

July 4, 2000

Attention: Dennis Adams - Nutritional Services Sub-committee Chair for the Priorities Committee - Broward County HIV Health Services Planning Council

The following is information (9 pages) on the need for more nutritional services for people living with HIV, estimations of the total money needed for 2001-2002 (for nutritional services and food bank), and suggestions for contract language for food bank, home delivered meals and nutritional services.

### **Selected References**

1) AIDS Digest V2 #1471 Thu, 22 Jun 2000 11:29:40 -0500 (CDT) Thursday, June 22 2000

#### **Hyperlipidemia and Insulin Resistance Due to HIV Infection and its Therapies**

Carl Grunfeld, MD, PhD, University of California at San Francisco

<<http://hiv.medscape.com/update2000/lipids>>

Introduction: As is the case with many other infections, HIV infection is accompanied by disturbances in lipid and glucose metabolism. These metabolic abnormalities are further confounded by changes induced by antiretroviral drugs. There is increasing concern that these changes will lead to an epidemic of cardiovascular disease. While cardiovascular disease will no doubt increase, current data indicate that the absolute levels are likely to remain low on average, although patients with additional risk factors are certainly more susceptible. These complications of therapy must be taken into account in deciding when to treat, and risk factor reduction should become routine part of care for the HIV population now living longer as result of highly active antiretroviral therapy (HAART).

2) Medscape.com <http://www.medscape.com>

#### **Link Found Between AIDS Medications and Diabetes May 23, 2000**

Journal of Biological Chemistry/MedscapeWire

AIDS drugs that dramatically prolong the lives of many HIV-infected people also quickly block the body's ability to store glucose, scientists have found. Their research explains why people who take HIV-protease inhibitors are prone to develop diabetes. It suggests that doctors might need to alter the way they test HIV-infected patients for diabetes. And it suggests a way to develop new AIDS drugs without the diabetes risk.

"We hope these findings will help improve AIDS therapy while preventing what can be serious complications from a very effective HIV treatment," says Mike M. Mueckler, PhD, the lead scientist for research that will be published in the July or August issue of Journal of Biological Chemistry. The unedited article is available on the journal's Web site (<http://www.jbc.org/cgi/reprint/C000228200v1>). Mueckler is a professor of cell biology and physiology at Washington University School of Medicine in St. Louis, Missouri, and associate director of the medical school's Diabetes Research and Training Center.

The Food and Drug Administration rapidly approved HIV protease inhibitors in 1996 because the drugs produce a dramatic drop in the level of HIV RNA in patients' blood. They prevent an enzyme from functioning that HIV needs for multiplying and producing a more active infection.

However, studies in the past 2 years have suggested that long-term use of HIV protease inhibitors comes at a high price. Up to 83% of people taking the AIDS drugs develop excess belly fat and skinnier arms, legs, and faces. Moreover, abdominal obesity is associated with type 2 diabetes. A recent pilot study found that 46% of HIV-infected patients receiving HIV protease inhibitors had impaired glucose tolerance, a predictor of future diabetes development. An additional 13% developed type 2 diabetes within 18 months of taking the drugs.

By comparison, about 6% of Americans develop this version of diabetes after years of difficulty handling glucose, the fuel that fat and muscle cells store for future bursts of activity. Type 2 diabetes results from an inability to produce enough of the hormone that stimulates glucose uptake by these cells, as well as from failure of the cells to respond to the hormone insulin. Excess glucose circulating in the bloodstream can damage organs, producing blindness, kidney failure, and other complications.

After reviewing results from animal studies, the researchers decided to investigate whether the AIDS drugs inadvertently cripple a protein that serves as the porthole for glucose entry into fat and muscle cells, which store it as fat or glycogen. Genetically modified mice that lack the protein, called glucose transporter 4 (glut4), can't store fat. Other mice that have half the normal level of glut4 respond poorly to insulin and are prone to develop type 2 diabetes. Mueckler and colleagues studied the effect of 3 commonly used HIV protease inhibitors on fat cells. They found that human fat cells in test tubes absorbed less glucose after exposure to the drugs at a concentration of 10 micromoles. This drug concentration occurs in the blood of people receiving HIV therapy.

To determine how the drugs inhibit glut4, the researchers analyzed the steps in the molecular pathway that the body uses to prompt glucose storage. The HIV inhibitors didn't prevent fat cells from responding to insulin. Nor did they keep glut4 from traveling to the cell exterior to prepare for glucose uptake. Instead, the protease inhibitors prevented the transporter from operating. This finding was made by inserting the gene for glut4 into eggs of African clawed toads (*Xenopus laevis*), which automatically display the transporter on their surface.

The results suggest that doctors need to reconsider how they assess the diabetes risk of people receiving HIV protease inhibitors. The researchers estimate that the drugs may hinder glut4 activity within minutes. Yet doctors currently give glucose tolerance tests without considering patients' HIV medication schedules. "More [HIV-infected] patients are probably glucose-intolerant than we are aware of because of the way diabetes testing is done," Mueckler says.

The researchers are searching for new drugs that won't cripple glut4 function. In addition, they are investigating how the current protease inhibitors thwart the transporter function.

They also will try to determine whether poor glut4 function causes fat redistribution in patients receiving HIV protease inhibitors. Because glut4 malfunctions in patients taking the inhibitors before body fat is redistributed, the transporter might incite this reorganization. "That would make sense if fat stored in the outer portions of the body is made from blood glucose, whereas stores of belly fat come from fat in the blood," Mueckler says, noting that abdominal obesity is associated with type 2 diabetes.

3) Medscape.com - <http://www.medscape.com/SCP/IIM/1999/v16.n11/m5780.diet/m5780.diet-01.html>

### **HIV-1 Protease Inhibitors: A Review CME**

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Abstract: Deaths due to AIDS are declining at remarkable rates in the developed world, largely because of promising new therapies that include protease inhibitors (PIs). The PIs are most effective in suppressing HIV-1 when used in combination with nucleoside reverse transcriptase inhibitors. The use of the PIs in combination regimens for the treatment of HIV infection has led to decreased hospital admissions, fewer opportunistic infections, and a total savings to the health care system. Current guidelines from the Department of Health and Human Services and the International AIDS Society-USA recommend the preferred regimen as one containing a highly active PI (eg, ritonavir, indinavir, or nelfinavir) and two nucleoside reverse transcriptase inhibitors.

**Introduction:** The remarkable decline in AIDS-related deaths in the developed world is mostly attributable to promising new therapeutic regimens. Each discovery of a successful new regimen increases our understanding and the potential for controlling or possibly curing this worldwide killer.

Before late 1995, medicine could only offer modestly suppressive regimens of limited durability to combat HIV infection. Early medical regimens included the nucleoside reverse transcriptase inhibitors (NRTIs), of which zidovudine is the prototype. However, this class of antiretroviral agents had the potential for rapidly acquired resistance. Zidovudine monotherapy had limited effectiveness, except in the area of maternal-fetal transmission.[1,2]

In 1995, a new class of antiretroviral agent, protease inhibitors (PIs), became commercially available. The PIs are most effective in suppressing HIV-1 when used in combination with NRTIs. Compared with older regimens, PIs used in combination with current therapies reduce viral loads (the number of viral particles in the blood) below detectable levels in greater numbers of patients for longer periods.

According to the 1998 consensus statement published by the Department of Health and Human Services (DHHS), the use of PIs in combination with at least two other agents is now first-line therapy for HIV infection.[3] However, because they were approved through the FDA accelerated review process, PIs were not subjected to the typical prolonged scrutiny that a new agent usually undergoes before marketing. This leaves unresolved complex issues regarding the proper use of these agents, such as development of resistance, tolerability, adherence, and cost. Improper use may lead to cross-resistance and the loss of effectiveness for the entire class. We review current reports on the PIs, including data presented at recent HIV and infectious disease conferences.

**Mechanism of Action:** After isolation and crystallization of the HIV-1 protease enzyme in 1988, researchers have been developing chemical compounds to effectively inhibit the action of this key enzyme.[4]

HIV-1 protease is an enzyme essential for viral replication.[5] It is responsible for the terminal maturation of infectious virions. Inhibition of this enzyme results in the production of immature, noninfectious viral particles. The immature virions are then cleared from the cell by mechanisms not yet well understood. PIs act only to block maturation of the viral particles and do not affect cells already infected. Although PI therapy does not prevent destruction of already infected CD4+ lymphocytes, further spread of infection to uninfected cells is prevented.[6,7]

The PIs are potent inhibitors of HIV-1 and HIV-2 protease in vitro.[8] Enzyme levels required to inhibit HIV proteases are 1,000 times less than those required to inhibit essential human proteases such as renin, pepsin, and cathepsin.[8]

Currently, there are four commercially available, FDA-approved HIV-1 PIs: saquinavir (hard- and soft-gel capsules), ritonavir, indinavir, and nelfinavir. Several others are in various stages of clinical and preclinical development.

**Pharmacokinetics:** To be successful, a PI must be readily bioavailable and not rapidly eliminated. Each of the commercially available PIs is extensively metabolized by the cytochrome P-450 isoenzyme system.[9,10] With the exception of saquinavir, they all possess excellent bioavailability. Although the saquinavir soft-gel formulation has improved bioavailability, the compound remains the least predictable of the commercially available products. In addition, bioavailability of the other agents differs, depending on whether it is given in the fasting or fed state. For example, indinavir is better absorbed when given in the fasting state, whereas others are better absorbed after a meal or snack (Table 1).[11-15]

**Drug Interactions:** **All PIs are substrates that inhibit and/or induce cytochrome P-450 isoenzymes, especially P-450 3A4.** The inhibition of this pathway raises the plasma concentrations of coadministered PIs, an interaction currently being exploited or explored in different combinations. Tables 2 and 3 summarize the drug-drug interactions.[3,11-15]

All of the currently available PIs interact with several classes of agents. The nonsedating antihistamines terfenadine and astemizole and the gastrointestinal prokinetic cisapride should not be administered with the PIs because of an increased risk of cardiac arrhythmias. Due to the possibility of increased rifampin toxicity and, in some cases, decreased PI serum levels, the concurrent use of rifampin and PIs is contraindicated. Rifabutin should not be used with ritonavir or saquinavir, but can be used in reduced dosages (50% of the rifabutin dose) with indinavir and nelfinavir.[11-15]

**Adverse Effects: The PIs have been associated with new onset of diabetes mellitus, worsening of preexisting diabetes, hyperglycemia, and insulin resistance suggestive of type 2 diabetes mellitus in some patients.[16-21] Hyperglycemia may occur regardless of familial risk of development of diabetes.** In some cases, the hyperglycemia resolved after discontinuation of the PI, whereas in others it persisted. Oral hypoglycemic agents are generally sufficient for treatment. Insulin is rarely required. Diabetic ketoacidosis rarely occurs.[18]

HIV-infected patients with hemophilia (type A or B) may be at increased risk for bleeding. Episodes of spontaneous skin hematomas and hemarthrosis, in some cases requiring additional doses of factor VIII, have been reported.[11-15] In more than 50% of the cases, the PI was continued or restarted after the episode. A clear causal relationship has not been established.

The PIs have also been associated with an unusual adverse reaction involving the deposition of fatty-like tissue at the base of the posterior neck ("buffalo hump") and the abdominal area ("protease paunch").[18,22-27] The syndrome is associated with peripheral lipodystrophy, central adiposity, female breast enlargement, hyperlipidemia, and insulin resistance.[18,22-27] The relationship between the PIs and this syndrome is hypothesized to be a 60% homology between the PI's binding region and two human proteins involved in regulation of lipid metabolism.[28]

The following outlines an educated estimate of Ryan White funding needed for the 2001-2002 year and suggestions for contract language for food bank, home delivered meals and nutritional services:

#Clients	Average Units/Client	Average Cost/Unit	1999-2000 Funding	2000 Funders	Calculated '01-'02 \$ Needed	Increased # Clients	Additional Increased # Units/Client	Documented Increased \$/Unit	Community Need Total Add \$	Calculated 2001-2002 \$ Needed	Total 2001-2002 \$ Needed
<b>Food Bank</b>											
2,451	15	37	1,374,484	0	1,374,484	0	0	0	0	1,374,484	1,374,484
Increase in number of clients should balance decrease in number of clients with AIDS.											
<b>Nutritional Services</b>											
1,358	4	13	76,012	0	76,012	2,882	8,646	13	112,398	76,012	188,410
4,240 (no. of meds clients) - 1,358 (no. in calculated amt.) = 2,882 additional clients <b>Increased no. units=</b> 2,882 X 1 (/Client Screening) + 4 units for 50%(1,441)= 5,764 + 2,882= 8,646											
<b>Home Delivered Meals</b>			<b>No Title II Information on-hand</b>								

**Food Bank**

**1) Expected Outcome: Food security that lessens barriers to care for eligible people living with HIV/AIDS**

Objective-----  
Provision of nutritious foodstuffs/meals or food vouchers **that meet nutritional standards for HIV-positive people and are both culturally and ethnically diverse**

- Activities
- 1a. On-site RD or LDN approval based on established AIDS Nutrition Services Alliance Guidelines (ANSA) dated 2/16/99.
  - 1b. Client advocacy group approval
  - 1c. Documentation of residential, financial and HIV status
  - 1d. Documentation of symptomatic HIV infection with opportunistic infection or an AIDS diagnosis. (MD or PA {physician's assistant} assessment with listed conditions including disease stage, height and weight)
  - 1e. Reassessment every 9-12 months
  - 1f. Documentation of clients served

**2) Expected Outcome: Safe (sanitary and uncontaminated) foodstuffs to lessen the risk of food and water-borne illness.**

Objective-----  
Compliance with all applicable local, state and federal standards **and food safety standards established by the national Nutrition Services Alliance Guidelines (ANSA)**  
**Educate food bank clients on methods to reduce the risk of food and water-borne illness**

- Activities
- 1a. On-site RD or LDN approval based on Hazard Analysis Critical Control Point system (HACCP) standards
  - 1b. Yearly documentation by state and successful food safety & sanitation inspection by independent auditor (RD with expertise in this area) noting compliance with standards for HACCP food handling and storage
  - 1c. On-site display of food safety and sanitation materials
  - 1d. Document number of clients receiving individual or group instruction on food safety, food handling, and food preparation

**3) Expected Outcome: Coordination of food bank services with local programs to lessen duplication of services**

Objective-----  
Coordinate food bank services with other local food programs

- Activities
- 1a. Documentation of coordination efforts with local food providers

**4) Expected Outcome: Culturally sensitive and competent services**

Objective-----  
Provision of culturally and competent services along with a variety of quality food

- Activities
- 1a. Decrease in number of grievances
  - 1b. Client satisfaction and cultural comfort surveys
  - 1c. Handouts available in English, Spanish and Creole
  - 1d. Evidence or documentation of provider addressing culture and language differences within personnel

**5) Expected Outcome: Increased client utilization and absorption of foodstuffs**

Objective-----	Activities
<b>Provision of appropriate food for clients with special needs</b>	1a. Development of screening tool to determine clients special needs 1b. Food bank will screen each client for potential nutritional concerns a minimum of once a year 1c. Documentation of RD or LDN assessment of clients needing special diets 1d. Documentation of clients with special needs receiving appropriate foodstuffs

**Home Delivered Meals:**

**1) Expected Outcome: Home-delivered meals, which will lessen the risk of weight loss and hospitalization, for eligible people living with HIV/AIDS**

Objective-----	Activities
Provision of home-delivered meals to needy Broward County people living with HIV/AIDS	1a. Documentation of residential and financial status 1b. Documentation of symptomatic HIV infection with opportunistic infection or an AIDS diagnosis. (MD or PA {physician's assistant} assessment with listed conditions including disease stage, height and weight) 1c. Acuity screen/Karnofsky score that indicates functional impairment 1d. Documentation of homebound or temporary disability status and client inability to prepare own meals, without anyone who can prepare meals for her/him 1e. Reassessment every 3-6 months

**2) Expected Outcome: Food security that increases nutritional status and lessens the risk of weight loss for people living with HIV/AIDS**

Objective-----	Activities
Provision of nutritious meals <b>that are ethnically diverse, which meet nutritional standards for HIV-positive people</b>	1a. On-site RD or LDN approval of meal adequacy based on established AIDS Nutrition Services Alliance Guidelines (ANSA). 1b. Client advocacy group approval 1c. Yearly RD or LDN documentation of menu review for nutritional adequacy 1d. Education and counseling is available to clients upon request. 1e. Documentation of clients served 1f. Documentation of requested/provided nutrition education and nutrition counseling services

**3) Expected Outcome: Increased client utilization and absorption of foodstuffs**

Objective-----	Activities
<b>Provision of appropriate food for clients with special needs</b>	1a. Development of screening tool to determine clients special needs

- 1b. Meal agency will screen each client for potential nutritional concerns a minimum of once a year
- 1c. Documentation of RD or LDN assessment of clients needing special diets
- 1d. Documentation of clients with special needs receiving appropriate foodstuffs

**4) Expected Outcome: Safe (sanitary and uncontaminated) foodstuffs to lessen the risk of food and water illness.**

Objective-----  
 Compliance with all applicable local, state and federal standards  
**and food safety standards established by the national  
 Nutrition Services Alliance Guidelines (ANSA)  
 Educate clients on methods to reduce the risk of food and water-borne  
 illness**

- Activities
- 1a. On-site RD or LDN approval based on Hazard Analysis Critical Control Point system (HACCP) standards
  - 1b. Yearly documentation by state and successful food safety & sanitation inspection by independent auditor (RD with expertise in this area) noting compliance with standards for HACCP food handling and storage
  - 1c. Document number of clients receiving educational materials and instruction on food safety, food handling, and food preparation
  - 1d. USDA approved meals are preferred.
  - 1e. Provider maintains working knowledge of foodborne illnesses and HACCP

**5) Expected Outcome: Coordination of meal delivery services with local programs to lessen duplication of services**

Objective-----  
 Coordinate meal delivery services with other local food programs

- Activities
- 1a. Documentation of coordination efforts with local food providers

**Nutritional Services (Nutritional services, including nutrition screening, nutrition education, nutritional assessment and counseling, may be determined based on provider facility. For instance, Medical Nutrition Therapy (MNT) is most effective when given at a medical facility while nutrition screening, nutrition education and mini-consults for food appropriateness and acceptance may be most helpful in a food bank setting.) Activities, objectives and outcomes may differ from setting to setting.**

**1) Expected Outcome: Provision of appropriate nutritional services to support and compliment medical treatment and lessen barriers to care for eligible people living with HIV/AIDS**

Objective-----  
 Provision of Medical Nutrition Therapy (MNT) **meeting the standards  
 for the American Dietetic Association's (ADA) HIV/AIDS protocols.**

- Activities
- 1a. Documentation of clients' residential, financial and HIV status
  - 1b. Completed nutritional risk screens documenting yearly client nutritional risk factors along with accurate height and weight
  - 1c. Documentation of screening tool results targeting clients with special needs
  - 1d. On-site RD or LDN to initiate MNT protocol standards
  - 1e. RD or LDN client assessment every 12 months
  - 1f. RD or LDN client follow-up consults as needed
  - 1g. RD or LDN client reassessment every 3-12 months based on disease status
  - 1h. Documentation of clients served

**2) Expected Outcome: Decreased incidence of food and water-borne illness.**

Objective-----	Activities
Provision of nutrition education including all aspects of food safety	1a. On-site RD or LDN to increase awareness of risk for water and food-borne illness and to provide food and water safety education 1b. On-site food safety and sanitation materials 1c. Documentation of clients receiving individual or group instruction on food safety, food handling, and food preparation 1d. Documentation of client's readiness to practice food and water safety and sanitation practices

**3) Expected Outcome: Culturally sensitive and competent services**

Objective-----	Activities
Provision of culturally and competent services	1a. Limit number of grievances 1b. Client satisfaction and cultural comfort surveys 1c. Handouts available in English, Spanish and Creole 1d. Evidence or documentation of provider addressing culture and language differences within personnel

**4) Expected Outcome: Coordination of nutritional services with local programs to lessen duplication of services**

Objective-----	Activities
Coordinate nutritional services with other local providers	1a. Documentation of coordination efforts with local providers

**5) Expected Outcome: Increased nutritional risk HIV-positive clients receive appropriate nutritional services to lessen the risk of weight loss**

Objective-----	Activities
Provision of appropriate nutrition education for clients at increased nutritional risk	1a. Documentation of screening tool results targeting clients with special needs 1b. Documentation of culturally relevant nutrition education plans and/or referral to RD or LDN for nutritional assessment 1c. Documentation of baseline height/weight along with monthly weights 1d. Documentation of follow-up nutrition education sessions as necessary 1e. Documentation of nutrition education group sessions 1f. Documentation of client's readiness to follow clinicians suggestions to maintain or increase weight, optimize nutrient intake, etc.)

**6) Expected Outcome: Increased client utilization and absorption of foodstuffs and decreased medication side-effects**

Objective-----Activities

Provision of appropriate MNT including nutritional assessment, nutrition education and counseling for clients with special needs (malabsorption, lipodystrophy, medication side-effects, severe or chronic diarrhea, wasting, etc.)

- 1a. Documentation of screening tool results targeting clients with special needs
- 1b. Documentation of baseline height/weight and bi-yearly bioelectrical impedance analysis (BIA) along with monthly weights
- 1c. Documentation of medically and culturally relevant nutritional care plans including meal prescription timing and foods to optimize drug therapy effectiveness
- 1d. Documentation of follow-up sessions as necessary (2 to 6 times per year for asymptomatic or symptomatic with AIDS)
- 1e. Documentation of clients readiness to include/avoid foods based on side effects of medication or symptoms of infection

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