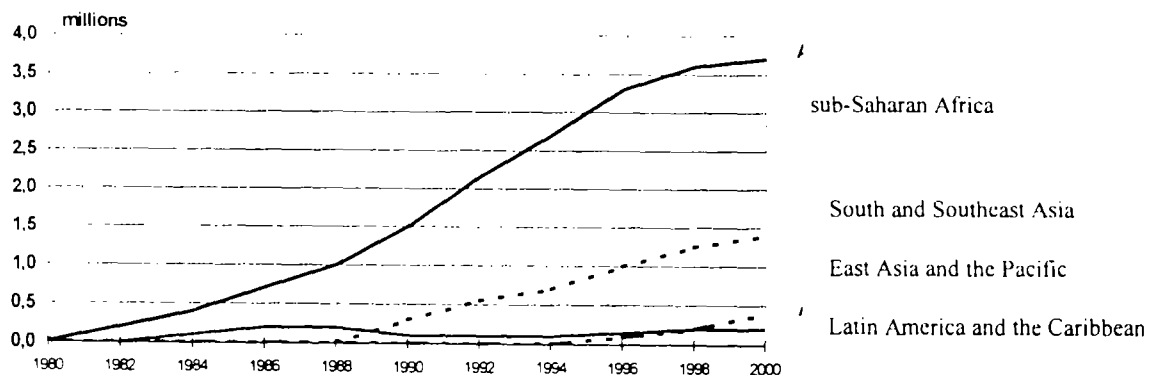
May 1999

WHY THE PRESENT THERAPEUTIC SOLIDARITY INITIATIVE?

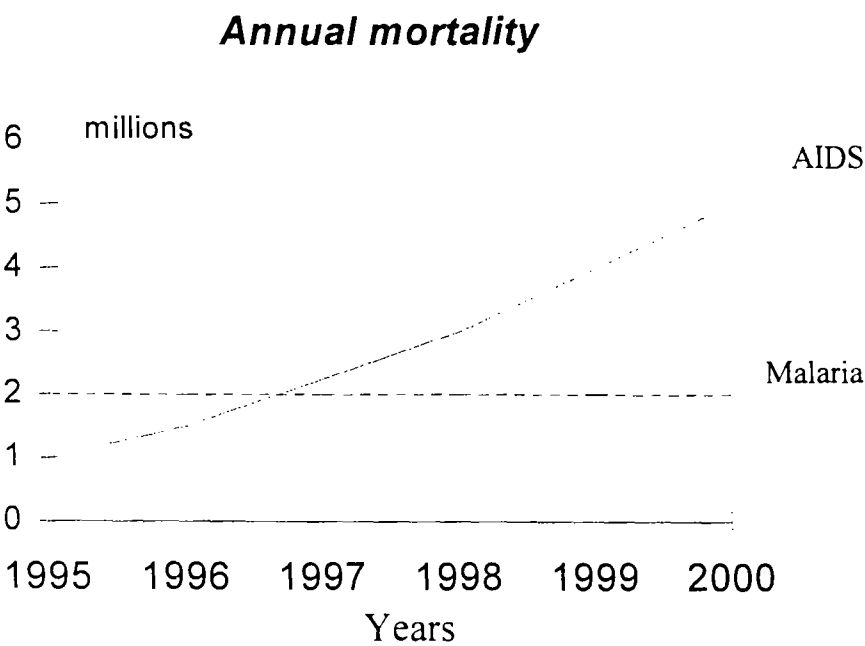
A) Aids is an epidemic which is continuing to grow...

Around the world, 33 million people must now live with HIV infection. Although this is an epidemic which has been more or less stabilized in industrialized countries, AIDS has become a major problem in the developing world. The number of people affected is constantly rising there, and over 90% of people living with HIV/AIDS are in these countries. Every day, another 16,000 people are infected — over one thousand of them children. Africa is the hardest hit by the epidemic. It has two-thirds of the global total of infected individuals — over 20 million of them.

Annual increase in the total of new HIV infection



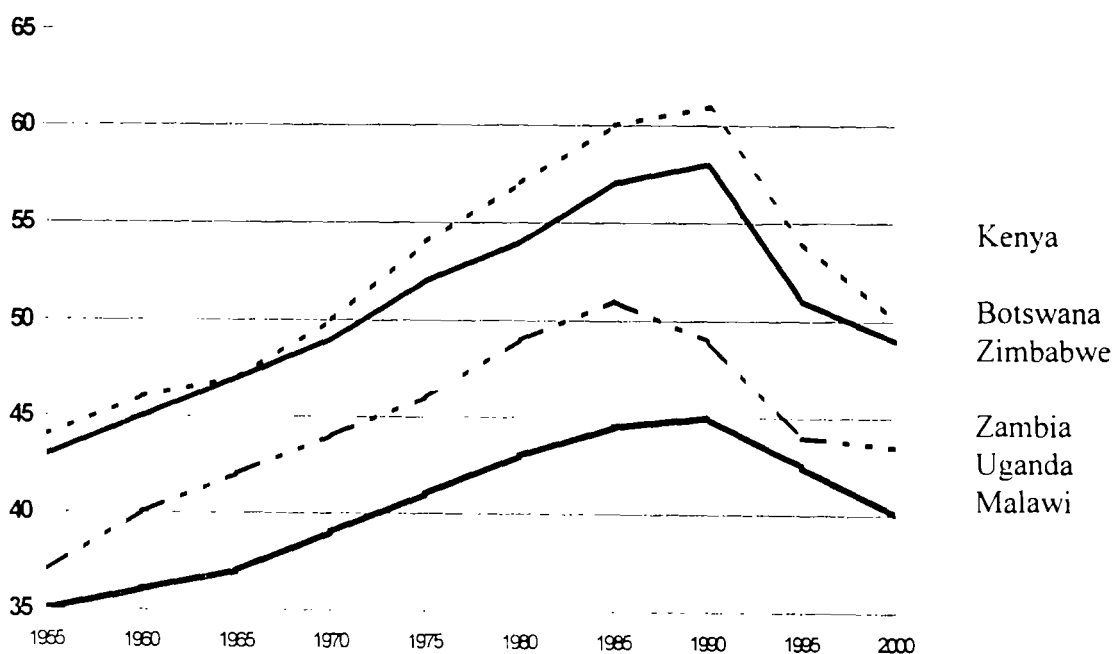
In 1997, for the first time, AIDS caused more deaths – over two million – than malaria. This trend will inevitably increase over the years to come if we do nothing, as the following table makes clear:



According to the latest estimates, life expectancy in numerous developing nations, which had improved over the years, is now being profoundly compromised by AIDS.

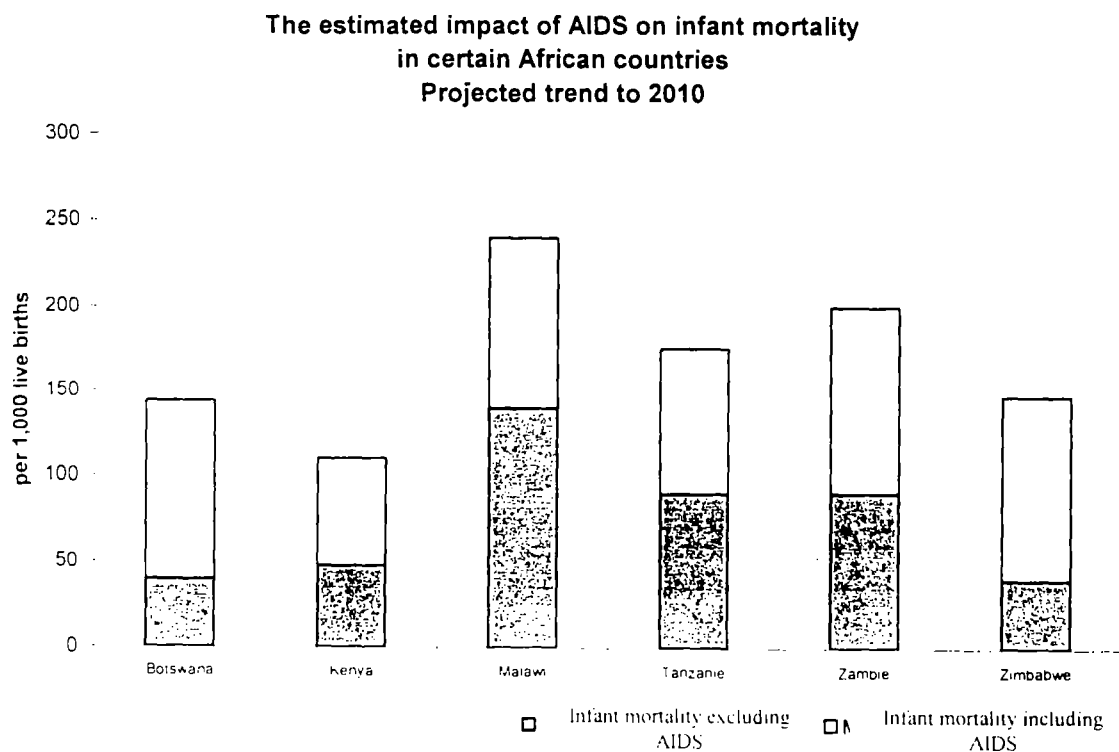
In January 1998, the World Bank organized a meeting to assess the impact of HIV infection on development. This meeting highlighted the fact that in the countries hardest hit by the epidemic, life expectancy at birth had fallen back to the level prevailing in the 1960s, thus wiping out the hard-won gains of the preceding thirty years.

*Projected figures for life expectancy at birth in
certain countries of Sub-saharan Africa*



(from the 1980s onward, the epidemic is of massive proportion)

Likewise, the major progress accomplished in the field of infant and child mortality in recent decades is now under threat. For example, it is reported that deaths of babies under 12 months old have risen by 25% in Zimbabwe and Zambia. By 2010, the projected trends point to an increase of 138% in infant mortality in Zimbabwe, and of 109% for children aged under five years. In Côte d'Ivoire, mortality rates for babies and young children will have risen by more than two-thirds.



B) ... and which threatens development

AIDS, over and above its purely medical aspect, is a condition which causes economic and social upheavals which are all too often ignored.

From the medical point of view, AIDS is characterized by a lengthy period during which it is communicable, without visible symptoms, and prolonged morbidity, factors which help explain the uninterrupted and massive epidemic.

AIDS is a disease which hits families insofar as it uses a dual vector for transmission –horizontal and vertical. It destroys social and family balances. It alters the distribution of tasks and roles, often to the detriment of children. Work done by children, which becomes vital to the family, leads to cessation of their formal education, thus compromising long-term development.

In addition, the death of one of the parents – especially the mother – leads to the problem of the “AIDS orphans”, whose social isolation is made worse by the stigma attached to AIDS. According to WHO figures, by the year 2000 there will be between 10 and 15 million children aged under 15 whose mothers will have died from AIDS.

AIDS is a disease which hits economic development, due to the youth of its victims, who are precisely at the age at which they would normally procreate and produce. The four cornerstones of “lasting human development” are all threatened by the AIDS epidemic. In addition to health and economic development, it compromises basic human freedoms through the stigma associated with it, and the acquisition of knowledge, through the cessation of schooling which it causes.

Those rare surveys that have been devoted to the macroeconomic consequences of AIDS have encountered great difficulty in assessing its real impact, which is especially profound on the informal economy, on the family, and on certain economic sectors...

But regardless of sector, the AIDS epidemic is the cause of major inroads into productivity due to the physical weakness and absenteeism of the sufferers and to the need to replace labor lost through death, requiring the training of new personnel. Those sectors which employ qualified labor – workers difficult to replace – are particularly severely affected. The threat is worse still in countries whose economy is based on a single major sector.

The overall macroeconomic impact of AIDS leads in this way to changes in the conditions of production – particularly in terms of a reorientation of economic activity towards areas less dependent on labor – and a decline in production.

In terms of macroeconomics, AIDS radically disturbs the family economy, affecting all the following aspects:

- Household production and income, because AIDS reduces the productivity of the sufferer, and therefore reduces the family's revenue (in goods or in money) both before and after his or her demise. Alongside this, the patient's friends and relations, especially women, have their time taken up by the healthcare which must be provided, and this also reduces their economic activity.
- Consumption – investment – savings: the balance between these three parameters, given the reduced level of income, is fatally compromised as immediate consumption comes to be given priority (healthcare, funeral expenses, and so on).
- The processes of community solidarity: the illness or death of a once-active adult brings about a radical change in the balance of the exchange of services and mutual help within the family and the surrounding community. The affected family, which is helped by the community, no longer has the resources to contribute itself to that community's processes of social solidarity.

The combination of these major economic, demographic, social and cultural effects aggravates inequality, increases the risks of social exclusion – especially for women – and inevitably threatens the political stability of the countries concerned.

Failure to act amounts to a ratification of the existing situation, which is dramatic and cannot in the long run remain circumscribed within southern countries.

C) An epidemic which knows no frontiers

If this situation persists, it will, in the long run, pose a threat to international geopolitical balances.

The existence of opportunities to receive medical care in just one part of the globe will tend to legitimize movements of populations towards the prosperous nations.

Although the epidemic has been held in check in the North, while spreading unchecked in the South, it is a delusion to believe that it is possible to put three-quarters of the world's population in quarantine. Epidemics know no frontiers, and this is even truer in an era of massive population movements around the world. For this reason, it is in the interests of industrialized nations – the only ones with the necessary resources – to control this pandemic.

The gravity of the consequences of the epidemic at global level puts in perspective the cost of treatment, which hitherto may have appeared prohibitive. It is clear that it is less costly for the international community to act – thereby preserving past achievements – than to suffer the consequences of AIDS.

The international community therefore has every reason to act: epidemiological, economic and political reasons.

D) What should be the response of the international community? Towards an approach combining prevention and care with the aim of achieving real effectiveness.

In order to control this epidemic, it remains necessary to mobilize resources for prevention; this must continue to be a priority for the international community.

The current scale of the disease means that we can no longer dissociate prevention and care (much less to see them as opposed) — even in terms of cost effectiveness. Prevention and care are the two mutually complementary and mutually reinforcing aspects of the fight against HIV. It is self-delusion to believe that a policy based on prevention can be effective in any lasting or efficient way if it is not associated with genuine opportunities to get care. Provision of care for this condition encourages detection of its existence. The fact that the vast majority of people living in the developing world are ignorant of whether they are HIV+ or not is a major obstacle to effective prevention, and this situation could be changed if there were a real possibility of obtaining treatment.

By offering a therapeutic response, treatment strengthens the credibility of the whole biomedical system, which has hitherto been powerless in the face of AIDS.

Lastly, the experience of countries which already benefit from such treatments proves that the provision of healthcare makes it possible to mobilize all those suffering from the infection, making them essential players in the fight against AIDS.

The essential purpose of the Fund

The essential purpose of the Fund is to promote the implementation of coherent programs for the prevention of HIV/AIDS and the provision of care for those suffering from the virus, facilitating access to medication, including anti-retroviral therapies.

Care would make it possible:

- to improve and prolong the lives of HIV carriers,
- to reduce mortality rates for HIV sufferers,
- to make a substantial reduction in the rate at which the virus is transmitted from mothers to their children.

The cost of care is still prohibitive for most developing nations, and the complete mismatch between demand and the possibilities of supply rules out any possibility of provision of immediate and complete medical care for all sufferers.

This harsh reality means that we must proceed gradually, step by step, but we must also target the involvement of beneficiary countries in a dynamic taking them forward to the development of the means to provide care to those living with HIV and AIDS.

This development dynamic, known as the *breach strategy*, entails a hard choice between the various project proposals, and additionally, an even harder choice to identify priorities.

Priority for the prevention of mother to child transmission and care of mothers and children

With the aim of combining prevention and treatment, a consensus has arisen from the very many exchanges of views which focuses on the importance of treating pregnant women in order to prevent the transmission of the virus from mother to child, with services offered to them after birth.

The concept is to put in place a comprehensive program for the prevention of infection and provision of care in a defined population area.

- The objectives of the program are the following:
 1. Provision of information and voluntary counseling and testing for pregnant mothers:
 2. Provision of preventive treatment to reduce mother to child transmission.
 3. Provision of medical treatment for opportunistic infections for all HIV positive women.
 4. Provision of a complete medical care program for children.
 5. As far as is practically feasible, the use of anti-retroviral therapies to treat women and children at major risk of rapid development of the infection.
 6. The offer of an alternative to breast-feeding.

COMPREHENSIVE PROGRAM FOR PREVENTION AND CARE

VOLUNTARY COUNSELING AND TESTING

SCREENING FOR PREGNANT MOTHERS

HIV- women

HIV+ women



counseling and prevention
Provision of services for partners
IEC
Marketing for Condom

provision of integrated medical treatment
and social support

Prior to childbirth

After childbirth

Psycho-social support
Standard prenatal care
STD diagnosis and treatment
AZT chemoprophylaxis

Mother (couple)

Child

Psycho-social support
Provision of artificial feeding
Nutrition
Prevention and treatment of opportunistic infections
monitoring of biological/immune system
ARV if necessary

monitoring of
biological/
Immune system
PCR
Nutrition
prevention I.O
ARV if necessary

Towards international mobilization

The proposal of an international therapeutic solidarity initiative was first put forward at the 10th International AIDS conference, held in Africa, at Abidjan on December 7-11, 1997 by the President of the French Republic, Jacques Chirac, and the Secretary of State for Health, Bernard Kouchner.

This was initially a French proposal intended to mobilize the entire international community.

At the Luxembourg Summit (December 1997), the Council of Europe urged the European Commission to look at ways in which an International Therapeutic Solidarity Fund could be set up under the aegis of UNAIDS.

At the Birmingham Summit (May 1998), the Heads of State and Government, in the final G8 communiqué, welcomed this proposal.

Alongside this, on Thursday, October 22, 1998, the European Parliament, sitting in plenary session, voted to adopt an amendment allowing an increase in the 1999 budget to combat AIDS in the developing world, including a formal reference to programs for provision of access to care in connection with the ITSF.

The European Council of Health Ministers was informed of the current state of progress on the initiative at its meeting on November 12, 1998.

The proposal to set up the ITSF is a step in the same direction as the United Nations program on AIDS, which targets the reduction of inequalities in access to medical care, and has been supported extensively by organizations whose purpose is to combat AIDS in both Northern and Southern nations.

The proposal to create the ITSF is also in line with the approach adopted by WHO, to quote recent remarks made by Dr Gro Harlem Brundtland, its new Director General, when she pressed for *“more equitable access to prevention and care- including anti-retroviral therapies”*. The central issue, Dr Brundtland emphasizes *“is no longer whether these sophisticated drugs should be distributed, but how they should be distributed ... ”*. (Regional Committee for the Western Pacific, Southeast Asia and Africa. September 1998).

Recent meetings with US representatives (White House, CDC, NIH, USAID) in Washington and Chicago, and discussions with World bank vice presidents for Africa and for the development have shown stronger interests for partnerships.

INTERIM STRUCTURE FOR 1999-2000
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**AN ORGANIZATION CREATED WITHIN
THE “FONDATION DE L’AVENIR
POUR LA RECHERCHE MÉDICALE APPLIQUÉE”**

[Foundation for Applied Research in Medicine]

*A foundation officially approved for the holding and management of funds allocated
to ITSF programs*



TECHNICAL COMMITTEE

Chairperson:	Professor PECKHAM (UK)
Vice Chairperson:	Professor HENRION



INTERNATIONAL ADVISORY COMMITTEE

Chairperson:	Professor PECKHAM (GB)
Vice Chairpersons:	Professor HENRION
	Professor Awa COLL SECK (UNAIDS)
	Jeanne KOUAME (Côte d’Ivoire)

ACTION IN COTE D'IVOIRE

The FSTI action in Côte d'Ivoire has a dual objective:

I - To improve the access of people infected with HIV/AIDS to antiretroviral treatment services set up by the Ivorian government in partnership with UNAIDS.

Modalities:

The national solidarity fund set up by the Ivorian government provides funding for up to 75% of the cost of antiretroviral therapy, according to the criteria and modalities defined by Ivorian authorities.

The intervention of the Fonds de Solidarité Thérapeutique International consists of reinforcing the action of the Ivorian fund by providing 80% of the remaining cost to the patient.

People concerned:

500 people, including, in particular, those who have participated in therapeutic trials. These people will therefore be able to benefit from antiretroviral treatments for a period of two years in the context of the access to care initiative conducted by the Ivorian government and UNAIDS.

Financial assistance: 2.5 million French Francs (250 million CFA Francs).

II - To develop a comprehensive HIV prevention and treatment programme for the family unit (starting at the antenatal visit).

Modalities:

This aspect integrates several actions over a two-year period, in particular:

- prevention of sexual transmission of HIV and other STDs, especially syphilis,
- prevention of perinatal HIV transmission,
- preventive and curative management of intercurrent and opportunistic infections in seropositive women,
- antiretroviral treatment for seropositive woman at greatest risk of rapid progression of their HIV infection,
- screening and therapeutic management, including, whenever necessary, by antiretroviral drugs, of infected infants born to seropositive mothers.

Partners:

The support provided by the FSTI to the Ivorian national fund is developed in partnership with:

- the PAC-CI programme (PNLS/ANRS/Coopération Française – Cote d'Ivoire)
- the RETRO-CI project of the Centers for Disease Control (USA)
- the Fondation Glaxo Wellcome France.

This comprehensive HIV/AIDS prevention and management programme will be effective at two sites - Yopougon and Koumassi - in which therapeutic trials have been conducted since 1995 and which are considered to be sites of expertise in terms of mother-to-child HIV transmission interventions. These sites, in collaboration with the FSTI, will provide training for other interventions. This programme is part of a complementary approach to other programmes to be developed in Côte d'Ivoire (UNICEF, etc.).

People concerned:

20,000 pregnant women accepting an HIV screening test and their children and partners.

Financial assistance: 7.5 million French Francs (750 million CFA Francs).

This programme will be evaluated by UNAIDS in collaboration with local teams of Côte d'Ivoire, ANRS (France) and Centers for Disease Control (USA).

ASPECT 1:

IMPROVE ACCESS TO TREATMENT SET UP BY THE GOVERNMENT OF
COTE D'IVOIRE
IN PARTERSHIP WITH UNAIDS

FSTI support to aspect 1

Objective:

To improve the access to antiretroviral therapy services set up by the Ivorian Government in partnership with UNAIDS.

Funding of treatment according to a two-agent protocol (UNAIDS initiative) in subjects with 75% health cover by the Ivorian Fund:

Ivorian Government	FSTI	Patient
75%	20%	5%

ANTIRETROVIRAL DRUG ACCESS INITIATIVE IN COTE D'IVOIRE

The antiretroviral drug access initiative was organised by Decree No. 98-204 dated 30 April 1998, and resulted in the creation of several bodies.

National Fund

The antiretroviral treatment support fund is designed to improve the accessibility of people infected by HIV to antiretroviral treatments, by providing a financial contribution to the organisations in charge of purchasing antiretroviral drugs, as specified on the list drawn up by decree of the Minister of Public Health.

The Ivorian Government has already provided an initial contribution of 600 million CFA Francs, i.e. approximately 1 million US dollars for a first drug endowment.

The fund is housed by the Caisse Autonome d'Amortissement

The Fund's resources come from :

- state subsidies
- contributions from bilateral and multilateral cooperation organisations
- donations and bequests from Ivorian or foreign individuals, private companies or public bodies
- donation campaigns organised amongst the general population.

Management Committee

The National Fund is run by a Management Committee composed of representatives of the Minister of Public Health, the Minister of Economy and Finance, the Executive Director of PNLS/STD/TUB, the Director-General of Caisse Autonome d'Amortissement, the coordinator of the initiative, a religious leader, and a representative of HIV infected patients.

Advisory Committee

The purpose of the Advisory Committee of the pilot project for the antiretroviral drug access initiative in Côte d'Ivoire, which is supported by UNAIDS, is to ensure the proper coordination of the national antiretroviral drug policy.

Technical Secretariat

This is responsible for compiling dossiers to be presented to the Advisory Committee and to help the initiative's coordinator carry through decisions taken by the Minister of Public Health.

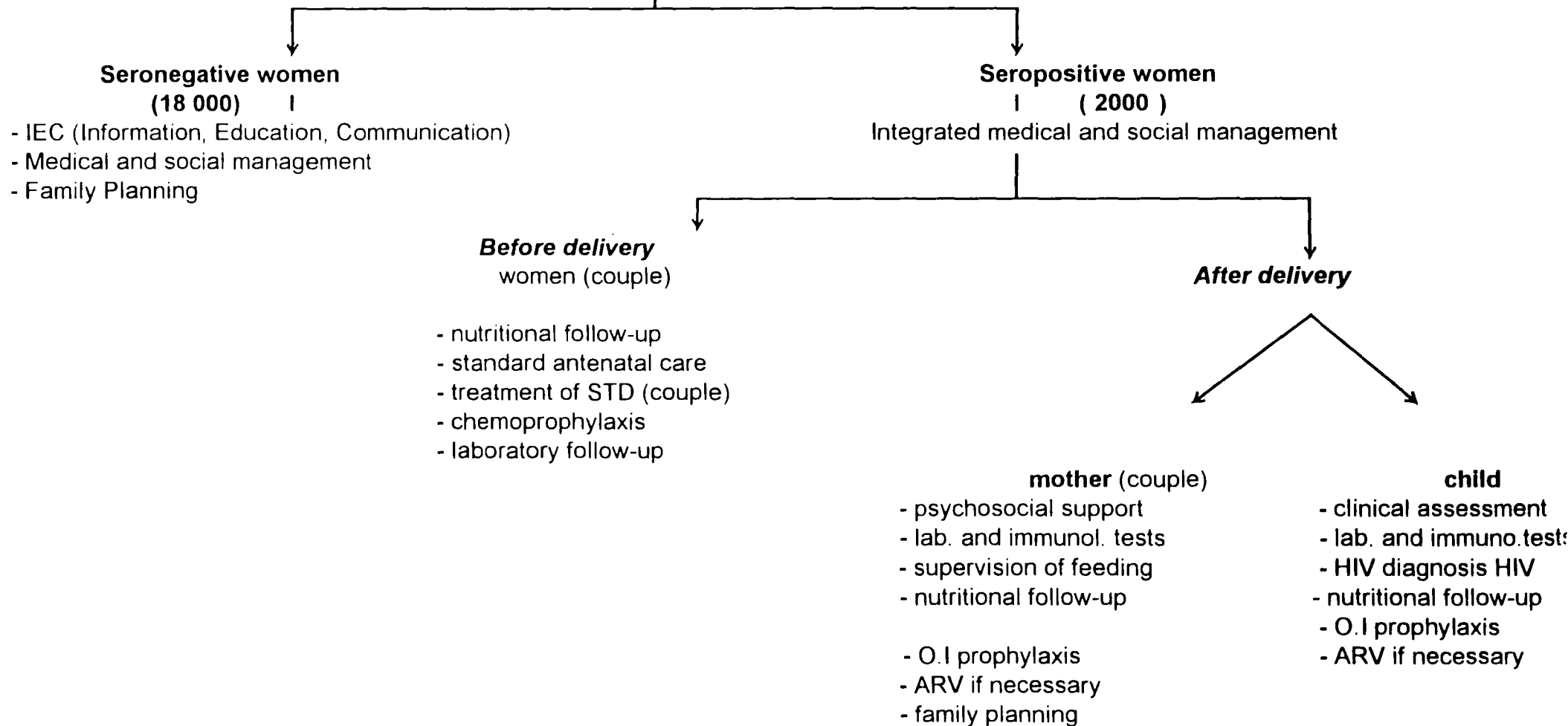
ASPECT 2:

DEVELOP A CONSISTENT INTERVENTION
TO PREVENT AND TREAT HIV INFECTION
IN THE FAMILIAL CELL, FROM ANTENATAL CONSULTATION

Mother to child prevention and management programme

Antenatal Counselling

SCREENING OF PREGNANT WOMEN in public health clinics (STD/HIV) - N = 20,000



Aspect 2: Intervention of the different partners

	Ivorian Govt	Retro-CI	FSTI	Glaxo Wellcome	Pac-CI	UNAIDS	Other
Screening of women		***		***	***		
Syphilis screening				***	***		
VIH screening partners		***		***	***		
Syphilis treatment			***				
AZT		***	***				
ARV women	***		***				
Opportunistic infections women			***				
Laboratory and immunological follow-up		***					
HIV diagnosis infants		***	***				
Treatment infants	***		***				
Opportunistic infections infants			***				
Artificial milk				***			
Milk supplement				***			
Psychosocial support				***			
Family planning			***				***
Support to associations			***				***
Running costs	***	***	***		***		
Training				***			***
Evaluation		***	***		***	***	

April 1999

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October 19, 1999

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Handwritten notes: "Rhe" with a box containing an "x", "PEP", and a large checkmark.

Emergency Treatment to Stop AIDS Virus

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Issue in Depth: The AIDS Epidemic

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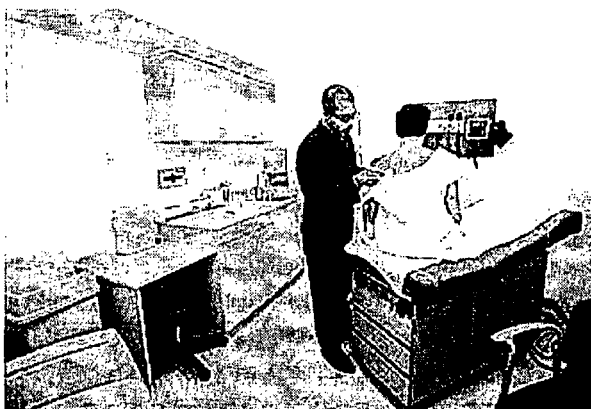
By **DAVID FRANCE**

Frustrated by the continued spread of H.I.V., a growing number of AIDS doctors are trying out an experimental treatment: an application of drugs meant to abort infection in a person who was recently exposed to the virus through unsafe sex.

Called post-exposure prophylaxis, or PEP, the emergency treatment incorporates the same powerful, toxic drugs commonly given to people with AIDS. Only in this case, the drug regimen is initiated in the hours after suspected exposure, and months before a blood test can verify infection.

There is no proof that the treatment works, and few insurance companies are likely to cover the cost, about

\$2,500 including 30 days of drugs, lab tests and doctors' visits. But on the basis of successful experiments on animals and studies of transmission from mother to child, many clinicians think it is at least plausible.



Marilynn K. Yee/The New York Times

Dr. Gabriel Torres, above in his medical office in Manhattan, has been using an experimental treatment for people who believe they have just been exposed to the AIDS virus.

Advertisement

"The body of evidence now available provides pretty solid indirect evidence that this works in preventing infection," said Dr. David Henderson, a deputy director at the Warren G. Magnuson Clinical Care Center, part of the National Institutes of Health, in Bethesda, Md.

The experimental treatment seeks to attack the virus after it attaches to a lymph cell but before it has a chance to burrow into the nucleus and begin reproducing, within two to three days. The aim is to contain and eradicate the viral invasion before it can embark on its destructive path through the body. For this reason, the clinicians say, prompt treatment is essential. Most clinics aim to treat in the first few hours of a suspected exposure, and 72 hours is considered the absolute latest.

Round-the-clock PEP clinics have proliferated in the past 18 months, with public or nonprofit ones opening in Los Angeles, San Francisco, Boston and Providence. Patients can call at any hour after an exposure, and be connected to a screening counselor -- who weeds out people with improbable risk behavior, like kissing -- and a doctor and all-night drugstore, if necessary.

Next month in New York City, Dr. Bernard Salick plans to begin a pilot PEP program at his for-profit clinic on Irving Place near Union Square, the first one based at a private practice. Even before opening, the demand there is astounding.

"The number of calls we get is beyond belief," said Dr. Gabriel Torres, a medical director at the practice who has been trying the treatment on his own patients.

"I had a guy calling me on day 2 from Albany who was driving at 90 miles an hour to get to me in time. I kept saying, 'Just pay attention to the road!' "

It will take thousands more cases and many more years before any conclusions can be drawn about how well, or even whether, the method works.

"No matter how effective these medications are in a preventive mode," said Dr. Michelle Roland, director of San Francisco General Hospital's Positive Health Program, "they are never going to be 100 percent effective."

Still, early indications are favorable. In San Francisco, a city-run PEP clinic treats an average of one new patient a day, and a joint study by the city and San Francisco General Hospital found no H.I.V. transmission among 436 sexually active patients who had received the treatment.

"I certainly believe there is some efficacy to this, or I wouldn't do it," said Dr. Joshua Bamberger, the medical director for special projects at the San Francisco Department of Public Health.

The Federal Centers for Disease Control and Prevention said last year that it "cannot definitively recommend for or against" the treatment, citing a lack of research.

"It's a very interesting area that we're all watching very closely," said Dr. Robert Janssen, the deputy director of the centers' Division of H.I.V./AIDS Prevention, Surveillance and Epidemiology. This summer, the centers established a national registry for doctors to report their PEP experiences. It will be years before the data can be analyzed, Dr. Janssen said.

The standard PEP regimen is similar to the one used for a decade whenever a health care worker is accidentally exposed to infected blood or needles. It uses two antiretroviral drugs, AZT and 3TC, for 7 to 30 days, depending on how early the treatment is started. Many doctors also add one of the powerful new class of anti-H.I.V. drugs called non-nucleoside reverse transcriptase inhibitors, like Sustiva or navirapine.

Advocates are encouraged by successes in blocking H.I.V. in other settings. Transmission rates from mother to child have been reduced to less than 5 percent from 25 percent with prophylactic treatments. Retrospective studies of the thousands of health care workers who have taken PEP suggest that such workplace treatments are 81 percent effective in thwarting infections.

**An
experimental
treatment is
used before
H.I.V. is
diagnosed.**

Extrapolating from these findings, the New York State Department of Health last year recommended that PEP be routinely prescribed in emergency rooms to rape victims whose assailants cannot be found.

But until recently, the treatment was not widely available to people who fell into more typical risk categories: those who engaged in unprotected intercourse with a partner known or suspected to be H.I.V.-positive, whether through carelessness or condom error. These lapses are especially

dangerous among gay men in cities like New York and San Francisco, where one-third of them harbor the virus.

Still, the overwhelming majority of people getting PEP treatment were never infected to begin with. H.I.V. is not easily transmitted; fewer than 1 percent of those exposed to the virus through rectal or vaginal contact will become infected, and the numbers are smaller for oral or penile contact.

Side effects can be severe in the short term, including nausea, headaches and hallucinations affecting three-quarters of patients, the health institutes report. Long-term effects are believed to be minor, as long as the drugs are taken for short periods.

Public health experts have raised some concern about PEP, which they fear may be misconstrued as something of a morning-after alternative, a pharmacological substitute for latex condoms and good sense.

Especially troublesome, they say, is the prospect that its availability may undermine a commitment to proven prevention methods like abstinence, needle-cleaning and safer sex. If so, it risks causing more transmissions than it is averting.

So far, there is little evidence that this is happening. The San Francisco study found that 56 patients returned within a year for another round of PEP. But Dr. Bamberger said it was clear in follow-up interviews that their behavior had not altered because of the availability of medication.

Still, this fear has kept most PEP clinics from promoting their services too widely, their directors say. Boston's Fenway Community Health Center has treated 74 PEP patients, mostly gay men, in the past year and a half, but has refused to advertise the program in the community for fear of sending the wrong message.

"We're happy to offer the information to people who ask, but we don't want to do social marketing," said Fenway's medical research director, Dr. Ken Mayer. "We are very concerned about the specter of some people using lots of medication and knowingly exposing themselves to H.I.V. If you rely on it as the magic bullet, a chemical condom, people are going to get burned."

Each PEP clinic also provides extensive counseling to patients, capitalizing on what Dr. Mayer called an "educable moment."

The PEP procedure itself, with its toxic side effects, may also help to underscore the need to return to vigilant behavior, he said.

That was the case with Dr. Dan Feldman, 30, a neuropsychology fellow at the Weill Medical College of Cornell University, in New York. Just 36 hours after he had reason to believe he had been exposed to H.I.V., his doctor put him on a 30-day PEP course.

"It's been a good reinforcer for staying with safe sex," Dr. Feldman said. "I kept thinking, 'Thank God I'm just doing it for 30 days and not the rest of my life.' "



Congress of the United States
House of Representatives

Washington, DC 20515

November 18, 1998

President William J. Clinton
The White House
Washington, D.C. 20500

Dear Mr. President:

Thank you for your leadership in the fight against AIDS. Earlier this year we joined 61 of our House colleagues in writing Secretary Donna Shalala urging her to expand Medicaid for asymptomatic, HIV-positive individuals. Today, we are writing to urge you, once again, to expand Medicaid for this population. If the Administration is not prepared to expand Medicaid administratively, we urge you to include this expansion in your fiscal year 2000 budget request.

HIV treatment guidelines issued by the Department of Health and Human Services (HHS) last year recommend the use of antiviral therapy *early* in the course of HIV infection, before development of symptoms. Yet because Medicaid does not define individuals with early infection as disabled, many low income individuals are unable to receive HIV-related drugs and health care through the program.

In our August letter, we noted that new research presented at the 12th World AIDS Conference in Geneva provided additional evidence that early therapy for individuals infected with HIV saves lives and is cost effective. Researchers from the University of California, San Francisco found that, "expansion of the US Medicaid system to provide wider access to combination antiretroviral therapy would prevent thousands of deaths and AIDS diagnoses, leading to 14,500 more years of life for persons with HIV disease over five years." The study found that cost neutrality was within reach and that "the program is affordable from a federal perspective."

A General Accounting Office report issued last month provides further justification for expansion of Medicaid. In HIV/AIDS Drugs: Funding Implications of New Combination Therapies for Federal and State Programs, the GAO predicts a steadily increasing demand for AIDS Drug Assistance Program (ADAP) services. The GAO reports that 22 states have already implemented emergency measures to contain ADAP costs; 10 states have capped program enrollment; and 9 states have restricted access to protease inhibitors. The same GAO report notes several studies which have demonstrated the cost-effectiveness of drug therapy for HIV disease.

We believe there is sufficient evidence that Medicaid can be expanded for asymptomatic, HIV positive individuals on a cost neutral basis, and that such a

November 18, 1998

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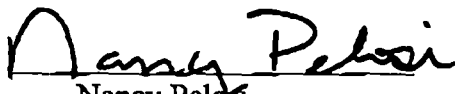
program change can be made administratively. However, if the Administration is unwilling to approve such an expansion, we urge you to request a legislative change in your FY 2000 budget proposal that would make this expansion possible. This proposal would be consistent with responsible long-term fiscal management and allow for more full implementation of the HIV treatment guidelines issued by HHS.

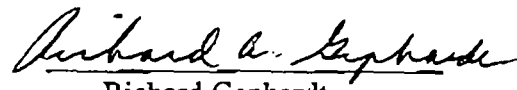
The combination of downward pressure on domestic discretionary spending due to the Balanced Budget Act caps and the continually growing demand for early therapy for HIV disease makes an expansion of Medicaid for HIV-positive individuals the only long-term answer for meeting the treatment needs of people with HIV disease.

Once again, we urge you to take this needed step to extend medically indicated, life enhancing care to people with HIV disease by expanding Medicaid eligibility to asymptomatic, HIV-positive, low income individuals. Thank you for your consideration of this important request.

Again, thank you for your enthusiastic support for AIDS research, care and prevention.

Sincerely,


Nancy Pelosi

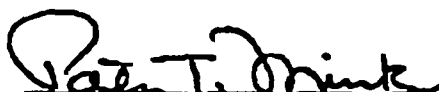

Richard Gephardt


Maxine Waters


Henry Waxman


Xavier Becerra


Pete Stark


Patsy Mink

Senate

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CAPE - AEP - +1

Dental 10

TV + 8

TV + 3

RAAP + 50

TV + 10

TV + 9

To Sandy
Date 7-22-97 Time 10:15 am

WHILE YOU WERE OUT

M. Julie Mukuga
or Intern at Tom Friedman's Office
Phone 456-5579

Area Code	Number	Extension
TELEPHONED	☒	PLEASE CALL ☒
CALLED TO SEE YOU		WILL CALL AGAIN ☐
WANTS TO SEE YOU		URGENT ☐

RETURNED YOUR CALL ☐

Message Can she use your desk
at DEOB 4th Floor until
you move in?

Operator

July 18, 1997

The Honorable William Jefferson Clinton
The White House
Washington, DC 20500

Dear Mr. President:

We are writing to express our grave concern about legislative efforts currently underway to repeal Section 1555 of the Federal Acquisition Streamlining Act (FASA) through the appropriations process. We represent people living with HIV and AIDS, and state and local entities, which provide health care, prescription drugs and social services to individuals living with HIV/AIDS and other uninsured and vulnerable Americans. FASA, which was passed in 1994 as part of Vice President Gore's reinventing government initiative, holds the promise of offering public hospitals, state AIDS Drug Assistance Programs, community health centers and other Ryan White funded entities important opportunities to purchase HIV drugs at deep discounts, thereby allowing them to expand access to these drugs to more individuals. We need the Administration's help in stopping the legislative effort to repeal FASA so that these opportunities can be realized.

The Senate Treasury-Postal Appropriations bill now pending Senate floor action contains language to repeal the FASA law. Repeal language is likely to be added to the House Treasury - Postal Appropriations bill through amendment as early as next week. The Administration opposed FASA repeal language, which was contained in the supplemental appropriations bill earlier this year. We have been working closely with key Senators on a compromise alternative to the repeal which would allow prescription drugs for life-threatening diseases to move forward on the discount drug schedule. This compromise closely resembles compromise language offered to the Senate Treasury-Postal Appropriations Subcommittee by the Office of Management and Budget.

Our efforts to develop an amendment strategy with this compromise language have been thwarted by untested and unsubstantiated arguments that expanding access to drug discounts to state and local entities will undermine the drug discounts now enjoyed by the Veterans Administration (VA) health care system. We have concerns that these arguments may, in fact, have originated with the Veteran's Administration itself as well as with veterans advocacy groups. Even Senators who are very sympathetic to the need to reduce the prices of prescription drugs for individuals with life-threatening illnesses are hesitant to be characterized as threatening the quality of veteran health care.

There is no evidence that expanding access to federal discounts will raise drug prices for the Veteran's Administration health care system. Moreover, the guidance governing the implementation of this program can be structured to ensure that the VA's drug discounts are protected. This is clearly a political weapon being utilized by the pharmaceutical industry to ensure the repeal of FASA. We respectfully request that the Administration take action immediately to communicate its position on FASA to the Congress through the Veteran's Administration. This position should articulate the Administration's support for FASA,

especially for expedited implementation of the discounted prescription drug schedule for drugs which treat life-threatening diseases, as well as a clear message that FASA will not hurt the nation's veterans or their health care.

The need for this kind of Administration action is urgent. The Senate is likely to pass the Treasury-Postal Appropriations bill on Monday with the repeal language intact. The only recourse at this late stage is to include language that would exempt life-threatening pharmaceuticals in the managers' package negotiated by Senators Campbell and Kohl – the Chair and Ranking Member of the Treasury, General Government and Civil Service Appropriations Subcommittee. Several Senators have weighed for this exemption including Senators Wyden, Kerry and Boxer. We urge you to coordinate with these interested parties to ensure the inclusion of this exemption.

We cannot afford to allow programs, which could reduce the price of HIV drugs to be eliminated by the self-interested political actions of the pharmaceutical industry. We need leadership from your Administration to protect the very existence of this program, and we need that leadership now.

Sincerely,

AIDS Action Council
AIDS Policy Center for Children, Youth & Families
Housing Works
Human Rights Campaign Fund
National Alliance of State and Territorial AIDS Directors
National Association of Counties
National Association of County Health Officials
National Association of People with AIDS
National Association of Public Hospital and Health Systems
National League of Cities
Public Hospital Pharmacy Coalition
San Francisco AIDS Foundation
U.S. Conference of Mayors

cc: The Hon. Albert Gore, Vice President
Franklin Raines, OMB
Nancy-Ann Min DeParle, HCFA
Sandy Thurman, White House
Bruce Reed, White House
Josh Gotbaum, OMB
Richard Thurman, OMB
Steve Kelman, OMB
Jesse Brown, Veteran's Administration

Chris Jennings, The White House
Donna Shalala, HHS
Sen. Herb Kohl
Sen. Ron Wyden
Sen. Barbara Boxer
Sen. John Kerry



HUMAN
RIGHTS
CAMPAIGN

TO: Ms. Sandy Thurman

FAX NUMBER: (202) 632-1096

FROM: The Human Rights Campaign
Legislative Department, PAC Department, Field Department

Winnie Stachelberg, Legislative Director
Kevin Layton, PAC Director/Chief Legislative Counsel
Donna Red Wing, Field Director

Nancy Buermeyer
Bill Darker
Becky Dinwoodie
Candace Gingrich
Terrance Heath

Doug Hess
Seth Kilbourn
Tiffany Newton
Kris Pratt
Susanne Salkind

DATE: July 18, 1997

RESPOND TO: Seth Kilbourn

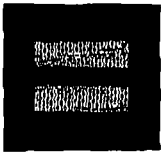
PAGES TO FOLLOW: 3

PHONE: 202.628.4160
FAX: 202.347.5323

Message:

WORKING FOR LESBIAN AND GAY EQUAL RIGHTS.

1101 14th Street NW, Suite 200 Washington, DC 20005
phone (202) 628 4160 fax (202) 347 5323 e-mail hrc@hrcusa.org



HUMAN
RIGHTS
CAMPAIGN

1101 14th Street NW
Washington, DC 20005
phone 202 628 4160
fax 202 347 5323

Memo

Date: July 18, 1997
To: Appropriations Staff Person
From: Seth Kilbourn, Senior Health Policy Advocate
Re: Federal Acquisition Streamlining Act

OPPOSE REPEAL OF THE FEDERAL ACQUISITION STREAMLINING ACT (FASA)

BACKGROUND

Section 1555 of the Federal Acquisition Streamlining Act (FASA) of 1994 establishes cooperative purchasing authority within the General Services Administration (GSA). Through cooperative purchasing, state and local governments, public hospitals, and certain other entities would be allowed to buy products at prices currently available to federal agencies under the Federal Supply Schedule (FSS).

The supplemental appropriations bill, signed by the President in June, imposed a moratorium on FASA implementation through the end of this session of Congress. During the moratorium, it was expected that hearings would be held on the merits of the program to give organizations benefiting from the program a chance to be heard.

Despite that agreement, the Senate Appropriations bill on Treasury, General Government and Civil Service includes an entire repeal of Section 1555.

COST SAVINGS FOR HIV DRUGS

Section 1555 would help local public health departments, public hospitals, and state AIDS Drug Assistance Programs (ADAP) realize significant cost savings in their purchase of pharmaceuticals, including much needed and very costly drugs for the treatment of HIV. FASA could offer cost savings of between 30% and 60% on the purchase of major HIV drugs, enabling ADAPs and public hospitals to expand access, offer more drugs to more people, and avert financial losses.

Currently, State ADAPs and public hospitals are overburdened in their ability to supply needed HIV-related drugs. ADAPs are limiting the number of drugs available, imposing restrictive medical eligibility criteria, and otherwise limiting the size of their programs in order to avoid fiscal crisis. The costs of providing protease inhibitors and the amount of uncompensated costs incurred by public hospitals is extremely high.

TALKING POINTS

- Implementation of cooperative purchasing could save state and local taxpayers across the country hundreds and millions of dollars every year, at a time when federal budget constraints are increasingly squeezing state and local budgets.
- Cooperative purchasing is **optional**. Vendors are not required to participate and are not required to offer products and services to local entities at the federal rates. Their ability to sell to federal agencies through the federal supply schedule would not be affected by that decision.
- 75% of vendors which sell to the federal government are small businesses. The cooperative purchasing program could allow them to expand their market share by attracting more state and local business. Implementation of cooperative purchasing of pharmaceuticals would have no impact on small businesses because there are no small pharmaceutical manufacturers.
- The impact of the cooperative purchasing program on the pharmaceutical market would likely be very small. State and local purchasers of pharmaceuticals represents about 4.4% of the total prescription drug market. Many of those purchasers could not participate in the program because of state and local procurement laws; and many already purchase pharmaceuticals at prices below the federal schedule. In the end, less than 1% of the total prescription drug market would be effected by cooperative purchasing.
- Because there are competing interests in the debate over cooperative purchasing, making a limited number of federal supply schedules would allow for an evaluation of the program's impact and a more informed debate about further implementation.
- The new drug therapies for HIV disease are very expensive (\$10,000 - \$12,000 per patient per year). Cooperative purchasing is a federal and local partnership which would enhance the ability of local governments and communities to use scarce resources more efficiently; it is a potential tool to get more life saving medications to people living with HIV/AIDS.

YOUR HELP IS NEEDED

We ask that you:

- Support a manager's amendment in the Senate Treasury appropriations bill that would provide for a two year demonstration project, whereby the federal supply schedule would be available to local entities for the purchase of pharmaceuticals to treat life-threatening diseases. These pharmaceuticals would include prescription drugs for the treatment of HIV and HIV-related conditions. The majority manager of the bill is Senator Ben Nighthorse Campbell; the minority manager is Senator Herb Kohl. The demonstration project would enable the Department of Health and Human Services and the Veteran's Administration to evaluate the impact of cooperative purchasing and make an informed decision about extending it beyond the two year project.

PUBLIC HOSPITAL PHARMACY COALITION
(A Coalition of the National Association of Public Hospitals & Health Systems)

**WHY IMPLEMENTATION OF COOPERATIVE
PURCHASING SHOULD NOT RAISE DRUG PRICES**

There is a misconception among certain groups that implementation of the cooperative purchasing program under Section 1555 of the Federal Acquisition Streamlining Act would force drug manufacturers to raise their prices. This issue has been the subject of two studies — one by the Prime Institute of the University of Minnesota¹ and the other by the General Accounting Office.²

- A manufacturer's participation in cooperative purchasing is completely voluntary. If a manufacturer cannot afford to extend its federal discounts to state and local buyers, it can simply elect not to participate. Its ability to sell to federal agencies through the federal supply schedule (FSS) would not be affected.³
- Notwithstanding the voluntary nature of the program, manufacturers have stated that they would likely join for competitive reasons. Opting out, they claim, is unrealistic because they could lose their state and local accounts to competitors that choose to opt in.⁴
- These same competitive pressures should encourage manufacturers to keep their FSS prices at their current levels or to lower their prices to attract more state and local business. If manufacturers keep their prices at current levels, average savings for public hospitals would be 25% and much higher for smaller purchasers.⁵ Predictions that the entire industry would have to raise prices do not make sense (absent collusion) since the alleged pressure to inflate prices would have motivated the companies to stay out of the program in the first place.

¹ Prime Institute/University of Minnesota, Section 1555 of the Federal Acquisition Streamlining Act: Impact of Cooperative Purchasing on the Pharmaceutical Market (Jan. 1977) [hereinafter Prime Institute Report].

² General Accounting Office, Drug Prices: Effects of Opening Federal Supply Schedule for Pharmaceuticals Are Uncertain (June 1997) [hereinafter GAO Report].

³ GAO Report at 8; Prime Institute Report at 5.

⁴ GAO Report at 8.

⁵ GAO Report at 18-19; Prime Institute Report at 10.



- In addition, the size of the state and local market is very small. Even if every state and local agency that purchases drugs were to participate in the cooperative purchasing program, this group of purchasers would constitute only 4.4 percent of the total prescription drug market. In reality, an even smaller market would be involved since 40 percent of state and local purchasers would be unable to participate in cooperative purchasing due to state procurement restrictions. In addition, a survey of public hospitals shows that nearly 20 percent of current purchases are at prices already below FSS prices, thereby further reducing demand for drugs through cooperative purchasing. In light of the above factors, the savings available to state and local purchasers of drugs would represent at most only 0.52 percent of the total drug market and would probably be much lower since it is unlikely that all vendors and purchasers would choose to participate in cooperative purchasing in the first place.⁶
- Finally, manufacturers must consider numerous factors in setting the prices of their products. Anticipated profits based solely on a market analysis is only one factor considered by industry. Other factors include the patent status of the drug and its competitors, the existence of generic and therapeutic substitutes, an opportunity to familiarize residents and medical students with the drug, and other factors. To speculate that the effects of cooperative purchasing would supersede all of these other factors is unreasonable.⁷

For more information, contact Bill von Oehsen (202-624-7249) or Ted Skafsky (202-624-7346).

21462831.W51

⁶ GAO Report at 10-12; Prime Institute Report at 6-11.

⁷ GAO Report at 18; Prime Institute Report at 12.

Estimated Costs of Providing Protease Inhibitors to an Eligible HIV Population at Select NAPH Member Hospitals

Hospital	Total Annual Cost	Total Percentage Reimbursed	Total Annual Uncompensated Cost (drugs only)	Total Annual Uncompensated Cost (drugs and testing)
Cook County BHS Total HIV Caseload: 2,700 Eligible Caseload: 1,800 Cost per Patient: \$5,074	\$ 9,134,680	75.0%	\$ 2,283,670	\$ 2,508,670
Grady Health System Total HIV Caseload: 4,000 Eligible Caseload: 1,500 Cost per Patient: \$5,000	\$ 7,000,000	40.0%	\$ 2,800,000	\$ 3,560,500
Harris County Hospital District Total HIV Caseload: 4,500 Eligible Caseload: 2,200 Cost per Patient: \$5,000	\$ 11,000,000	21.0%	\$ 8,690,000	\$ 9,993,500
Jackson Memorial Hospital Total HIV Caseload: 2,500 Eligible Caseload: 1,750 Cost per Patient: \$4,980	\$ 8,715,000	30.0%	\$ 8,100,500	\$ 6,468,000
Los Angeles County DOH Total HIV Caseload: 12,826 Eligible Caseload: 6,413 Cost per Patient: \$6,000	\$ 38,478,000	90.0%	\$ 3,847,800	\$ 4,264,645
Total	\$ 74,327,680		\$ 23,721,970	\$ 26,795,315
Average	\$ 14,865,536		\$ 4,744,394	\$ 5,359,063

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AMENDMENT NO. _____ Calendar No. _____

Purpose: To provide for a cooperative drug purchasing demonstration program for certain drugs, and for other purposes.

IN THE SENATE OF THE UNITED STATES—105th Cong., 1st Sess.

S. 1023

Making appropriations for the Treasury Department, the United States Postal Service, the Executive Office of the President, and certain Independent Agencies, for the fiscal year ending September 30, 1998, and for other purposes.

Referred to the Committee on _____
and ordered to be printed .

Ordered to lie on the table and to be printed

AMENDMENT intended to be proposed by Mrs. HUTCHISON

Viz:

- 1 At the appropriate place in the bill, insert the follow-
- 2 ing new section:

- 3 SEC. ____ COOPERATIVE DRUG PURCHASING DEMONSTRA-
- 4 TION PROGRAM.

- 5 (a) IN GENERAL.—Section 201 of the Federal Prop-
- 6 erty and Administrative Services Act of 1949 (40 U.S.C.
- 7 481) is amended by adding at the end the following:

- 8 “(f)(1) Subject to paragraphs (2), (3), (4), and (5),
- 9 the Administrator may provide for the use of Federal sup-

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1 ply schedules of the General Services Administration as
2 described in paragraph (2) by any of the following entities
3 upon request:

4 “(A) A State, any department or agency of a
5 State, and any political subdivision of a State, in-
6 cluding a local government.

7 “(B) The Commonwealth of Puerto Rico.

8 “(C) The government of an Indian tribe (as de-
9 fined in section 4(e) of the Indian Self-Determina-
10 tion and Education Assistance Act (25 U.S.C.
11 450(e))).

12 “(2) Subject to paragraph (4), paragraph (1) shall
13 apply to any drug, available through a Federal supply
14 schedule contract that falls within the Federal Supply
15 Classification Code 65 (Medical, Dental and Veterinary
16 Equipment and Supplies) to the extent that such drug—

17 “(A) is purchased for the treatment of life-
18 threatening conditions as determined by the Sec-
19 retary of Health and Human Services and the Sec-
20 retary of Veterans Affairs; and

21 “(B) is not used in the general practice of med-
22 icine.

23 “(3) Any entity referred to under paragraph (1) (A),
24 (B), or (C) may purchase a drug under this section for
25 any entity, including a hospital that satisfies the criteria

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1 under section 340B(a)(4)(L)(i) of the Public Health Serv-
2 ice Act (42 U.S.C. 256b(a)(4)(L)(i)).

3 “(4)(A) During the 2-year period beginning on the
4 date of enactment of this subsection, the authority speci-
5 fied in paragraph (2) shall be limited to drugs purchased
6 for the treatment of life-threatening conditions as deter-
7 mined by the Secretary of Health and Human Services
8 and the Secretary of Veterans Affairs. During such period,
9 the Secretary of Health and Human Services and the Sec-
10 retary of Veterans Affairs shall assess the effect of imple-
11 menting paragraphs (1) and (2) with respect to drugs pur-
12 chased for the treatment of life-threatening conditions.
13 The assessment shall include an analysis of the effect on
14 prices paid by Federal agencies for such drugs.

15 “(B) The Administrator shall review the assessment
16 and consider the recommendations of the Secretary of
17 Health and Human Services and the Secretary of Veter-
18 ans Affairs before exercising authority under paragraph
19 (2) with respect to drugs purchased for the treatment of
20 life-threatening conditions. In the event of conflicting rec-
21 ommendations, determination of whether to exercise the
22 authority shall be made by the Director of the Office of
23 Management and Budget.

24 “(5) The authority under this section shall terminate
25 and this section shall have no force and effect on the date

SENT BY:

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1 occurring 2 years after the date of enactment of this sub-
2 section.".

**DEMONSTRATION PROPOSAL THAT WOULD ALLOW
FOR EVALUATION OF COOPERATIVE PURCHASING AND ASSIST
TAXPAYERS IN PAYING FOR HIV AND OTHER LIFE SAVING DRUGS**

Proposal

- (1) Pharmaceutical schedule (Multiple Award Schedule 65 IB) is opened up to state and local agencies, including public hospitals, on a demonstration basis with respect to drugs used to treat HIV and HIV-related conditions.
- (2) After two years, the demonstration project shall be expanded to drugs used to treat other life-threatening conditions subject to the approval of the Department of Veterans Affairs and the Department of Health and Human Services.
- (3) A state or local hospital is defined to ensure that only bona fide public hospitals with indigent care obligations are eligible to participate.

Explanation

- (1) According to a study by the Public Hospital Pharmacy Coalition (PHPC), including pharmaceuticals in the federal cooperative purchasing program could save state and local hospitals more than 25 percent on drug costs while having negligible impact on the price of drugs purchased by the federal government and other entities.¹¹ Proceeding in this fashion on a demonstration basis would assist financially-strapped hospitals in being able to offer expensive new therapies such as protease inhibitors used to treat HIV and other pharmaceuticals for life-threatening conditions. This approach would also not affect small businesses since virtually all pharmaceutical vendors and distributors are large businesses.
- (2) The demonstration project will yield data that shall be subject to review by the VA and HHS so that all sides to the issue can be studied. Expansion of the program to include other pharmaceuticals used to treat life-threatening conditions would also be subject to the approval of the VA and HHS.
- (3) To ensure that the proposed demonstration projects are limited to bona fide public hospitals, it is important that the definition of a state or local hospital be carefully drafted. The proposed definition would include hospitals that have already been

¹¹ Prime Institute/University of Minnesota, Section 1555 of the Federal Acquisition Streamlining Act: Impact of Cooperative Purchasing on the Pharmaceutical Market 10 (Jan. 1997).

deemed by Congress to be governmental,^{2/} and would exclude all other hospitals that arguably have a claim to being eligible (e.g., hospitals that receive Medicare or Medicaid funding, etc.) but fall outside the scope of a reasonable definition.

- (4) Besides assisting public hospitals, this program would stretch taxpayer dollars further for AIDS Drug Assistance Programs (ADAPs) and other state and local AIDS programs. According to a recent national survey, state ADAPs are facing a projected budget shortfall of \$131.7 million dollars. This shortfall could be substantially reduced through cooperative purchasing.
- (5) Early, aggressive use of triple combination therapy will shortly become the standard of HIV/AIDS care to be recommended by the NIH and PHS. The draft guidelines, as now written strongly recommend that all people with HIV who have fewer than 500 CD4 cells and any detectable viral load be treated with triple combination therapy including a protease inhibitor. It also strongly suggests that any therapy that does NOT reduce viral load to below the level of detection does more harm than good.
- (6) Although including the pharmaceutical schedule in the cooperative purchasing program is controversial, limiting the demonstration project to only HIV-related drugs will assure that lives are not unnecessarily lost and HIV expenses are not unnecessarily incurred while Congress evaluates whether the program should be broadened. Both GSA and GAO have recommended that, under the appropriate circumstances, schedules be opened up on a partial basis rather than in their entirety.
- (7) It is inappropriate for Congress, on the one hand, to be seeking an increase in federal funding for AIDS drugs and, on the other hand, to be repealing a program that uses competition to reduce the cost of such drugs.

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^{2/} See 42 U.S.C. § 256b(a)(4)(L)(i). This definition would include state, county and city hospitals, hospital commissions, hospital authorities, hospital districts, public benefit corporations, and reorganized quasi-public, non-profit corporations. Other hospital structures would be excluded.

Section ____ Cooperative Purchasing Demonstration Program.

IN GENERAL - Section 201 of the Federal Property and Administrative Services Act of 1949 (40 U.S.C. 481), is amended by adding the following new subsection (b):

"(b)(1) **DEMONSTRATION** - The Administrator may provide for the use of Federal supply schedules of the General Services Administration as described in paragraph (2) by any of the following entities upon request.

- (A) A State, any department or agency of a State, and any political subdivision of a State, including a local government.
- (B) The Commonwealth of Puerto Rico.
- (C) The government of an Indian tribe (as defined in section 4(c) of the Indian Self-Determination and Education Assistance Act (25 U.S.C. 450(e)).

(2)(A) **HIV AND LIFESAVING DRUGS** - Paragraph (1) shall only apply to pharmaceuticals, available through Federal supply schedule contract that fall within the Federal Supply Classification Code 65 (Medical, Dental and Veterinary Equipment and Supplies) to the extent that such pharmaceuticals:

- (i) are purchased for the treatment of life-threatening conditions as determined by the Secretary of Health and Human Services and the Secretary of the Department of Veterans Affairs; but
 - (ii) exclude those pharmaceuticals used in the general practice of medicine.
- (B) Prior to that date which is two years after enactment of this Act, the authority specified in subparagraph (A) shall be further limited to drugs purchased for the treatment of HIV and HIV related conditions as determined by the Secretary of Health and Human Services and the Secretary of the Department of Veterans Affairs. During this time, the Secretary of Health and Human Services and the Secretary of the Department of Veterans Affairs shall assess the effect of implementing paragraph (1) with respect to drugs purchased for the treatment of HIV and HIV related conditions. The assessment shall include an analysis of the effect on prices paid by Federal agencies for these drugs. The Administrator shall review this assessment and consider the recommendations of the Secretary of Health and Human Services and the Secretary of Veterans Affairs prior to exercising the authority set forth in subparagraph (A) with respect to drugs purchased for the treatment of life-threatening conditions. In the event of conflicting

recommendations, determination of whether to exercise this authority shall be made by the Director of the Office of Management and Budget.

(3) **PUBLIC HOSPITAL DEFINED** - A hospital shall be considered to qualify for use of the Federal supply schedules under paragraph (1)(A) if it satisfies the criteria described in 42 U.S.C. § 256b(a)(4)(L)(i)."

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