

The Study of

Glucose Metabolism

on HIV Infected

Drug Users

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# The Study of Impaired Glucose Metabolism in HIV infected Drug Users

## Overview

As the many treatments for Human Immunodeficiency Virus (HIV) become more effective, patients infected with it life expectancy has been greatly lengthened. Therefore the factor of aging diseases comes into play.

The goal of this study that I am currently involved in as an intern, is to select the HIV infected patients (HIV+) and some chosen non-infected patients, and monitor them for signs of Impaired Glucose tolerance (IGT) and Type 2 diabetes. To determine the prevalence of such characteristics the enrolling subjects will be carefully screened to check for eligibility based on their PI Therapy, Hepatitis C infection (HCV), Sociodemographic characteristics,

Body mass Index (BMI) and genetic/family history of diseases or tendencies.

Some of the current scientific inclinations that are to be addressed include:

1. Drug users who have taken PI for more than one year will have a greater prevalence of IGT and type 2 Diabetes.
2. Drug users with hepatitis C infection will have a greater prevalence of IGT and Type 2 Diabetes.
3. Older aged, non white race, high BMI, and family history of diabetes will be associated with IGT and Diabetes

Also to determine any impact of HIV infection other hypotheses will be addressed such as:

1. PI therapy will be associated with the development of IGT and type 2 Diabetes
2. In individuals with IGT, PI use will be associated with progression to frank diabetes
3. HCV infection will be associated with the development of IGT and 2 Diabetes.

## **Background and Significance**

HIV and Aging. There is already existing evidence that persons age 50 or older account for 11% of all of the known AIDS cases in the United States. The incidence of AIDS in older adults also steadily continues to increase. But also on the other hand the current AIDS mortality rate is substantially dropping giving lead to the idea that HIV+ patients are living longer lives therefore the ability to study the role of aging diseases in the population is now becoming a possibility in HIV+ persons.

**Type 2. Diabetes.** Type 2. Diabetes is commonly characterized by hyperglycemia from insulin resistance and/or an inadequate insulin secretory response. Both micro- and macro vascular complications of diabetes are known to occur several years before diabetes is diagnosed. Being that early treatment may substantially lower the risk of end-organ damage screening of high-risk populations is highly warranted. Thus, identifying risk factors for diabetes in IDU -infected drug users is a high research priority.

**Impaired Glucose Tolerance.** IGT is an abnormal metabolic state intermediate between normal glucose homeostasis and full blown diabetes. Individuals with IGT have insulin resistance and are at an extremely high risk for developing diabetes. IGT is also an independent risk factor for cardiovascular disease. Past prospective studies have shown that on average, approximately 2-6% of individuals with IGT develop type 2 Diabetes per year. Factors predictive of progression to diabetes include non-white race, fasting and post-load glucose levels, and body mass index (BMI). It is not known whether these findings are generalizable to HIV+ drug users, or what impact PI therapy and HCV infection have on the development of type 2 diabetes.

**PI Therapy and Diabetes.** There have been several cross sectional studies of HIV+ patients treated with PI Therapy. It has been estimated that the prevalence of IGT to be 16-46% and of diabetes to be 2-13%. Even so the variability in diagnostic criteria, a lack of appropriate controls groups, and poor characterization of

the study population limited their studies creditability. The entire procedure in which PI use develops relative glucose intolerance is not completely understood. It is always been described that the prevalent insulin resistance among HIV+ patients is attributed to the direct inhibitory effects on cellular glucose transport by PIs. Also the changes in fat distribution associated with the commonly known highly active antiretroviral therapy (HAART) use seems to have a role in the susceptibility to diabetes.

**Opiate Use, Alcohol Intake and Diabetes.** There seems to be evidence that both opiate and alcohol use are associated with IGT and type 2 diabetes. Heroin users have been reported to have increased concentrations of glycosylated proteins. They have also been shown to have elevated fasting insulin levels, and an abnormal insulin response to a glucose load. Impairment of glucose tolerance has also been reported in patients receiving methadone, and methadone-addicted rats. Heavy alcohol consumption, common among drug users, may also increase their risk of type 2 Diabetes.

HIV, HCV, and Diabetes. An association between HCV infection and diabetes has also been observed in all infected individuals. In a cohort study of 228 HIV-infected drug users recruited from methadone maintenance treatment, we found the prevalence of diabetes to be higher among HCV co-infected individuals (13%) than among drug users with infection alone (0%) In another study of HIV-infected persons on HAART, HCV infection was independently associated with insulin resistance measured using the Homeostasis Model Assessment (HOMA IR). In addition, HCV co-infection and PI use have been identified as independent risk factors for developing hyperglycemia in HIV-infected patients on their first HAART regimen.

Summary. As a growing number of HIV-infected drug users experience a prolonged lifespan, the evaluation of co-morbid conditions associated with aging takes on increased importance. This review suggests that HIV infected drug users may be at heightened risk for IGT and type 2 diabetes in association with PI

therapy and HCV infection. It is critical that knowledge about this preventable morbidity is expanded to reduce the burden of disease on these individuals and society.

C. Progress. We have enrolled 229 women participating in Ms., a longitudinal study of menopause and its sequel and 215 men participating in CHAMPS, a longitudinal study of aging, HIV, and drug use, who did not have diabetes by history. Baseline oral glucose tolerance tests (OGTTs) with insulin levels have been performed in all participants to detect IGT and diabetes. Insulin resistance was estimated using the homeostasis model assessment (HOMA-IR), and insulin secretion was calculated using the incremental ratio of insulin to glucose at 30 min. Follow-up OGTTs 2 to 18 months later have been performed in 118 subjects.

Study Setting. Research visits take place at the AIDS Research Program's ambulatory research facility at Montefiore, which includes staff offices, examination rooms, freezers and centrifuges. OGTTs are performed at the Einstein GCRC, which includes five examination rooms and a state-of-the-art core laboratory.



Study Participants. Subjects for the Diabetes Study are being recruited from among 620 women enrolled in Ms. and 643 men enrolled in CHAMPS. In each parent study, 50% of participants are HIV-infected. Within each, 50% have a history of drug use in the last 5 y, and 50% have a history of high risk sexual behavior.

Research Visits. Ms. and CHAMPS semi-annual research visits consist of a standardized interview, laboratory studies, and a brief physical exam. Interviews for both studies use the same validated instruments to elicit sociodemographic data, medical history, and drug use behavior. Laboratory measures include HIV serology, Cell lymphocyte analyses, HIV viral load, fasting lipid profiles, and total and regional body composition using dual x-ray absorptiometry (DXA). Weight, height, waist and hip circumference are also measured.

**Importance of the Knowledge to be gained**

This study will contribute to knowledge about the menopausal transition in women from ethnic and racial minorities, as well as among current and former drug users and HIV positive women. The knowledge can be helpful in understanding how problems encountered during and after menopause can be treated or medically or through other means such as education and counseling, therefore reducing the burden on the women and the social and medical care systems.

The knowledge gained in the proposed study will also be helpful in improving understanding of the interaction of illicit drug use, alcohol, HIV and HIV treatment, and the aging process in women who are predominately poor and belong to racial and ethnic minorities. In particular, understanding how conditions such as high blood pressure, elevated cholesterol, diabetes, and obesity may be both consequences of and complicate the treatment of HIV infection.

**Table 1. Oral Glucose Tolerance Test Results**

Parameter	Result, mean	
	<b>HCV (-) N = 239</b>	<b>HCV (+) N = 168</b>
<b>Fasting glucose level, mg/mL</b>	96.4 (1.5)	93.4 (1.4)
<b>120-minute glucose level, mg/mL</b>	117.2 (2.9)	115.3 (3.4)
<b>Fasting insulin level, μU/ML</b>	21.2 (5.5)	17.0 (1.0)
<b>Impaired glucose tolerance, N(%)</b>	36 (15)	27 (16)
<b>Diabetes, N (%)</b>	14 (6)	12 (7)

This graph shows the average of the results of the OGTTs based on the Data collected so far.

**Table 2. Participant Characteristics**

	<b>HIV (-) N =239</b>	<b>HIV (+) N =168</b>
Median age, y (range)*	48 (35-73)	52 (37-75)
Male, N (%)*	84 (35)	101 (60)
Race/ethnicity, N (%)	123 (52)	100 (60)
Black	25 (10)	22 (13)
White	81 (34)	44 (26)
Hispanic	10 (4)	2 (1)
Other		
Unemployed, N (%)*	189 (79)	146 (87)
Ever injected drugs, N (%)*	67 (28)	131 (78)
Use Heroin in last 5 years, N (%)*	59 (25)	60 (36)
Use Heroin last 6 months, N (%)*	18 (8)	33 (20)
Use Cocaine last 5 years, N (%)	115 (48)	94 (56)
Use Cocaine last 6 months, N (%)*	49 (21)	50 (30)
Currently on Methadone, N (%)*	23 (10)	29 (17)
Positive CAGE test for Alcoholism, N (%)*	90 (38)	87 (52)
HIV-Infected, N (%)*	133 (56)	115 (69)
Median CD4+ Count (range)*†	462 (0–1332)	374 (60-1391)
Antiretroviral use, N (%)†	30 (23)	26 (23)
Naïve	37 (28)	23 (20)
HAART, PI-naïve	66 (50)	66 (57)
HAART with PI		

This table shows the characteristics of all participants respectively



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