HIV/AIDS AND DIABETES: MINIMIZING RISK, OPTIMIZING CARE

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Recent literature about diabetes and disorders of glucose metabolism in people with HIV/AIDS contains conflicting messages. Some studies indicate an increased risk of diabetes mellitus (generally referred to simply as "diabetes") in people taking HAART, specifically protease inhibitors (PIs). Other studies indicate that nucleoside reverse transcriptase inhibitors (NRTIs) are the culprit. It is clear that traditional risk factors for diabetes, such as family history of the disease, obesity, and sedentary lifestyle, are important in people with HIV. Other issues, such as the role of fat deposition ab-

normalities, HIV/hepatitis C coinfection, and dyslipidemia (a metabolic disorder), require further investigation.

People with HIV can work to prevent diabetes by maintaining a healthy weight and increasing physical activity. Diabetes treatment, with oral agents or insulin, can be initiated when preventive efforts are not sufficient. This article reviews current research and areas for future study in the relationship between HIV, insulin resistance, and diabetes, presents basic principles of diabetes management, and highlights specific concerns for HIV positive diabetic women.

Diabetes and Insulin Resistance

Type 1 diabetes is typically diagnosed in children and young adults. The disease is caused by destruction of the pancreatic islet beta cells, which produce insulin. People with type 1 diabetes therefore have a lifelong dependence on insulin therapy. Type 2 diabetes is usually diagnosed later in life, and is the result of tissue (muscle, liver, fat) insensitivity to insulin. The pancreas overcompensates by increasing insulin secretion, but eventually it cannot keep up. More than 90% of the approximately 18 million known diabetics in the U.S. have type 2 diabetes.

The long-term consequences of uncontrolled diabetes are devastating. They include vascular disease (heart attacks and stroke) and kidney disease (diabetic nephropathy), which may eventually lead to end-stage renal disease requiring dialysis. Diabetic retinopathy causes vision changes and eventually blindness, and diabetic neuropathy, which causes painful burning and tingling or numbness in the limbs, can be debilitating. Skin infections, especially of the feet, take longer to heal in diabetics than in non-diabetics, placing diabetics at higher risk for amputation.

Diagnosis

Glucose, the main sugar that the body makes from food, is carried through the bloodstream to provide energy to all of the body's cells. The fasting blood glucose test measures the level of glucose in a blood sample taken after the patient has fasted for at least eight hours (for example, first thing in the morning). A fasting blood glucose of 126 mg/dL or higher in blood samples taken on two separate occasions is diagnostic of diabetes. A randomly sampled blood glucose level greater than 200 mg/dL, in conjunction with symptoms of diabetes (such as blurry vision, weight loss, or frequent urination), is also diagnostic of diabetes.

The oral glucose tolerance test

can also be used to diagnose diabetes. This test requires ingestion of a 75-gram glucose load (usually in the form of a sweet liquid), with the blood glucose level checked two hours later. If the blood glucose is greater than 200 mg/dL, and a subsequent fasting blood glucose is greater than 126 mg/dL, the diagnosis of diabetes is confirmed.

There are other "pre-diabetes" conditions that have garnered attention in the era of HAART therapy. Insulin resistance, the precursor to diabetes, is measured clinically via tests of impaired glucose tolerance and impaired fasting glucose. Impaired glucose tolerance is determined by performing an oral glucose tolerance test, as described above. A blood glucose of 140–199 mg/dL two hours after the 75-gram glucose load indicates impaired glucose tolerance. Impaired fasting blood glucose is diagnosed with a fasting blood glucose of 100–125 mg/dL. Fasting insulin levels are often checked in clinical trials to determine insulin resistance but are not used clinically.

Insulin Resistance, Diabetes, HIV/AIDS, and HAART

As people with HIV live longer with highly active antiretroviral therapy (HAART), their care providers must be more vigilant about chronic conditions like diabetes and high blood pressure that can cause significant damage if not well controlled. Since the late 1990s, when glucose abnormalities began to appear in people taking HAART, multiple studies have examined the relationships between HIV/AIDS, HAART, insulin resistance, and diabetes.

Several mechanisms contribute to insulin resistance, and subsequently diabetes, in individuals with HIV. These include chronic inflammatory changes caused by HIV, and side effects of antiretroviral medication, such as the interference of protease inhibitors (PIs) in the activity of glucose

transporters, the damage to mitochondria caused by NRTIs, fat deposition in the liver, and abnormal levels of free fatty acids caused by lipodystrophy (fat redistribution in the form of central obesity, or excess belly fat, and fat loss from the limbs).

Data from the Multicenter AIDS Cohort Study

A large study of diabetes in men with and without HIV by Todd Brown, MD, of Johns Hopkins University and colleagues showed higher baseline prevalence of diabetes in men with HIV taking HAART than in men without HIV. Of 1,278 men from the Multicenter AIDS Cohort Study (MACS), 47 of 411 men with HIV using HAART (14%) had diabetes at baseline compared with 33 of 710 men without HIV (5%). Of the 680 study participants who were followed prospectively, men on HAART had an incidence rate of diabetes of 4.7 per 100 person-years (PY), compared with 1.4 cases per 100 PY in men without HIV, indicating a four-fold increased risk of developing diabetes for men on HAART, adjusted for age and body mass index (BMI). With regard to specific PIs, only ritonavir (Norvir) was associated with an increased risk of either diabetes or hyperglycemia (high blood sugar); however, the authors noted that 94% of subjects taking ritonavir were using it in combination with another PI.

Another interesting finding was that among 229 HAART users who were followed in the study, 157 men whose nadir (lowest ever) CD4 cell count was less than 300 cells/mm^3 developed either hyperglycemia or diabetes, compared with 72 men whose lowest CD4 cell count was greater than 300, for a relative risk of 1.67 among those with a low nadir CD4 cell count.

Brown and colleagues also published data from the MACS group regarding insulin resistance among 1,288 men, 533 with HIV and 755 without HIV. Having HIV was independently associated with insulin re-

sistance and fasting hyperinsulinemia (excess levels of insulin in the blood). Length of cumulative exposure to NRTIs, but not PIs, was also associated with insulin resistance. NRTIs have also been linked to peripheral fat wasting in other studies. Although the exact mechanisms are unclear, both metabolic and body shape abnormalities clearly stemmed from NRTI use.

Data from the Swiss HIV Cohort

A study from Switzerland by Bruno Ledergerber, MD, of the University Hospital, Zurich, and colleagues revealed much lower incidence of diabetes than the U.S. studies. The Swiss HIV Cohort, established in 1988, followed 6,513 persons (about one-third of whom were female) and collected plasma glucose levels and information on diabetes diagnoses starting in March 2000. During the study, 123 patients developed new-onset diabetes, an incidence of 4.42 per 1,000 PY. The investigators found male sex, older age, African or Asian ancestry, AIDS diagnosis, and central obesity to be associated with diabetes.

With regard to antiretroviral therapy, the Swiss investigators found that ongoing therapy with an NRTI, NRTI/PI, and NRTI/PI with a non-nucleoside reverse transcriptase inhibitor (NNRTI), but not NRTI/NNRTI therapy, increased the risk of incident diabetes two to three fold. In terms of specific drugs and drug combinations, indinavir (Crixivan), lamivudine (Epivir; 3TC) plus stavudine (Zerit; d4T), didanosine (Videx; ddi) plus stavudine, and didanosine plus tenofovir (Viread) were associated with new diabetes cases.

The study authors observed a much lower rate of incident diabetes than studies in the U.S. have shown, but noted that the population in the Multicenter AIDS Cohort Study was older and had a higher median BMI than their population. In addition, the definition of diabetes in the MACS study was based on a single fasting glucose determination, whereas in the Swiss study, individual physicians were contacted if a blood glucose level was high to determine whether the patient had been diagnosed with diabetes.

CALCULATING BMI

Body mass index, or BMI, is an indicator of total body fat, which is related to an individual's risk for obesity-related illnesses like diabetes. The following formula is used to calculate BMI:

$$\left(\frac{\text{body weight in pounds}}{\text{height in inches} \times \text{height in inches}} \right) \times 703 = \textbf{BMI Score}$$

When compared with the categories shown below, BMI scores can help alert individuals and their clinicians to possible weight-related health risks.

BMI Category	BMI Score
Underweight	Below 18.5
Normal weight	18.5–24.9
Overweight	25–29.9
Obese	30–39.9
Morbidly obese	40 and above

Note: This formula is not a reliable measure for children, may overestimate total body fat in highly athletic people (because muscle tissue weighs more than fat), and may underestimate total body fat in the elderly and others who may have lost muscle mass.

Data from the D:A:D Study

The D:A:D (Data Collection on Adverse Events of Anti-HIV Drugs) study is a multinational, prospective, observational study with data collection from over 33,000 patients at 212 clinics in Europe, the U.S., Australia, and Argentina. The study was designed to examine the cardiovascular disease risk associated with antiretroviral therapy. Data on diabetes were collected as a secondary endpoint of the study.

Of the 33,389 study patients, 952 had diabetes at baseline, for a prevalence of 2.85%. During the follow-up period, 744 patients were diagnosed with diabetes, an incidence of 5.72 per 1,000 PY of follow up. Of these cases, over 60% were diagnosed by obtaining two fasting blood glucose values greater than 126 mg/dL; the remainder had a diabetes diagnosis and started a new glucose-lowering drug.

New cases of diabetes were associated with longer total duration of antiretroviral therapy, and in particular, with stavudine therapy. Zidovudine (Retrovir; AZT) and didanosine were also associated with an increased risk. Exposure to the PI ritonavir and the NNRTI nevirapine (Viramune) were associated with a slightly decreased risk. The authors proposed that stavudine has direct effects on diabetes risk by increasing insulin resistance, in addition to indirect effects through the development of lipodystrophy.

In the study group, men were more likely to develop diabetes than were women; other factors included older age, higher BMI, and African ancestry. In further multivariate analyses, high total cholesterol, low HDL cholesterol (the "good" cholesterol), and manifestations of lipodystrophy, either as peripheral fat loss or central fat gain, were associated with new-onset diabetes.

Data from the Women's Interagency HIV Study

The Women's Interagency HIV Study (WIHS), established in 1994, is a large study based in six U.S. cities that

tracks the disease progression of women with and at risk for HIV using semi-annual study visits. Data regarding diabetes was published at three different time points, with increasingly detailed information each time.

One such study, by Jessica Justman, MD, of Columbia University's HIV Center for Clinical and Behavioral Studies and colleagues, examined the incidence of diabetes in the WIHS group from 1994 to 1998. Participants included 1,435 women living with HIV and 350 HIV negative women. The investigators compared women in three groups: those who used PIs in a regimen containing one PI and at least one NRTI and/or NNRTI, those who used NRTIs and/or NNRTIs but no PIs, and those who received no anti-retroviral therapy at all.

Sixty-nine new cases of diabetes were reported among all study participants, for an incidence of 1.5 per 100 PY overall. Breaking down the incidence by HIV status and antiretroviral therapy group, the incidence of diabetes in women without HIV was 1.4 per 100 PY, incidence among women using NRTIs and/or NNRTIs was 1.2 per 100 PY, and incidence in HIV positive women not taking antiretroviral therapy was also 1.2 per 100 PY. The incidence of diabetes was highest in women taking PIs, at 2.8 per 100 PY— a statistically significant difference. The authors also noted that the highest risk of developing diabetes occurred among women who were obese.

Another study from the WIHS group, published in 2005 by Ann Danoff, MD, of the New York University School of Medicine and colleagues, was a cross-sectional examination of the prevalence of diabetes, prediabetes, and insulin resistance among a subset of WIHS participants. The substudy enrolled 258 women, most of whom (72%) were overweight or obese, and 81% of whom were African American or Latina. Eighty-eight women did not have HIV, 74 women had HIV and were not on HAART, and 96 women had HIV and were taking

HAART. Study participants underwent oral glucose tolerance testing and measures of fasting blood glucose and insulin to determine the prevalence of diabetes, prediabetes, and insulin resistance. The investigators determined diabetic status, then compared diabetic status among women with and without HIV and women using or not using HAART.

Contrary to the prior study, there was no significant difference in the prevalence of prediabetes or diabetes based on HIV status, nor was there a significant difference in prevalence of prediabetes or diabetes based on HAART use among HIV positive participants. Only higher BMI was associated with prediabetes and diabetes. The investigators hypothesized that in a sample composed mainly of overweight women, the impact of BMI on prediabetes and diabetes overshadowed any small differences related to HIV or HAART use.

A third study from the WIHS group, published in 2007 by Phyllis Tien, MD, of the University of California, San Francisco, and colleagues, was the most robust. Data were collected prospectively from 2,088 women (1,524 women with HIV, 564 without HIV). The investigators used fasting blood glucose greater than 126 mg/dL or use of a medication for diabetes for diagnosis, rather than patient self-report of diabetes. Use of HAART was classified as no therapy, monotherapy, combination therapy, PI-based HAART, or non-PI-based HAART. Length of cumulative exposure to HAART drugs was determined. Additional data were collected on race/ethnicity, smoking status, BMI, hip and waist size, and hepatitis C antibody status. In the entire study group of 2,088 women, 152 women developed diabetes (116 women with HIV, 36 women without HIV), and 1,710 women (1,213 with HIV, 497 without HIV) completed the study without diabetes. (The remaining 226 women were lost to follow up or died.) Of the 116 women with HIV

who developed diabetes during the study, 82 reported using HAART immediately prior to diagnosis.

The incidence rate for diabetes was 1.96 per 100 PY in women without HIV, compared with 1.53 per 100 PY in women with HIV and not on HAART, 2.5 per 100 PY in women on PI-based HAART, and 2.89 per 100 PY in women on non-PI based HAART. These differences were not statistically significant. Further analyses showed that longer cumulative exposure to NRTIs (more than three years) was associated with a higher risk of new-onset diabetes; longer cumulative exposure to PIs or NNRTIs was not associated with higher risk. With regard to specific NRTIs, there was no association between cumulative exposure to abacavir (Ziagen), stavudine, or zidovudine and new-onset diabetes. However, a higher incidence of diabetes was associated with greater than one year of exposure to lamivudine.

The study authors suggested that the differences between the results of the earlier and later WIHS studies were due to widespread use of indinavir in the earlier studies. Indinavir use is associated with insulin resistance, even in HIV negative people who have taken the drug in clinical trials.

Hepatitis C, HIV, and Diabetes

Studies have shown an association between hepatitis C virus (HCV) infection and the development of diabetes in people without HIV. A study by Shruti Mehta, PhD, of Johns Hopkins University and colleagues examined hyperglycemia in people with HIV, with specific attention to HAART and HCV status.

The study enrolled 1,230 people with HIV receiving their first HAART regimen. Of the 1,230 participants, 845 (69%) were on a PI, 269 (22%) were on an NNRTI, and 116 (9%) were on both; 579 (47%) did not have HCV, and 651 (53%) had HCV. The investigators looked for hyperglycemia in the study participants, defined as a random blood

glucose of greater than 200 mg/dL, confirmed either by repeat blood glucose testing or diagnosis of diabetes in the participant's medical history.

The investigators found new-onset hyperglycemia in 5.8% of participants with HCV/HIV coinfection and 2.8% of participants with HIV only—a statistically significant difference. The data also showed highest incidence of hyperglycemia in people taking PI-based HAART compared with those on NNRTI-based or PI- and NNRTI-based HAART. This highest incidence of hyperglycemia (at 6.4%) was seen in participants who were HIV/HCV coinfected and receiving a PI. The authors concluded that HIV and HCV coinfection and PI use increase risk of hyperglycemia, independent of age, race, and body weight.

A cross-sectional study by Andrea Howard, MD, of the Albert Einstein College of Medicine and Montefiore Medical Center and colleagues involved 267 people with HIV and 179 people without HIV from the Menopause Study and the Cohort of HIV at-risk Aging Men's Prospective Study (CHAMPS). Of the 446 subjects enrolled, 265 (59%) had HCV, and 98 participants (22% of the total) had impaired glucose tolerance or diabetes. HCV infection was associated with insulin resistance, even after adjusting for traditional risk factors for insulin resistance such as higher BMI, sedentary lifestyle, and older age. Among the HIV positive participants in this study, insulin resistance was greatest in those with higher CD4 count (greater than 500 cells/mm^3) and higher BMI. This study found no difference in insulin resistance with regard to antiretroviral therapy use. It is still unclear how HCV is linked to insulin resistance, although it has been hypothesized that the infection interferes with insulin signaling, the process by which insulin affects target cells.

Managing Diabetes

In their excellent review article on the metabolic complications of HIV infection, David Wohl, MD, of the University of North Carolina at Chapel Hill and colleagues summarize the risk factors for disorders of glucose metabolism in HIV infection: obesity, lipoatrophy, PIs, NRTIs (especially stavudine), older age, family history of diabetes, non-white race, and HCV coinfection. A review by Todd Brown and Joseph Cofrancesco, MD, of Johns Hopkins University also includes low nadir CD4 count as a risk factor. Various medications, including steroids, growth hormone, certain antipsychotics, and the appetite stimulant megestrol acetate (Megace) also contribute to glucose abnormalities.

Wohl and colleagues recommend clinical monitoring with fasting blood glucose testing before initiating HAART and every three to six months thereafter. Furthermore, they recommend an oral glucose tolerance test in patients with risk factors for diabetes, including fat redistribution. In terms of switching antiretroviral therapy, there is some data suggesting that NNRTIs and certain PIs, such as atazanavir, cause less insulin resistance; however, all treatment decisions should be made on an individual basis with the primary care provider.

Self-Care

While diabetes treatment involves physicians, nurses, dieticians, and other health care professionals, self-care is crucial for managing diabetes. Good self-care includes following the recommendations discussed below regarding diet, exercise, monitoring, and medications.

Diet, exercise, and smoking cessation. Diabetics are advised to perform moderate-intensity exercise for 150 minutes per week (if approved by their clinician). Both aerobic and strength training activities are beneficial. Diabetics should strive to maintain a healthy weight with a diet that limits saturated fats, concentrated sweets, and alcohol. Individualized nutritional plans can be made in conjunction with a registered dietician.

Smoking cessation is crucial to reduce the risk of diabetic complications, especially heart disease. For more information about quitting, see "Smoking and Your Health: How to Quit (and Why You Should)" in the Winter 2008 issue of *BETA*.

Monitoring blood glucose levels. Diabetics on insulin therapy are typically advised to check their blood glucose at least three times a day. Home blood glucose monitoring may also help diabetics who are not on insulin therapy achieve their blood sugar goals, but the optimal frequency of monitoring is not known. Blood glucose should be between 70 and 130 mg/dL before meals and no more than 180 mg/dL one to two hours after meals.

Home blood glucose monitoring should be used in conjunction with the hemoglobin A1C test, which measures the average blood glucose over a few months. The goal for diabetics is an A1C lower than 7%, which corresponds to an average blood sugar level below 170 mg/dL. In addition to blood glucose monitoring, diabetics should have regular cholesterol and blood pressure checks.

Monitoring for diabetes complications is individualized and may include an electrocardiogram (ECG or EKG) or a stress test to check for cardiovascular complications, based on risk factors and symptoms. Yearly blood and urine tests to check kidney function are recommended, and eye exams to evaluate diabetic retinopathy and simple clinical tests for nerve damage (especially in the lower limbs) should also be performed annually.

Diabetics should also monitor for symptoms of hyperglycemia, which include blurry vision, frequent urination, severe thirst, and unintentional weight loss. Symptoms of hypoglycemia (low blood sugar) include racing heart, sweating, shakiness/weakness, hunger, and headache.

Because diabetes increases the risk of foot infections and ulcers, diabetics are advised to check their feet daily for any signs of injury or infection. (The

primary care provider should also examine a diabetic client's feet at every visit.) Feet should be carefully washed and dried daily, and socks and supportive footwear are highly recommended. Trimming toenails straight across the tops of the nails can help prevent infections.

Medications. Type 1 diabetics require intensive insulin therapy to achieve and maintain tight glucose control and minimize diabetic complications. The management of type 2 diabetes typically starts with metformin (Glucophage) and lifestyle modifications, including changes to diet and exercise habits and smoking cessation. Metformin decreases production of glucose by the liver, limits absorption of glucose, and improves insulin sensitivity (increasing the uptake and use of glucose). If lifestyle changes and metformin alone do not bring blood glucose under control within two to three months, another oral medication, such as a sulfonylurea agent (e.g., Glipizide, Glyburide), which increases insulin secretion, or a glitazone (e.g., rosiglitazone [Avandia], pioglitazone [Actos]), which increases insulin sensitivity, may be used.

These are the two most commonly used classes of oral medications for controlling blood glucose; however, other classes with a variety of mechanisms of action are available. Side effects and contraindications to all oral therapies should be discussed with the primary care provider. Insulin therapy is an excellent treatment option for type 2 diabetics and is available in short-, intermediate-, and long-acting forms. Initial insulin therapy usually involves one dose of an intermediate- or long-acting form, and treatment can be intensified as needed.

For patients with high blood pressure in addition to diabetes, blood pressure should be controlled to less than 130 mmHg systolic and 80 mmHg diastolic (130/80), which may require medication. LDL cholesterol ("bad" cholesterol) should be less than 100 mg/dL, and even lower in very high-risk patients. If LDL cholesterol cannot be brought under control with diet and exercise, then a lipid-lowering agent should be considered. Some patients with diabetes and other risk factors for heart disease benefit from aspirin therapy (in consultation with the primary care provider).

Diabetics are also advised to receive a yearly influenza vaccine and at least one pneumococcal vaccine to prevent pneumonia.

Additional Considerations for Diabetic Women

Blood glucose control and the menstrual cycle. Some diabetic women have decreased insulin sensitivity around the time of menstruation, which may lead to difficulty with glucose control; more intensive monitoring may be needed.

Management of yeast infections. Yeast infections are very common, with about three-quarters of all women having one at least once in their lives. Symptoms include vaginal itching and thick, white vaginal discharge. Diabetes, especially poorly controlled diabetes, is a risk factor for yeast infections; high glucose levels promote yeast attachment and growth, and also interfere with immune responses in the host. *Candida albicans* is the most common pathogen, but other forms of *Candida,* such as *Candida glabrata,* that are less susceptible to conventional treatment are commonly found in diabetics. First-line treatment typically involves creams or ointments that are applied directly to the affected areas. Oral treatments are also available but may have interactions with oral medications for diabetes; consultation with a primary care provider is advised. Whether an oral or topical medication is chosen, treatment must include achieving optimal blood glucose control.

Contraceptive options for diabetic women. Diabetic and non-diabetic women have the same contraceptive options, including barrier products (such as diaphragms and male and female condoms), intrauterine devices (IUDs), hormonal methods, and tubal ligation. However, the latter two options carry some risks that HIV positive diabetic women should discuss thoroughly with their health care providers. (In addition, only condoms protect both women and their male sex partners against HIV and other sexually transmitted infections.)

Combination oral contraceptive pills have a low failure rate when taken correctly and consistently, and there are minimal metabolic abnormalities associated with their use. However, there are known interactions between oral contraceptives and some PIs and NNRTIs. Hormone levels may increase or decrease in the presence of these drugs, and the effectiveness of oral contraceptives may be diminished; using an additional method of contraception is recommended.

Women with type 1 and type 2 diabetes are advised to use the lowest-dose combination oral contraceptive available, but there is no known worsening of diabetes with oral contraceptive use. That said, there are other risks associated with oral contraceptives, including increased risk of deep venous thrombosis and pulmonary embolism (blood clots in the extremities and lungs), especially in women who smoke. The interaction between oral contraceptives and some PIs and NNRTIs may raise the risk of these side effects. All decisions about oral contraceptives should therefore be made by the individual woman in conjunction with her doctor.

Other hormonal contraceptive products, such as rings, patches, and injectable medroxyprogesterone acetate (DepoProvera), have not been studied extensively in women with HIV, but their hormone components are similar to those of oral contraceptives. A backup method is advisable, and decisions regarding their use—and potential interactions with antiretroviral drugs—should be made with the primary care provider.

Tubal ligation ("having your tubes

tied") is another contraceptive option available to diabetic women. Most cases are laparoscopic, using a special camera and several small incisions rather than open surgery. Blood sugar control should be optimized prior to surgery to minimize operative complications. Tubal ligation is considered to be a permanent procedure, and women should discuss the benefits, drawbacks, and what to expect post-surgery with their medical providers.

Heart disease in diabetic women. There is evidence that women with diabetes are at higher risk for cardiovascular complications of diabetes than are men. A study in Finland with 1,296 diabetic and 835 non-diabetic middle-aged participants studied the effects of type 2 diabetes on risk for heart attacks and heart disease–related deaths, specifically comparing these effects in males and females. After 13 years of follow-up, the investigators reported a significantly higher relative risk of a major cardiac event in diabetic women compared with diabetic men. More women at baseline had risk factors for heart disease (high blood pressure, elevated BMI, and high triglycerides with low HDL cholesterol), but even controlling for these added risks, there was still a higher burden of heart disease in diabetic women than in diabetic men. Poor blood glucose control contributed to heart disease in both groups.

Conclusion

Study data are mixed regarding the influence of NRTIs compared with PIs on insulin resistance, and the exact mechanisms of the development of insulin resistance and diabetes in HIV disease are still unclear. Until these questions are answered, HIV positive people and their health care providers

must understand the importance of maintaining optimal weight through regular exercise and a healthy diet for diabetes prevention.

Additionally, close monitoring of blood glucose, with supplemental testing for people at high risk, will help identify cases of diabetes early so that appropriate treatment can be initiated. Through lifestyle changes and monitoring, HIV positive people can avoid the complications of uncontrolled diabetes and instead concentrate on living well with HIV.

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