acria UPDATE

vol. 16 no. 2

AIDS COMMUNITY RESEARCH INITIATIVE OF AMERICA

Living with HIV: Facing the Challenges

In this issue we examine the unique health concerns faced by people living with HIV – from changes in appearance and the health risks associated with altered fat distribution, to anemia and depression in women living with HIV, to key oral health considerations. With two articles on aging and HIV, ACRIA continues to examine treatment for the growing number of older adults with HIV. We also have a great report from the recent Conference on Retroviruses and Opportunistic Infections (CROI) that includes an update on new antiretroviral drugs in clinical trials and the FDA approval pipeline.

Dr. Marshall Glesby, a former medical director at ACRIA, thoroughly discusses current thinking and treatment for altered fat distribution found in people with HIV. This thoughtful article notes not only clinical concerns but also the emotional impact of changes in appearance. Dr. Glesby urges further research into why these changes occur and how best to prevent them.

Dr. Richard Havlik discusses common changes in body systems and organs due to aging and the unique impacts of HIV disease and treatment. In a related article, Andrew Shippy and Dr. Jerry Ernst examine and discuss in greater detail the characteristics and management of several illnesses in older adults living with HIV. These articles are part of a series of nearly 100 publications in professional journals and presentations of ACRIA's *Research on Older Adults with HIV* (ROAH) findings at conferences and symposia. ACRIA will also soon issue a new educational booklet on older adults and HIV that will be useful to both HIV-positive seniors and their providers.

The articles in this issue raise several issues of importance in long-term management of HIV and we'd love to know what you think, so please email us at info @acria.org with your thoughts.

Daniel Tietz, Editor-in-Chief

contents

spring 2007

Treatment of Body Shape Changes

by Marshall J. Glesby, MD, PhD

Ten years ago, shortly after the approval of protease inhibitors, clinicians began reporting changes in the body shape of people with HIV. The first reports of what came to be known as *lipodystrophy* noted fat loss in the face, arms, legs, and buttocks, along with fat gain in the abdomen and sometimes in the breasts and back of the neck ("buffalo hump"). The loss of fat (*lipoatrophy*) was specifically fat beneath the skin, known as *subcutaneous* fat. In contrast, the gain of fat in the abdomen tended to be fat around the internal organs, known as *visceral* fat. People also frequently had high triglycerides and cholesterol levels and sometimes high blood sugar or diabetes. These problems raised concern about the long-term risk of heart disease in people with lipodystrophy.

Fast-forwarding ten years, we still do not clearly understand the underlying causes of these changes in fat distribution. But careful studies comparing people living with HIV to people without HIV have changed how we think about lipodystrophy. In these studies of both men and women, those with HIV were found to have less subcutaneous fat in their limbs than those without HIV but no more visceral fat in their abdomens. In fact, HIV-infected people in these studies who had lipoatrophy were not more likely to have increased visceral fat gain than those without lipoatrophy. These results suggest that lipoatrophy is the unique feature seen in people with HIV and is a separate process from fat accumulation. While people living with HIV did not appear to have abnormal accumulation

(continued on page 3)

acria UPDATE

Editor in Chief
Daniel Tietz

Editors
Mark Milano
Luis Scaccabarrozzi

Medical Editor
Jerome A. Ernst, MD

Publications Manager
Mark Milano

Publications Associate
Laura Engle

ACRIAis an independent, non-profit, community-based AIDS medical research and HIVhealth literacy/treatment education organization dedicated to rapidly improving the length and quality of life for people living with HIV/AIDS. Bulk copies of *ACRIAUpdate* are available free to agencies that provide services to people living with HIV/AIDS. For more information, call 212-924-3934 ext. 129.

ACRIA
230 West 38th St., 17th Floor
New York, NY10018
Phone: (212) 924-3934
Fax: (212) 924-3936
Internet address: www.acria.org

ACRIA STUDIES IN PROGRESS

Transacin (NGX-4010) for Peripheral Neuropathy
People with HIV who have peripheral neuropathy will use either Transacin (capsaicin) patches or very low-dose patches for 30 or 60 minutes a day for 3 months. Participants must be 18 or older and have had pain in both feet for at least 2 months.

TH9507
People aged 18-65 who have excess abdominal fat will take either TH9507 (an investigational growth hormone releasing factor), or a placebo for 26 weeks. The two groups will then switch for 26 more weeks.

Lauriad for Oral Thrush
People with oral candidiasis will take either Lauriad (miconazole) tablets once a day or clotrimazole troches 5x a day for 2 weeks. Participants must be 18 or older and be on stable HAART for at least 2 months.

Crofelemer for Diarrhea
People 18 and older who have persistent diarrhea will take crofelemer for up to 17 days.

Avandia and Serostim
People with insulin resistance will take Avandia (rosiglitazone), or Serostim (growth hormone), or both for 6 months to see how they affect glucose, insulin levels and body shape.

KP-1461
People aged 18-60 who have taken an NRTI, NNRTI and PI, and have developed resistance or stopped the drugs for other reasons, will take KP-1461 (a new type of NRTI) with no other ARVs for four months.

SPRING: Aptivus in Diverse Populations
People 18 and older (half white and half non-white, half men and half women) who have taken an NRTI, NNRTI and PI (not Aptivus) and who have resistance to at least two PIs, will take a standard dose of Aptivus or receive therapeutic drug monitoring to find the best dose for them.

IMPACT: Reyataz Resistance
People who have developed resistance to Reyataz will come in for one day of blood tests to study the I50L mutation.

TMC 125 Expanded Access
People 18 and older who have limited treatment options and resistance to approved NNRTIs, and who have taken an NRTI, NNRTI and at least two PIs, may qualify for early access to this experimental NNRTI.

Maraviroc Expanded Access
People 16 and older who have taken HAART and who have few treatment options may qualify for early access to this experimental CCR5 attachment inhibitor.

For more information on these trials, contact Dr. Douglas Mendez at 212-924-3934 ext.126 or Dr. Yuriy Akulov at ext. 124.

Editor's Note
All material in *ACRIAUpdate* is presented for educational and informational pur- poses only, and is not intended as medical advice. All decisions regarding one's personal treatment and therapy choices should be made in consultation with a physician.

Treatment of Body Shape Changes *(continued from first page)*

of fat *on average* in these studies, there does appear to be a subset of people who do have abnormal accumulation of visceral abdominal fat with or without buffalo hump, breast enlargement, and excess fat in the neck and upper chest. The picture remains somewhat confusing, but it is fair to say that the term lipodystrophy, which does not accurately describe the type of change in fat, is falling out of favor in the medical community.

In thinking about possible treatments for these changes in fat distribution, it is best to think about lipoatrophy and fat accumulation as separate processes that might both be occurring within an individual. But first it's worth considering why we might want to treat these changes in fat. Among the obvious reasons are that people with altered fat distribution are usually quite concerned about the change in their appearance, especially those who have lost fat in the face. Their self-esteem may be affected, and they may feel that their HIV status will be obvious to others.

These concerns may cause some people to stop or skip doses of their antiretrovirals or even prevent them from starting HIV therapy when it is needed. People who have lost significant fat from the buttocks may have discomfort when sitting; women with breast enlargement may develop back pain. Others with increased neck fat may have difficulty moving their heads or with posture. In addition, the metabolic problems that often accompany the fat changes have potential to increase the risk of diabetes and heart disease. Treating the fat changes could have favorable effects on these metabolic disturbances and reduce the risk of these complications.

Treatment of Lipoatrophy

Switching Antiretrovirals

A number of studies indicate that use of either Zerit or Retrovir (AZT – also in Combivir and Trizivir) increases the likelihood of developing lipoatrophy. Other drugs in this class (known affectionately as "nukes") – Epivir, Ziagen, Viread – do not appear to be linked to lipoatrophy. It is possible that using a protease inhibitor (PI) with either Zerit or Retrovir speeds up the loss of fat, but this has not been proven conclusively. Although some studies have suggested that PIs may play a role in lipoatrophy, most studies that have looked at switching from a PI to a different type of drug, such as a "non-nuke" like Sustiva or Viramune, have not shown gains of fat.

"Body shape concerns may cause some people to stop or skip doses of their antiretrovirals or even prevent them from starting HIV therapy when it is needed."

ACTG 5142, a study presented at the 2007 Conference on Retroviruses and Opportunistic Infections (CROI) reported some surprising results, and questioned the dogma that PIs contribute to lipoatrophy more than non-nukes. One aim of the study was to see if avoiding nukes would lower the chance of developing lipoatrophy. People took Sustiva plus two nukes, or the PI Kaletra plus two nukes, or Sustiva and Kaletra without any nukes. After 96 weeks, 32% of people on Sustiva plus two nukes had significant lipoatrophy, compared to only 17% of those on Kaletra plus two nukes and 9% taking Sustiva and Kaletra alone. But the lipoatrophy was mainly seen in those taking Zerit (42%) or Retrovir (27%) – there was no significant difference in lipoatrophy between those taking Viread and those not taking any nukes.

While the choice of nuke was important, overall twice as many people taking Sustiva developed lipoatrophy compared to those taking Kaletra, regardless of which nuke they took. But those who took Sustiva and Kaletra without any nukes saw their blood lipids (cholesterol and triglycerides) rise significantly more than those taking nukes.

These results are in contrast to a prior study that found higher rates of lipoatrophy in patients taking the PI Viracept compared to Sustiva. Taken together, these results indicate that it may be the particular combination of drugs that is most important, rather than which class they belong to. The impact of ACTG 5142 on first-line treatment recommendations, if any, remains to be seen – it will be important to tease out exactly which combinations have the least chance of lipoatrophy without increasing blood lipids. And of course, which regimens work best: 89% of people taking Sustiva had viral loads below 50, compared to 77% of those on Kaletra – another surprising result.

As a result of some of these observations, researchers have looked at the effects of switching from HIV drugs that are linked to lipoatrophy to other drugs. In most of these studies, people who switched from Zerit or Retrovir to Ziagen or Viread had modest gains in fat in their arms and legs compared to people who stayed on their original therapy. While researchers reported these gains using special scans, patients did not always notice changes in their appearance. Many of the studies lasted a year or less, so it is possible that with more time people who switched from the offending drug will gain enough fat back to make a noticeable difference.

(continued on next page)

Treatment of Body Shape Changes *(continued from previous page)*

Unfortunately, switching antiretrovirals is not an option for everyone. It is extremely important to consider an individual's HIV treatment history and whether he or she has resistance to certain drugs (or is likely to) before making a switch. Otherwise, there is potential for viral break-through.

Glitazones
Insulin is a hormone made in the pancreas that acts to lower blood sugars, especially after eating. Many people with lipoatrophy have insulin resistance, meaning that their pancreas needs to produce more insulin than normal to keep blood sugar under control.

Glitazone drugs are used to treat diabetes – they act to control blood sugars by improving the action of insulin in the body. A large Australian study of Avandia in people with HIV did not show any beneficial effect on limb fat. A smaller study that included only people who had both lipoatrophy and insulin resistance, however, did show modest gains in limb fat. A recent study of a similar drug, Actos, also showed modest gains in limb fat compared to placebo. Of note, people who continued to take Zerit did not benefit from Actos. It is still not clear whether Avandia or Actos will have a role in treating lipoatrophy.

Uridine
Laboratory studies suggest that uridine, a natural nucleoside compound, may protect fat cells from being damaged by Zerit and other nukes. NucleomaxX is a dietary supplement derived from sugar cane that is rich in uridine. The initial results of a small study of NucleomaxX in people taking Zerit or Retrovir showed modest gains of limb fat with the supplement. Based on how uridine is thought to work, this approach may work only in people taking Zerit or Retrovir. A larger study of NucleomaxX is now under way.

Plastic Surgery
Lipoatrophy involving the face can often be helped by injections of substances called "fillers" by dermatologists, plastic surgeons, or other clinicians with appropriate training. These fillers come in two major varieties: temporary and permanent. As the names imply, temporary fillers may require multiple injections at regular intervals, whereas permanent fillers are intended to be a permanent fix. While permanent may sound better, there may be disadvantages to these types of fillers – fat content in the face may change over time because of continuing fat loss or possible fat gain due to other interventions. This sometimes results in undesirable effects such as sagging of the skin.

"Fat loss in the face can often be helped by injections of substances called 'fillers.' Cheek implants are another option that has shown good results."

A comprehensive review of facial fillers is beyond the scope of this article. Briefly, there are now two temporary fillers that are approved for facial lipoatrophy: Sculptra and Radiesse. There are no studies comparing these two treatments. Cheek implants (hard pieces of silicone or other substances) are another option that has shown good results in people with facial wasting.

Treatment of Fat Accumulation

Exercise
There have been a few small studies of the effects of aerobic exercise and weight training on fat accumulation in people with HIV. These interventions led to modest decreases in central fat in many participants as well as improvements in metabolic problems such as elevated triglycerides and cholesterol. Persons with fat accumulation should certainly exercise for the overall health benefits if they are able to do so, although this may not necessarily take care of the problem of excess fat.

Switching Antiretrovirals
Early studies suggested that PIs might cause or contribute to fat accumulation. While this is still not clear, a number of studies have looked at switching PIs to other drugs such as Sustiva, Viramune, or Ziagen. In general, people who switched from a PI did not have major changes in central (abdominal) fat compared to those who stayed on PIs. Studies switching from Zerit or Retrovir to other drugs mentioned above, while promising for limb fat, have not had favorable effects on central fat.

Glucophage
Glucophage, another drug used to treat diabetes, has been studied as a potential therapy for fat accumulation, especially in people with insulin resistance. A small study of low-dose Glucophage in people with HIV-associated fat accumulation and insulin resistance showed a slight loss of central fat and a slight overall weight loss. A follow-up study of a higher dose plus a supervised exercise program also showed modest reductions in central fat. A study of Glucophage in people without insulin resistance that was presented at the 2006 CROI, however, showed no beneficial effect. In fact, in this study as well as several others, people receiving Glucophage had some worsening of lipoatrophy. Overall, people with significant lipoatrophy in addition to fat accumulation may want to avoid Glucophage.

Glucophage may be reasonable to try in people with fat accumulation who have diabetes or what is called impaired glucose tolerance. Impaired glucose tolerance refers to having a higher than normal blood sugar at the end of a 2-hour oral glucose tolerance test. While researchers were originally concerned that both Glucophage and nukes can cause lactic acidosis, a severe build-up of acid in the body, this has not been a problem in the small studies in people with HIV to date.

Serostim
The recombinant human growth hormone Serostim is approved for the treatment of AIDS-related wasting. Researchers have noted that, in addition to gaining weight primarily in the form of lean tissue (including muscle), people taking growth hormone often lose fat. These observations, as well as reports of people who had reductions of buffalo humps while receiving growth hormone, led to several small studies of Serostim in people with HIV-associated fat accumulation.

These studies, including one done at ACRIA in conjunction with Dr. Donald Kotler's research group at St. Luke's-Roosevelt, suggested that Serostim injections can cause selective reductions in visceral fat, sometimes accompanied by mild loss of subcutaneous fat. Follow-up studies comparing growth hormone to placebo have confirmed these findings, and the FDA is currently reviewing their results to determine if Serostim should be approved for the treatment of HIV-associated fat accumulation.

Most studies of growth hormone have used doses that are about ten times more than the body normally produces. At these doses, side effects are quite common but often manageable by reducing the dose. The most common side effects include fluid retention, swelling, and joint and muscle aches. Growth hormone can also cause high blood sugar and diabetes. As a result, the major studies of growth hormone have excluded people who have high fasting blood sugars or impaired glucose tolerance. Also, once Serostim is stopped, some of the fat that was lost tends to come back over the course of months. It is not known whether something can be done to prevent this rebound in fat or if the drug can safely be taken only when fat accumulates.

Since growth hormone can raise blood sugars and also may result in mild loss of subcutaneous fat, there has been interest in seeing if it can safely be combined with a glitazone drug, which might prevent the problem with blood sugars and possibly prevent the loss of subcutaneous fat. ACRIA plans to participate in a study funded by the National Institutes of Health to test this strategy in people with HIV-associated fat accumulation who have evidence of insulin resistance but not frank diabetes.

TH9507
TH9507 is a synthetic growth hormone releasing factor that, like growth hormone, is given by injection beneath the skin. It causes the pituitary gland in the brain to produce growth hormone. Because it more closely mimics the body's normal production of growth hormone, which may be reduced in people with HIV-associated fat accumulation, it may be an attractive option.

To date, TH9507 has led to an average 15% reduction in visceral fat. It has been generally well tolerated and notably did not lead to blood sugar elevations even in people with impaired glucose tolerance at study entry. ACRIA participated in a recent study of TH9507 and will also be a site for the confirmatory clinical trial required by the FDA.

Leptin
Leptin is a hormone-like substance produced in fat that acts in the brain to affect appetite and metabolism. A synthetic form of leptin, recombinant human leptin, has been studied in very small numbers of people with HIV-associated lipoatrophy who were found to have low amounts of leptin in their bloodstreams. In one very small study of eight people, twice-daily injections of leptin led to significant reductions in visceral fat and improvements in cholesterol and insulin resistance. The studies to date are very preliminary and hopefully will be followed up with larger studies.

Surgery
Because the abdominal fat accumulation is visceral fat that is deep inside, around the organs, liposuction is not a safe treatment option. Plastic surgery, including liposuction, can sometimes be done to remove neck fat, such as buffalo humps. While generally safe, buffalo humps often recur over many months. Insurance companies will sometimes pay for removal of neck fat, especially if its presence causes functional problems, such as difficulties with neck movement or sleep apnea (breathing problems during sleep).

Conclusions
It's important to think about lipoatrophy and fat accumulation as separate processes that may exist simultaneously in the same individual. There are several promising approaches that are being studied for each of these conditions, but our best hope is that use of newer HIV therapies will prevent the development of lipoatrophy in particular. The only way for us to better understand and treat these conditions is through further clinical research.

Marshall Glesby is an Associate Professor of Medicine and Public Health at Weill Cornell Medical College, Co-Director of the Cornell HIV Clinical Trials Unit, and Clinical Director of the New York-New Jersey AIDS Education and Training Center.

ACRIA Drop-In Support Groups

The popular groups formerly offered by Body Positive have found a new home. These peer-led drop-in support groups are held every Thursday and Friday from 6:30 to 8:00 p.m. at the LGBT Community Center, 208 West 13th St., NYC.

For more information, call Angelo Andino at 212-924-3934 x129.

Anemia and Depression in Women with HIV *by Kim-Monique Johnson, MSW*

"Women are the mules of the world."

Zora Neale Hurston

Women carry a heavy load when it comes to living with HIV. Poverty and access to health care are among the predominant factors causing poorer health outcomes for women with HIV. The HIV Cost and Services Utilization Study (HCSUS), a national study of people with HIV receiving regular medical care, found that women with HIV were disproportionately living in poverty. Nearly 64% of the women in the study had annual incomes below $10,000, compared to 41% of men. At the same time, many of these women were also the primary caretakers of children under the age of 18. Postponing medical care due to lack of transportation, being too sick, or having to take care of others are familiar reasons that women are more likely to receive delayed treatment than men.

The CDC reports that women are significantly more likely to die of AIDS than men because treatment is started late, if at all. After highly active antiretroviral therapy (HAART) became available in 1996, the decline in AIDS-related deaths was 44% for men but only 35% for women. More than ten years later, such dramatic differences have lessened, but women's survival rates after an AIDS diagnosis are still slightly lower than men's. The CDC reports that during the first two years post AIDS diagnosis, women in the U.S. live as long as men, but by year three their survival rate drops 2% compared to men's survival.

According to Punkin Clay Stephens, Assistant Professor of Epidemiology and Biostatistics at the School of Public Health, SUNY Albany, the real difference occurs *before* the AIDS diagnosis. "Once in treatment, women and men respond equally to medication. The issue is what happens early in HIV infection, before a person receives health care."

Herein lies the disparity. The CDC reports that 59% of men progress to an AIDS diagnosis after one year of testing HIV positive, compared to 64% of women (according to 2004 data from the 33 states that have confidential names reporting for both HIV and AIDS). Socioeconomic factors play an important role in access to care for women with HIV – poverty, substance use, or gender-based violence are all associated with delayed treatment and, possibly, disease progression.

Besides the factors above, what are the biological factors or comorbid illnesses that place women at increased risk of disease progression and increased mortality? Two such conditions, anemia and chronic depression, have recently received needed attention by researchers.

Women, HIV, and Anemia

Anemia has long been associated with HIV disease. A study of 31,000 people with HIV, done before the advent of HAART, found rates of severe anemia from 3% in people with asymptomatic HIV infection to 37% in people with AIDS. Despite its prevalence among HIV-positive women, it is often unrecognized and untreated. If left untreated, anemia is strongly associated with HIV disease progression and increased risk of death.

Fortunately, the rate of serious, death-related anemia has decreased since the advent of HAART. However, moderate anemia still affects approximately 30% of people using HAART. Researchers at Beth Israel Medical Center in New York and the Clinical and Epidemiology Research Center in Atlanta examined anemia and HIV disease. In their study of 4,183 patients receiving medical care, women had an 80% greater risk of anemia than men. In addition, the risk of anemia was 2.6 times greater for African-American patients compared to white patients.

"I'm sick and tired of being sick and tired."

Fannie Lou Hamer, civil rights activist

What is Anemia?

Anemia is a shortage of red blood cells that can occur when the body either produces too few red blood cells or loses too many. As important as the red blood cell count is, hemoglobin levels must also be monitored. Hemoglobin is important because red blood cells use it to carry oxygen from the lungs to the rest of the body, providing energy and strength. When hemoglobin levels are low, anemia can also occur.

Symptoms of anemia include extreme fatigue, dizziness or fainting, feeling cold, difficulty breathing, and depression. In terms of the HIV connection, anemia is linked to higher viral load and lower CD4 counts. For a woman coping with both anemia and HIV, it is not hard to imagine the impact on daily functioning, her quality of life, and her ability not only to receive treatment, but to remain in treatment.

Among the factors linked to anemia in people with HIV are:

- Being a woman
- Being African-American
- Having a lower CD4 count
- Having a higher viral load
- Taking Retrovir (AZT)

Recent studies show that maintaining normal hemoglobin levels in women is linked to successful treatment adherence and to maintaining undetectable viral loads after 6 months. In some cases, hemoglobin level may be as useful an indicator for predicting disease progression as CD4 counts and viral load.

Treatment Options

Dr. Keith Rawlings, President of the Integrated Minority Network, Inc. in Dallas, recommends the following strategies for managing anemia in people with HIV:

- Monitor hemoglobin levels and red blood count
- Monitor physical functioning and quality of life regularly
- Determine the treatable causes of anemia
- Initiate appropriate therapy

The key to corrective treatment is linked to the cause. Women who experience heavy menstrual bleeding may be at increased risk for anemia and may consider gynecological treatment options to decrease bleeding. Is the anemia caused by advanced HIV disease, thus warranting HAART, or is the anemia in fact caused by HAART? Answers may mean either *starting* a new drug, such as injectable erythropoietin (Epogen or Procrit), or *stopping* a drug that can cause anemia, such as Retrovir (AZT). Dietary changes, such as increasing foods rich in iron, vitamin B12, and folic acid, can also help.

Women. HIV, and Depression

Data from the Women's Interagency HIV Study (WIHS) were analyzed to consider the relationship between chronic depression, HIV disease progression, and mortality. From 1994 through 2001, 1,716 women with HIV from Brooklyn, Bronx, Chicago, Los Angeles, San Francisco, and Washington D.C. were interviewed and given blood tests as part of a research study published in the July 2004 issue of the *American Journal of Public Health.* The researchers were careful to control for other factors that might be associated with death, such as CD4 and viral load counts, antiretroviral therapy, and the use of drugs such as cocaine and heroin.

The study found that women with both chronic depression and HIV were almost twice as likely to die from AIDS-related causes as HIV-positive women who were not also battling chronic depression, even after controlling for CD4 counts. In 2002, another study in the *American Journal of Psychiatry* suggested that, like anemia, chronic depression may be a physical condition and not purely a mental health problem. The researchers examined depression, viral load, and the immune system in women with HIV and found a link between depression, increased viral load, and lower levels of natural killer cells.

"Women with chronic depression and HIV were almost twice as likely to die from AIDS-related causes as HIV-positive women who were not also battling chronic depression..."

According to Dr. Judith Rabkin, a clinical psychology researcher at Columbia University, depression manifests in women similarly to anemia:

- Between 5 and 20% of people with HIV also have major depression
- Women with HIV are more likely to suffer from depression than men
- Clinical depression has been consistently associated with poorer medication adherence

Another HCSUS study reported in the August 2001 *Archives of General Psychiatry,* found that almost half of the over 2,800 people studied experienced some form of psychiatric disorder, signaling the need for appropriate mental health care for women, who are more vulnerable to such conditions. Dr. Eric Bing, lead author of the HCSUS report, observes that multiple HIV-related symptoms are strong signals for health care providers to screen for depression. HIV infection by itself is not a *predictor* of depression; it is a complex *association*, not cause, leading providers to consider other factors, such as poverty, violence, and substance abuse, to determine risk and treatment for women.

Treatment Options

Appropriate and sensitive mental health treatment throughout HIV disease has been shown to decrease the death rate of HIV positive women with chronic depression by half.

Individual or group psychotherapy may help with depressive symptoms and provide needed support. Exercise, even though difficult due to fatigue, can actually provide a boost and has been linked to improving mood and energy. Antidepressants should be carefully selected so as not to interfere with antiretrovirals such as Norvir. Providers commonly use a class of antidepressants such as Paxil, Zoloft, and Celexa in the treatment of depression in HIV.

Conclusion

Identifying co-morbid conditions in women with HIV is critical for addressing the disparities in their survival rates compared to men. When two such conditions, anemia and chronic depression, are treated, it leads to improved quality of life and survival rates for women with HIV infection.

According to a recent CDC study of more than 19,500 patients with HIV in ten U.S. cities, women were slightly less likely than men to receive prescriptions for the most effective treatments for HIV infection. When women are 33% more likely to die than men due to delayed treatment, identifying treatable co-morbid conditions that can slow disease progression and risk of death is critical for women's survival.

Similarly, treating chronic depression also leads to increased quality of life and the ability to adhere to treatment. Women need providers who can help them separate the symptoms of HIV, anemia, depression, and the side effects of HIV drugs. Proper and consistent monitoring will lead to early detection, diagnosis, and treatment, which in turn are associated with a decrease in disease progression and mortality.

Both anemia and depression are common in women with HIV disease. Both are treatable, which can lead to increased energy, improved ability to function, and enhanced quality of life. Women, who often carry the weight of the world on their shoulders, need to know that help is available not only to lighten the load, but to help them live healthier and longer.

Kim-Monique Johnson is a health care consultant and is the NYS HIV Prevention Planning Group Community Vice Co-Chair.

Dealing With Fatigue

by Judith Rabkin, PhD

By itself, fatigue is not a "disease." When persistent and severe, however, fatigue (feeling tired all the time, lacking stamina, having too little energy to do things) can disrupt one's life, interfering with daily activities, socializing, or fulfillment of goals such as returning to work, enrolling in school, or improving life circumstances in other ways.

There is no standard definition or standard measure of fatigue. Being tired all the time may include both psychological components (such as depression) and physical components (climbing stairs tires you out). It is different from apathy, which is loss of desire to do anything, and from oversleeping, which is defined simply as increased sleep time. Common words to describe fatigue include lack of energy, sleepiness, tiredness, exhaustion, an inability to get enough rest in the absence of night-time insomnia, or inability to sustain a desired activity.

Everyone experiences fatigue at some point. It becomes a problem that warrants treatment when it occurs frequently, for sustained periods, and interferes with daily activities. Fatigue occurs in relation to multiple AIDS-associated conditions and also medications, but may also exist without apparent explanation.

Fatigue and HIV

Research studies from our group and others have shown that fatigue is a common and significant problem for a substantial number of people with HIV, and may be due to the virus, to HIV-related medications, or associated health problems or treatments. In various surveys, up to 40% of HIV+ respondents report fatigue, although it is not always persistent or disabling.

When it does persist, fatigue can interfere with many activities Physical activities such as exercise are often reduced, as are social activities, contributing to social isolation and fewer opportunities for pleasant events. People with fatigue may not have the energy to visit friends, or may cancel planned activities because they're too tired to go out.

Fatigue is a common reason for leaving work and going on disability, as well as inability or reluctance to return to work even when one's health is otherwise stable.

Together with other problems, fatigue may interfere with medication adherence, including doses missed for reasons such as falling asleep prematurely or sleeping through a scheduled dose. Fatigue also can interfere with concentration, memory, and the ability to sustain attention, which in turn may interfere with new learning. Overall, persistent fatigue in HIV is common and can be disabling.

> ***"Fatigue is a common problem for a substantial number of people with HIV, due to the virus, to HIV-related medications, or associated health problems or treatments."***

Medical Causes

Fatigue may be caused by specific medical conditions, including untreated insomnia, anemia, low levels of testosterone, or thyroid deficiencies. It makes sense to identify and treat these conditions directly before treating the symptom of fatigue. Routine bloodwork can be done to check whether such problems do exist.

Fatigue also may be the result of the drugs used to treat HIV or other conditions. Some psychotropic drugs (Remeron, for example) can cause fatigue. Hepatitis C itself often causes fatigue, and fatigue is one of the major and frequent adverse reactions to alpha interferon/ribavirin treatment of hepatitis. Some studies have shown a relationship between fatigue, higher HIV viral load and lower CD4 cell count, while others have not shown such a relationship.

Fatigue and Depression

People who are depressed often complain about low energy, lack of stamina, or feeling tired all the time. In fact, fatigue is one of the symptoms used to diagnose depression. In addition, fatigue is also associated with problems concentrating and focusing, which is another criterion used to identify depression. There may be the opposite connection as well: when fatigue restricts participation in pleasant events, reduces social activities and leads to long days alone at home, depressed mood is a likely result.

However, since both depression and fatigue are fairly common in people with HIV, they may overlap even if one doesn't cause the other. Each can and does occur without the other. Some people say they always feel tired, but are not persistently depressed. Some patients with depression do not report fatigue. So the two conditions may occur together or separately. If both are present, and the depression is moderate or severe, it is best to treat the depression first, on the principal that it is preferable to treat the cause of a problem rather than its manifestation. If fatigue remains, then it can be treated subsequently.

Treating fatigue

Several treatment approaches have been used to treat fatigue in the context of HIV infection. One approach is to use steroid hormones such as testosterone or DHEA. Studies, including those from our group, have shown that, among men, testosterone injections have a clearcut positive effect on energy level and stamina. Injected

testosterone is no longer commonly recommended, however, given the availability and greater convenience of gel preparations. Testosterone gel has not been systematically evaluated with respect to effects on fatigue in HIV+ men, although we often see patients seeking treatment for fatigue who have already tried gel testosterone preparations without effects on their fatigue. Furthermore, testosterone is not appropriate for men with prostate problems or men with bipolar disorder (extreme mood swings), and is not approved for use by women.

The results for DHEA are less consistent; some patients have found it helpful for fatigue but others have not, in research we have conducted. However, DHEA has few side effects, is sold over the counter without the need for a prescription (which means that health insurance does not cover the cost although it is inexpensive), and at higher doses than often sold can be helpful, at least for some people, for mildly depressed mood as well as low energy. DHEA increases testosterone level in women but not in men.

The other main class of medications used to treat fatigue in HIV+ people includes stimulants such as Dexedrine, Ritalin, and Cylert. In one study comparing Ritalin, Cylert, and placebo, both drugs were more effective than placebo – but overall, most study participants did not show significant improvement to any of them.

In the early 1990s (before HIV combination therapy was available) our group conducted a small study of Dexedrine in people with CD4 counts below 50, and found a major positive effect on energy as well as mood. However, most health providers are reluctant to prescribe these controlled substances because of concerns about physiological as well as psychological dependence, and they are generally not appropriate for patients with addiction histories. Stimulants as well as steroids also are not indicated for those with bipolar disorder (manic depression) since they may cause the onset of manic episodes.

In the past few years, a new stimulant medication has been marketed, known as Provigil. It isn't fully understood how it works in the brain, but it is different from other stimulants and shows no evidence of potential for addiction. In fact, it has been used with some preliminary evidence of success for treatment of cocaine addiction. Provigil is approved for the treatment of narcolepsy (a condition where one falls asleep suddenly and involuntarily during the day), sleep apnea, or shift work-related sleep disorder. Its use to treat fatigue in HIV is thus "off label," which is why research is needed concerning its effectiveness for HIV+ people with fatigue.

We conducted a preliminary study with 30 HIV+ men and women with persistent fatigue who were taking HIV medications. In this exploratory study, most participants found Provigil helpful, although the results are at best suggestive, since this was a small study and both doctors and patients knew they were taking Provigil. Side effects were uncommon, but when they occurred included feeling jumpy, "wired," or having a headache – not unlike drinking too much coffee. These side effects were gone the next day, and could be managed by lowering the dose. No patients discontinued the medication because of side effects. We monitored CD4 counts and viral load, and found no changes, providing some evidence that there are no harmful interactions with HIV medications. By the end of this 12-week trial, five patients started working again, two others increased their hours of work, and two enrolled in vocational training programs.

We are now conducting a larger placebo-controlled trial in people with HIV who have persistent fatigue that interferes with their everyday life. We hope to learn more about rates of response, who seems most likely to benefit from this treatment, how long the effects last, and whether it is helpful for problems with memory and attention. We also are conducting studies to make sure that Provigil is safe and effective in combination with HIV medications.

In conclusion, fatigue can be "real" and can represent a significant problem. It isn't just being lazy or not trying hard enough, especially if you are often too tired to do things and go places. Treatment can help, options are available, and quality of life can improve.

Judith Rabkin is a clinical psychology researcher at Columbia University.

Research Study

For HIV+ men and women with severe and persistent fatigue

All eligible participants see a psychiatrist regularly and are treated with Provigil (modafinil) for four weeks, although for some there may be a four week delay. Two additional months of treatment are offered.Compensation is provided for assessments.

Dr. Judith Rabkin (212) 543-5762
Columbia University Medical Center - NYS Psychiatric Institute

Peering into the Pipeline: New Drug Candidates *by Donna M. Kaminski*

As I further my medical training, I find that the management of HIV remains intricate, requiring both an increasing understanding of the disease and a growing tool set. So many resources come into play when deciding on a treatment regimen, including information on when to start, what to start with, side effects, and how and when to use resistance test results (which continue to mesmerize me with their bright green and red boxes). These tools, combined with an arsenal of over 20 HIV medications, have helped us to optimize treatment regimens. Yet even with these, resistance continues to limit treatment options. The need for a greater arsenal of HIV medications remains strong – luckily for us, it looks as if we have several promising candidates on the horizon.

Many HIV drugs approved to date have taken a good idea and given us more of the same. First came the reverse transcriptase inhibitors (also referred to the "nukes" and "non-nukes"), which block HIV's ability to convert its RNA to DNA. Then came the protease inhibitors, which expanded our treatment options because they worked at a different step in the HIV lifecycle. Many more protease inhibitors followed, but all worked in more or less in the same way. A fusion inhibitor followed in 2003. But all in all, the over 20 drugs approved to date work on just three steps in the life cycle of HIV.

For many treatment-experienced patients, resistance can still limit treatment options. We need new HIV meds that will work differently, targeting a different part of the HIV life cycle and working on virus that is resistant to multiple drugs, in addition to being safe and tolerable.

The 14th Conference on Retroviruses and Opportunistic Infections (CROI), held in Los Angeles from February 25-28, 2007, included over 1,000 posters, presentations, and abstracts. Of these, some of the most promising dealt with an alphabet soup of new drugs: MK-0518, GS-9137, TMC-278, and UK-427857. With the exception of TMC-278, these drugs work at new steps in HIV's life cycle, and may be important options for people with HIV that is resistant to existing medications.

The first two drugs, MK-0518 and GS-9137, are the first of a new class of HIV drugs that target the integrase enzyme, effectively blocking HIV from weaving its DNA into the host cell's DNA. UK-427857 (maraviroc) also works differently from approved HIV drugs, as it targets one of the coreceptors on the CD4 cells, blocking HIV from entering the cell. By interfering with new steps in the lifecycle of HIV, these drugs may work when approved HIV drugs do not. The fourth drug discussed at the conference, TMC-278, works like drugs already available (Sustiva and Viramune), but may have fewer side effects and may be as effective as Sustiva, one of the more potent HIV drugs.

This article will review current data on these four drug candidates, and look at where they are headed.

MK-0518

MK-0518, newly christened Isentress (raltegravir), was shown to be potent in people with resistance to many HIV medications. In two worldwide large Phase III studies, BENCHMRK 1 and 2, a total of 700 people who had taken HIV drugs for about 10 years were randomly assigned to receive 400 mg of MK-0518 or placebo twice a day, together with an individualized combination of HIV medications. People in both studies had viral loads over 30,000 and CD4 counts below 200. The studies will follow them for three years, but the initial four- and six-month study results were reported at CROI.

After four months, the studies reported that more than twice as many of those taking MK-0518 had viral loads below 50 as those taking placebo: 61% compared to 33% – compelling results in this highly resistant group. CD4 counts also rose, more than twice as much in people taking MK-0518.

People taking both Fuzeon and Prezista for the first time saw the greatest benefit from MK-0518. Of those, an impressive 98% had viral loads below 400 at four months, compared to 87% those taking placebo. When people took only one of the two (either Fuzeon or Prezista), 90% had viral loads below 400 copies, compared to 63% on placebo. As has been shown in many other studies, the best results occur when a new HIV drug is combined with other active drugs.

More good news: After six months, 61% of people taking MK-0518 who were resistant to all the approved HIV drugs were able to get their viral loads below 400 at four months, compared to only 5% without MK-0518. These results are significant, as few of the other drugs presented at CROI did as well in people with multidrug resistant virus.

With regard to side effects, people taking MK-0518 seemed to report similar side effects to those taking placebo. The most common side effects reported were diarrhea, headaches, or nausea. About 12% in both groups reported a serious side effect. On the whole, four months of MK-0518 use was concluded by the researchers to be generally well tolerated.

In a nutshell, MK-0518 appears to lower viral load significantly and increase CD4 counts in people who have had a

long history of HIV treatment, and may work well even in people with HIV that is resistant to all other HIV medications. As expected, it works best when combined with other active drugs (like Fuzeon and Prezista), and generally seems to be well tolerated. All in all, MK-0518 looks like an exciting future drug option that may receive FDA approval before the end of the year. For people who need the drug sooner, it is available now through an early access program. Doctors can call 877- 327-6751 for information on how to enroll patients.

GS-9137

In a smaller trial, Gilead's 0105 study looked at various doses of another integrase inhibitor, GS-9137 (elvitegravir). In this study, 278 people who had an average viral load of 36,000 and about 10 protease mutations in their virus took either 20 mg, 50 mg, or 125 mg of GS-9137 twice daily with a small dose of Norvir or a protease inhibitor that included Norvir. Everyone also took at least two other nucleoside analogs (NRTIs) with or without Fuzeon. 26% of those in the study used Fuzeon for the first time while in the study. After just two months, however, many taking the 20 mg dose had much smaller drops in viral load than those taking the larger doses, so the trial eliminated the 20 mg dose and switched those taking it to the 125 mg dose. (Their data were not included in the report; only those initially taking the 50 mg and 125 mg doses were followed.)

"MK-0518 appears to lower viral load significantly and increase CD4 counts in people who have had a long history of HIV treatment and may work well even in people with HIV that is resistant to all other HIV medications."

After four months, 38% of those on the 50 mg dose and 40% of those on the 125 mg dose had viral loads below 50, compared to 30% of those on placebo. These results, not as impressive as those for MK-0518, were perhaps due to the restrictions on the other HIV drugs allowed in the trial. No non-nukes were allowed, for example, so it's likely that a number of people with resistant virus were on virtual monotherapy. As has been the case with many drugs, GS-9137 works best when taken with at least one active HIV drug. People taking the 125 mg dose who had at least one other active drug saw a viral load drop of 2.1 logs. Those with no other active drugs saw only a 0.7 log drop. So having just one other active HIV med can make a huge difference when taking GS-9137.

Those taking GS-9137 also saw their CD4 counts rise. After four months, people taking the 50 mg and 125 mg doses had their CD4 counts increase by 52 and 61 respectively, compared to 28 cells in those taking approved drugs only. Side effects were similar in both groups. Between 1% and 3% of the groups stopped taking GS-9137 due to side effects. There also were similar rates of moderate to severe grade 3 and 4 side effects and abnormal lab results.

Gilead Sciences will be moving forward with a 150 mg dose of GS-9137 into larger phase III clinical trials, and hopes to see similar results to the 125 mg dose.

Maraviroc

HIV uses one of two coreceptors, R5 or X4, to get into a CD4 cell. Early in infection, HIV seems to prefer R5, but later may switch to the X4 receptor. Maraviroc works by blocking the R5 receptor. (This is different from Fuzeon, which prevents HIV from fusing with the CD4 cell's wall after a coreceptor is engaged.) Maraviroc therefore offers the exciting possibility of using a different target to block HIV from entering cells.

In the MOTIVATE 1 and 2 studies, 1,076 people living with HIV in Europe, Australia, and North America took 300 mg of maraviroc once or twice a day, or took a placebo. Both groups also took at least three other individually optimized HIV drugs. (People taking Rescriptor or a protease inhibitor other than Aptivus took 150 mg once or twice a day.) People in both studies had previously taken HIV drugs and had viral loads above 50,000 and CD4 counts below 200. People are to be followed for one year, and the initial six-month results were reported.

After six months, nearly twice as many people taking maraviroc had viral loads below 50 compared to those taking placebo with approved drugs: 41-48% of those taking maraviroc had viral loads below 50, compared to only 21-25% of those taking placebo. CD4 counts increased by 102-112 in those taking maraviroc, compared to an increase of 52-64 in those on placebo.

Between 84% and 89% of all patients experienced at least one mild side effect, and up to 91% reported experiencing any side effect. There was no significant difference between those taking maraviroc and those taking the placebo in the number of side effects experienced. In MOTIVATE 1, four people in each of the maraviroc-dosed groups died, as com-

(continued on next page)

Peering into the Pipeline *(continued from previous page)*

pared to none of those in the placebo group. In MOTIVATE-2, one person in the placebo group, two in the once-daily, and one in the twice-daily groups died. According to the investigators, the deaths were not related to the medications used.

It's interesting to note that in both studies, people who began with viral loads over 100,000 did just as well as those below 100,000. This is good news for people who can't get their viral loads below 100,000 on their current regimen. For those who have resistance to many HIV drugs, the twice-daily dose seemed to work better at reducing viral load than the once-daily dose. 29% of those with high-level resistance reached viral loads below 400 when taking the drug twice daily, compared to 18% in the once-daily group and 3% in the placebo group. Thus maraviroc seems to work best when taken with at least one antiretroviral to which one's HIV is not resistant. An official dose has not been decided upon, but these results will have to be weighed against the simplicity and convenience of the also effective once-a-day dosing.

"In both maraviroc studies, people who began with viral loads over 100,000 did just as well as those below 100,000."

A concern with maraviroc is whether using a drug active against the R5 receptor will prompt more HIV to switch to using the X4 receptor. In this study, 31 patients in the once-daily group and 32 patients in the twice-daily group had their virus switch to the X4 receptor, so they may be less responsive to future R5 receptor inhibitors. The Monogram Trofile Assay should help patients and doctors identify which type of receptor someone's HIV uses, and will be useful when deciding to start or continue maraviroc.

TMC-278

TMC-278, also known as rilpivirine, is a newly designed non-nuke in the same class as Sustiva and Viramune. In the Tibotec study presented at CROI, 90 people who had never taken HIV drugs before took either 25 mg, 75 mg, or 150 mg of TMC-278, or the standard dose of Sustiva. Everyone also took Truvada or Combivir. On average, people had viral loads about 70,000 and an average CD4 count of about 200. About a third of the people in the study were women.

After a year, it looks like TMC-278 may be as effective as Sustiva. Here's what we saw: 81%, 80% and 77% of those on the 25 mg, 75 mg, and 125 mg doses of TMC-278 respectively saw their viral loads drop to below 50. This is comparable to the 81% of those taking Sustiva. People saw CD4 count increases of 125-145. Larger clinical trials are needed to see how well TMC-278 works in various populations, but these initial results look promising.

TMC-278 may have fewer side effects than Sustiva, as far as these study results go. While similar numbers of people experienced nausea (18% and 20%), fewer people experienced central nervous system effects (dizziness, abnormal dreams, vertigo) and rash. Overall, 33% of people on TMC-278 experienced CNS effects compared to 53% of those on Sustiva, while 8% of those on TMC-278 experienced rash compared to 19% of those on Sustiva. In addition, TMC-278 may be easier on the lipids, or blood fats, than Sustiva. In this study people taking TMC-278 had their total cholesterol rise 5 mg, compared to 31 mg in the Sustiva group. The "bad" LDL cholesterol also did not increase in those taking TMC-278, compared to a 16 mg rise among those on Sustiva.

Further studies will need to be done on TMC-278 before we can have a full sense of how TMC-278 will work in larger populations, such as those who have previously taken antiretrovirals, etc. Tibotec is looking into larger clinical trials of the 75 mg dose among people who have never taken HIV meds before.

Conclusion

From the looks of things, we have some exciting new possibilities on the drug horizon. Maraviroc and MK-0518 are furthest along in development, and are *both* slated to be considered for approval by the FDA in the upcoming months. If approved, they may be available as soon as this summer or fall. GS-9137 is further behind in development, but is heading for the larger trials it needs to show its stuff. TMC-278 is also moving into larger trials, and may also help expand our arsenal of HIV drugs, with the benefit of fewer side effects. In total, what sounds like alphabet soup may provide just the right flavors we need to meet the challenges we face in HIV treatment.

Donna M. Kaminski formerly was ACRIA's Associate Director of Treatment Education, and is currently a second-year medical student.

Looking AIDS in the Mouth

by Charles Dorato, DDS

Being a practicing general dentist in Manhattan – specifically Greenwich Village – for 35 years, I've seen the worst of the AIDS epidemic and, if such a word can apply, the best. Back in the late í70s and early '80s, AIDS was a little-known entity with, sadly, dire consequences. Most of us did our jobs, but those were difficult times. HIV was territory that most dentists had never explored. We learned a lot and did what we could. While some of us insisted that we not strip away all semblance of dignity from people with the virus and deny them the simple basics of dental care, many dentists did not even want these patients in their waiting rooms.

The early days were full of flat-out sadness: the families of many gay men virtually denied their existence and shoved them away to NYC – even paid for them to stay away – yet came out of the woodwork when they passed on to grab whatever they could. I recall a 21-year from the upper east side whose parents didn't want him to go to the family dentist because he would have to tell him he was HIV positive, and they didn't want the dentist to know they had a gay son. Conversely, I saw an old Italian man – who for years wanted nothing to do with his gay son – carry him up the stairs of my office during his last days, not giving a damn what anyone thought.

My years as a dentist have taught me that the mouth is often the first part of the body to show the signs of certain diseases: diabetes, stress, allergies, etc. But the hardest to have to relate to any patient were anomalies tied to AIDS: thrush, Kaposi's Sarcoma, advanced oral herpes, etc. Back then, this was a death sentence, and as a dentist, I really wasn't prepared to pass on that kind of information. My information was often greeted with resentment: "What do you know? You're just a dentist!" There would be hysteria at times, as most of the gay community knew enough about the disease to know what to ask and to look imploringly in your face for any sign other than the worst.

HIV and Oral Health

Oral health problems that are normally minor can be exacerbated when the immune system is compromised. Let's face it, when problems in the mouth occur, pain is a common byproduct, and HIV patients just don't need this additional distraction and aggravation. I guess you can use oral problems as a barometer that you're not keeping up with your maintenance – an early-warning system, so to speak.

"I saw an old Italian man – who for years wanted nothing to do with his gay son – carry him up the stairs of my office during his last days, not giving a damn what anyone thought."

From a dental health point of view, dry mouth is probably the most common problem seen in people with HIV. It can be caused by HIV meds like Crixivan and Videx, or by HIV itself. And non-HIV meds like alpha interferon, antidepressants, blood pressure meds, antihistamines, etc., can also cause dry mouth.

Saliva is a great barrier and cleanser – it washes away bacteria and acids formed by foods that can cause serious gingivitis, or gum disease. Actually, the mouth is the filthiest part of the body, with the highest count of bacteria. And the last thing any immune-compromised person needs is the introduction of more bacteria into the body thru bleeding gums. One of the fastest ways anything can get into the body is through mucous membranes. And low saliva increases the risk of cavities, which can quickly grow and become abscesses, so regular checkups are essential for anyone with dry mouth.

Unfortunately, there aren't really many good medications to promote salivation. Just keeping hydrated and using fluoride rinses to keep decay at bay is the best thing I can recommend. There are mouth rinses and artificial saliva products out there now for dry mouth. Use them, or use sugar-free candies to stimulate saliva production. Have your dentist familiarize you with the tissues in your mouth so you can be aware of any strange lesions.

Thrush

Oral candidiasis, called thrush, is also common in people with HIV, and can appear in a number of different forms. Often people with thrush notice white patches on the tongue or elsewhere in the mouth. They may also have a burning sensation or pain, and food may taste strange, making it hard to eat. Candidiasis can also occur at the corners of the mouth and be mistaken for chapped lips. Other types may appear on the roof of the mouth and appear red rather than white.

No matter how it occurs, thrush should be treated promptly. People can use lozenges such as Mycelex, or pills like Diflucan. But no matter what treatment you use, itís important to take all the doses prescribed, even after the thrush appears to be gone, since resistant strains can develop and become much harder to treat. People who have recurrent thrush should keep meds on hand and learn how to identify the signs so they can restart treatment immediately, without waiting for their next appointment. Thrush that moves into the esophagus leads to an AIDS diagnosis, since it is a serious condition.

(continued on page 18)

The Interplay of Aging and HIV

by Richard Havlik, MD

As we age, there are common body changes that often result in physiological vulnerabilities and medical conditions as well as an increased risk of illnesses and diseases. For people with HIV, there is the added complexity of hidden effects from the virus itself or from the medications used to control HIV and prevent complications. It is not always possible to sort out a single cause for a specific problem in each individual, and multiple factors probably interact to influence the outcome. In this article I will discuss the effects of common aging processes, the known effects of the virus, and the results of certain HIV treatments. Fortunately, in many cases it is possible to address these comorbidities in beneficial ways.

The Immune System

Aging: Early in life, the thymus gland – which produces CD4 and other immune cells – begins to shrink, and the number of such cells diminishes as we grow older.

HIV: The virus attacks CD4 cells, and their reduced number makes people with HIV more vulnerable to infection, especially those who are older. So a normal process is accelerated and results in *immunosenescence,* or premature aging of the immune system.

Treatment: Combinations of HIV meds known as HAART (highly active antiretroviral therapy) can reduce but not eliminate the ongoing damage to CD4 cells. Sometimes older patients do not restore their CD4 counts to as high a level or as quickly as younger patients.

Body Shape

Aging: There is a gradual loss of muscle (lean body mass) with aging. Some of this is unavoidable (for example, longer completion times for older runners), but disuse as the result of a sedentary lifestyle also contributes. In addition, there is a redistribution of fat with more collection in the belly area, especially in men. This is the result of fat depositing around the abdominal organs, not under the skin. There is some loss of fat under the skin in the face and limbs.

HIV: Although in earlier days there was HIV-associated wasting disease, with HIV treatment there may not be enough virus left to affect muscle tissue directly. Disuse and disability are the more likely culprits. Sometimes the effect of peripheral neuropathy (nerve damage in the hands and feet) can mimic muscle problems when walking. HAART has been linked to changes in body shape (see article on page 1).

> ***"HAART can reduce but not eliminate the ongoing damage to CD4 cells. Sometimes older patients do not restore their CD4 counts to as high a level or as quickly as younger patients."***

Treatment: Newer HAART regimens, at least in developed countries, have replaced those most likely to cause unwanted body changes, but switching drugs may not change body shape. Even when these drugs are avoided from the onset of therapy, there are still other contributing factors. Recently there has been increased use of products that can be injected under the skin of the face to replace lost fat cells.

Bone

Aging: Loss of bone, especially for women during and after menopause, is quite common and can occur in men at older ages.

HIV: There are some reports of accelerated bone loss in people with HIV, and studies are under way using sophisticated measures to determine how frequently this occurs.

Treatment: Calcium tablets in addition to high-calcium diets have been recommended. In cases of major bone loss (osteoporosis), there are medications that can be taken a few times or even just once a month to reverse the condition.

Liver

Aging: Because liver cells regularly rejuvenate themselves, the adverse effects of aging per se on this organ are minimal. What is more likely the cause of liver damage is the chronic abuse of alcohol or Tylenol (acetaminophen).

HIV: Although the virus may be present in liver cells, most damage is from the common coinfection with hepatitis, especially hepatitis C. HIV meds can also lead to liver problems, particularly Viramune (in women with higher CD4 counts) and Aptivus.

Treatment: Besides recommending alcohol and drug abstinence, it is possible to treat hepatitis with available drugs or to avoid hepatitis A and B with a vaccine. Switching HIV meds may be necessary in some cases.

Kidneys

Aging: The kidneys are major organs for detoxification, and usually operate quite adequately even at older ages. Most reported problems with kidney function are complications of other conditions, such as high blood pressure, diabetes, or recurrent urinary tract infections.

HIV: HIV has been associated with a specific type of kidney disease known as HIV-associated nephropathy. Although this condition is relatively uncommon, it appears to be more frequent in African-Americans than in other groups.

Treatment: HAART has resulted in some improvement in kidney function. Viread

has been linked to minor loss in kidney function and should be avoided in people with kidney problems.

Blood Pressure

Aging: It is common to see a rise in blood pressure at older ages due to stiffening of the arteries. This is most evident with systolic blood pressure (the top value when reported), which increases cardiovascular risk. Diastolic blood pressure (the lower number) may stabilize with age, but elevations occur, leading to a diagnosis of high blood pressure (hypertension). Weight gain and salt intake over time are also factors.

HIV: It is controversial whether HIV itself can affect blood pressure, but HIV drugs can increase blood lipids (see below), leading to hypertension.

Treatment: Guidelines for treatment of hypertension have been established, and lowering blood pressure, both systolic and diastolic, has been found to decrease the risk of heart attack and stroke. Most blood pressure drugs can be used in people taking HIV meds, although the class called calcium channel blockers can be problematic with certain protease inhibitors.

Lipids (Blood Fats)

Aging: There tends to be an increase in cholesterol, including low density lipoprotein (LDL) cholesterol, or "bad" cholesterol, in people over 40. This rise may represent the cumulative effect of a high-fat diet in a genetically vulnerable individual. High density lipoprotein (HDL) cholesterol, or "good" cholesterol, is more stable. Both have an effect on the risk of heart attack. Triglycerides are the other major class of lipids, but the associated risk of heart attack is less definite.

HIV: In people who have progressed to AIDS, total cholesterol and LDL cholesterol tend to be lower. Successful HAART regimens usually restore lipid levels. Certain protease inhibitors, however, have been shown to elevate cholesterol and triglycerides, possibly leading to hypertension.

Treatment: Most experts recommend continuing the HAART regimen but adding a statin drug, such as Pravachol, but certain other statins interact with protease inhibitors and should be avoided. Another class of drugs, called fibrates, might be necessary if triglycerides remain substantially elevated. Switching to a different protease inhibitor or to a non-nucleoside reverse transcriptase inhibitor are other alternatives. As with blood pressure, cholesterol-lowering guidelines exist and it makes sense to apply them to people with HIV.

Blood Sugar

Aging: As we age, there is a tendency for problems in the way sugar is handled by the body, because the insulin necessary for metabolism is less effective. This can lead to diabetes, especially in those who are obese or have a family history of diabetes. In other individuals it is identified only with administration of a special test (a glucose tolerance test) and may not be a major problem. If this glucose abnormality is coupled with obesity, hypertension, high triglycerides, and low HDL cholesterol, it is referred to as the "metabolic syndrome."

"Recent reports suggest that there may be an increase in heart attacks in people with HIV…the virus itself may be having a direct negative effect on cardiovascular disease frequency."

HIV: Treatment with protease inhibitors has been associated with glucose intolerance. Such treatment could exacerbate a tendency toward the metabolic syndrome.

Treatment: If possible, a switch in regimen can be considered. With a successful HAART regimen, however, it may be better to continue the therapy and attempt to control glucose intolerance with weight reduction, exercise, and dietary changes. Such a strategy would also improve lipid and blood pressure abnormalities. There are also medications that are quite effective in controlling blood sugar.

Heart Conditions

Aging: In developed countries, the frequency of atherosclerosis (hardening of the arteries) and myocardial infarction (heart attack) increases with age. This is believed to be the cumulative effect of lifestyle and genetic factors present for a lifetime, rather than irreversible changes that are age-related. Besides hypertension, abnormal blood lipids, and diabetes, smoking is a strong predictor of cardiovascular disease and cancer.

HIV: Recent reports suggest that there may be an increase in the frequency of heart attacks in people with HIV. Although initially it was thought that this was most likely the result of the effect of HAART on cardiovascular risk factors, more recently it has been suggested that the virus itself may be having a direct negative effect on cardiovascular disease frequency.

Treatment: This observation would suggest that optimal HAART therapy is the best approach to minimizing heart attack risk, as well as continuing to address the known cardiac risk factors where possible.

Conclusion

Since HIV infection has become more controllable with HAART regimens and the life expectancy of people with HIV has increased, the issue of dealing with the comorbidities of aging has become much more important. Successful treatment should lead to longer life and successful aging for people with HIV.

Richard Havlik is a medical epidemiologist formerly with the National Institute on Aging.

Health Concerns for Older Adults

by Andrew Shippy and Jerome Ernst, MD

Even though, since the beginning of the U.S. epidemic, at least 10% of people with AIDS have been over the age of 50, our health and social policies have generally neglected this population. Now the proportion of people living with HIV who are older is rising; in some cities, 25% or more of all people with HIV are over 50. Ageism and stereotypes contribute to the belief, among the general pubic and among health care providers, that older adults are not at risk for HIV infection.

The HIV population is often described using only health care measures: office visits, lab tests, treatments received, outpatient visits versus hospital care, etc. The health picture presented in ACRIA's *Research on Older Adults with HIV* (ROAH) study of 1,000 people over 50 is driven by the voices of the participants. ROAH participants rated their current health on a scale of 0 to 10, with higher scores indicating better health. Participants' scores ranged from 1 to 10, with a mean score of 6.8, slightly above the midpoint of the scale. This indicates that most consider their overall health to be at least fair or good. In many ways this measure is analogous to asking, "How are you feeling today?" The answer of ROAH's participants is, "Not bad," or "Pretty good." Given the tremendous challenges that these individuals face in managing HIV along with their daily life activities, this suggests there has been some success in providing care, services, and funding.

The older adults in ROAH have been living with HIV for an average of 12.6 years. The range from date of HIV diagnosis is 3 months to 26 years. A little over half (51%), have an AIDS diagnosis, while only 13% currently have CD4 levels below 200. Thus the extraordinary success of antiretroviral treatment is evident in the ROAH data. Consistent with NYS standards of care, the majority (88%) visited their primary health care provider every 3 to 4 months. Nearly 85% are currently on HIV meds. Most patients (76%) receive care in public hospitals, in clinics, or at AIDS service organizations. There are no apparent differences in access to treatment among the major racial and ethnic groups or between men and women.

Getting Older With HIV

People with HIV are now living long enough to experience the disease as a chronic illness. As they age, they will encounter the challenges of competing health risks from aging, drug toxicity, and other diseases and conditions. HIV alone does not define the health status of these individuals. Without the opportunistic infections associated with AIDS and the collapse of the immune system, there is a need to focus on non-HIV-associated health needs. As people with HIV are living longer, they and their health care providers will be challenged by at least one if not several disease processes.

> ***"Ageism and stereotypes contribute to the belief, among the general pubic and among healthcare providers, that older adults are not at risk for HIV infection."***

Many diseases that are common in the over-50 age group mimic or parallel HIV symptoms, often resulting in the older person being misdiagnosed and HIV disease overlooked. For example, diabetic neuropathy looks like HIV neuropathy, and multifocal dementia mimics HIV dementia. The complications of a lifetime of poor health choices may affect the course of HIV in the older adult. People who are over 50 when they receive their HIV diagnosis are often diagnosed late in the course of their HIV infection. This can result in an AIDS diagnosis as the initial diagnosis.

ROAH findings highlight several important issues that need to be considered and will be examined in follow-up ROAH studies. Most participants (91.4%) reported at least one comorbidity, and 77% had two or more. The most common comorbidities were depression (52%), arthritis (31%), hepatitis (31%), neuropathy (30%), and hypertension (27%). Many medications commonly taken by older people – tranquilizers, antianxiety agents, drugs to treat Parkinson's disease, hypertension, heart disease, rheumatoid arthritis, and pain – can worsen depression.

High Blood Pressure

Hypertension, or high blood pressure, is a common condition that is more frequent as we age. Close to 2/3 of people over 60 will be affected by it; left untreated it can lead to an increase in strokes, heart attacks, heart failure, and death. When treated, the frequency of these complications is greatly lowered.

Blood pressure needs to be monitored regularly as we age. A reading of 120/80 is usually considered normal; readings that are repeatedly over 135/85 usually need to be treated. Several measurements are usually needed to verify the diagnosis since blood pressure normally goes up in the doctor's office due to the normal stress of seeing a doctor ("white coat hypertension").

People with high blood pressure need to live a healthier life, which usually requires losing weight, stopping tobacco use, moderating alcohol consumption (a couple of glasses of red wine may actually be beneficial), exercising at least three or four times a week for at least 30 minutes each time, and monitoring blood lipid levels like cholesterol and triglycerides. Stress reduction, lowering salt (sodium) intake, increasing fruits and vegetables, and decreasing fat in the diet are also beneficial. Most of these interventions can reduce hypertension as well as the risk of heart disease. Medications can help when these methods don't.

High Cholesterol

Lipids, or fats, often increase in the blood as we age and are another risk factor for heart disease and stroke. Cholesterol is but one lipid found in our bodies; the good cholesterol is called high density lipoprotein, or

HDL, and the bad one low density lipoprotein, or LDL. (An easy way to remember this is: HDL for "Healthy" cholesterol and LDL for "Lousy" cholesterol.) HDL helps remove cholesterol from the body while LDL helps deposit it in the walls of blood vessels, so we want HDL to be higher and LDL to be lower. The lower one's level of LDL, the lower the risk of heart disease, especially in those who already have heart disease. So, most physicians are urging patients to lower their LDL and raise their HDL as much as possible.

A diet low in fat is one way to do this. So is increasing one's intake of omega-3 fatty acids (found in flaxseed oil, certain fish – especially salmon – and walnuts). Statins are drugs that can be effective in doing this, but unfortunately many of them interact with HIV drugs. Your physician can help pick those with the least chance of such interactions. Exercising and stopping smoking can also lower LDL.

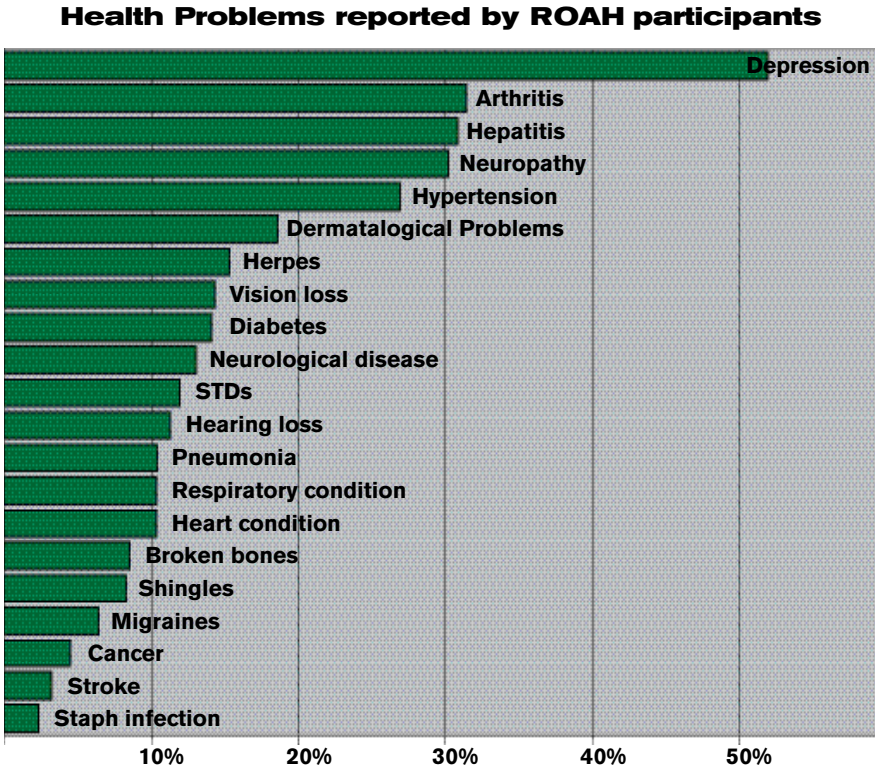
Diabetes

Diabetes is increasing in frequency in this country, including among people with HIV. The risk for diabetes increases the more a person weighs. It also increases when taking certain HIV drugs, especially the protease inhibitors. Type 2 diabetes, the kind that usually affects adults, is clearly tied to body weight, age, and genetics (coming from a family with diabetes increases one's risk).

Diabetes is managed by weight reduction, changing the diet, and, sometimes, oral medications (insulin injections are rarely needed in adult onset diabetes). Often, simple weight reduction is enough to normalize a person's blood sugar. Complications of diabetes include vascular diseases, such as heart disease and stroke, and damage to the vessels of the kidneys and the retina of the eye. Vascular compromise can lead to amputation of the lower limbs due to gangrene. The vascular complications are greatly increased in those who smoke. Diabetic neuropathy is also a complication of diabetes and often is difficult to differentiate from HIV neuropathy.

Cancers

There are many other diseases that become more common as we age. Breast cancer in women (and very rarely, men) is one of them, but no definite increased risk has been shown in women with HIV. Most women should begin having regular mammograms after the age of 40, and according to the latest guidelines those at higher risk are now being offered MRIs. People are at higher risk for beast cancer if they have already had it in one breast or have a family history of the disease. Genetic tests are available for those with a strong family history.



Prostate cancer is the most common cancer in men, but again with no known increase in people with HIV. Most men with prostate cancer have a low-grade disease and will die from another illness. The major problem today is determining who will develop an aggressive, life threatening cancer and who won't. This cancer is more common in older men, in men with a family history of the disease, and in African-American men.

Currently, a blood test – the PSA (prostatic specific antigen) test – is used to screen for prostate cancer, along with a digital rectal exam. The blood test is very sensitive, but some men with low PSA levels can have the disease while not everyone with high levels does. High levels usually indicate the need for a needle biopsy of the prostate, which may be followed by surgery, drug therapy, radiotherapy, cryotherapy or some combination, depending on the results. Men need to be well informed before they embark on screening tests for prostate cancer, given the difficulties interpreting the PSA test and the complications of prostate surgery, which can include impotence and/or urinary difficulties.

Conclusion

Growing old isn't without its risks. Some of these risks are increased in people with HIV disease; some are not; and for some, there isn't enough experience yet to know. The good health measures and preventive care recommended for people who are HIV negative also need to be followed by those who are HIV positive. As time goes on and more people with HIV live to old age, we may see different frequencies of the diseases of aging, or they may express themselves differently in those with HIV. Only time will tell.

Andrew Shippy is a Senior Research Scientist at ACRIA.

Jerome Ernst is ACRIA's Medical Director.

Looking AIDS in the Mouth *(continued from page 13)*

Canker Sores
Canker sores (aphthous ulcers) are something most people have had at some point in their life, whether or not they have HIV. But in people with HIV, they may be slow to heal, and can grow quite large. They are not contagious and their cause is not known.

If they don't heal on their own, they can increase in size and cause a great deal of pain. This can lead to difficulty eating and even make swallowing dangerous. So, while people with normal immune systems can wait for these sores to heal on their own, people with low CD4 counts should get treatment no matter how small the sores are. There are ointments available, such as Kenalog or Lidex, or a dexamethasone rinse can be used. Prednisone or thalidomide pills are also available for more advanced cases.

Herpes
Oral herpes is caused by the virus known as HSV-1. This is the virus that causes cold sores (different from HSV-2 which causes blisters on the genitals). In people with a normal immune system, herpes blisters usually heal in a couple of weeks without treatment.

But once again, in people with HIV, the lesions may be larger and more painful, and they may lead to secondary infections and interfere with the ability to eat. People with lower CD4 counts should consider antivirals like Famvir, Valtrex, or Zovirax. While there are ointments available, they often don't work as well as systemic meds.

Gingivitis
ANUG (acute necrotizing ulcerative gingivitis), is a painful, inflamed, punched-out appearance of the gums, in the same category as Vincent's infection (trench mouth). It is often caused by stress – something many chronically sick people have to deal with, so the cycle becomes self-perpetuating. Often the only recourse is to keep the mouth as clean as possible, or just treat the symptoms with an antimicrobial mouth rinse or pain meds.

Home care is most important. You can see the dentist every week for a cleaning, but if you don't do that work in front of that mirror, youíre asking for trouble. Brush, floss, get frequent cleanings – these simple things will go a long way to maintaining a decent quality of life. Maintenance, maintenance, maintenance.

It's been a privilege caring for people with AIDS since the beginning of this worldwide epidemic. Difficult at times, but mostly rewarding. Every single patient deserves special attention, regardless of personal feelings and agendas. Dentists should never forget the simple reason we all got into this to begin with – to heal the sick.

Charles Dorato is a dentist in Greenwich Village, New York.

ACRIA Offers National Technical Assistance Trainings

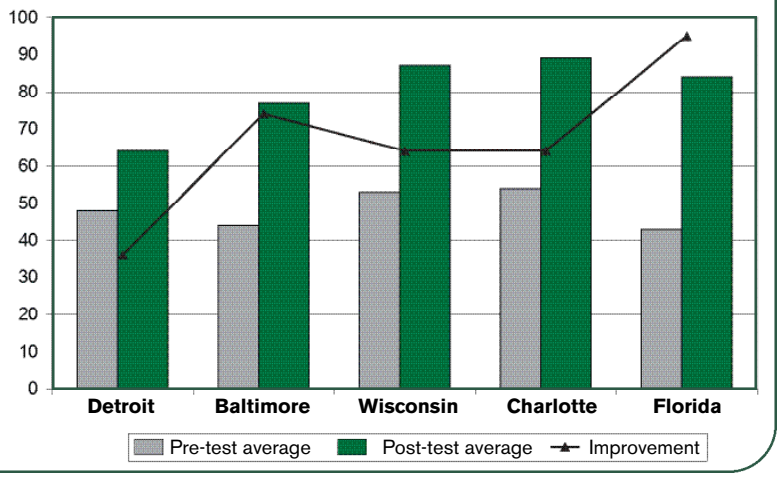
ACRIA is now offering our acclaimed National Training & Technical Assistance (NTA) on a regional basis across the country. We will tailor a 2, 3, or 4-day intensive training curriculum to the specific needs of agencies serving people with HIV in your area. In addition, all participants will receive our 400-plus-page Training Manual and other educational materials, and we will provide ongoing health literacy and treatment education technical assistance.

Topics covered in the training can include:

- HIV Transmission & Testing
- Understanding the Immune System
- HIV Overview
- HIV Treatment Update
- Resistance and Adherence
- HIV Treatment Guidelines
- Understanding Lab Results
- Managing Drug Side Effects
- Hepatitis C
- Women's Issues and HIV
- Clinical Trials
- Getting the Most from Your Healthcare Provider

Our latest training, in South Florida in late 2006, showed the best results ever: pre-tests resulted in an average score of only 43%, while post-tests showed participants' average score had risen to 84%. As the chart below illustrates, the NTA's positive results are improving over time.

For details, please call National Training & Technical Assistance Program Manager Lisa Frederick at (212) 924-3934, ext. 119, or email her at lfrederick@acria.org.



Older Adults Program

ACRIA's commitment to expanding services for older adults with HIV has now taken a practical turn, thanks to a generous grant from the M·A·C AIDS Fund. We are happy to announce the formation of Project SEE – Senior Education and Empowerment – in partnership with the Council on Senior Centers Services (CSCS), which represents 265 New York City senior centers and other organizations that provide services to senior citizens.

The goals of Project SEE are to ease access to services and support at senior centers, decrease dependence upon AIDS service organizations for HIV-positive seniors, and provide accurate and up-to-date HIV education and prevention information. The core goal is to break down preconceptions, misconceptions, and stigma related to HIV among staff and clients. Project SEE is aimed at nothing short of changing the culture of New York City's senior centers with regard to HIV.

ACRIA's HIV Health Literacy Program (HHLP) will work with CSCS to bring our education services, including technical assistance and tailored publications, into the senior centers of New York City. HHLP's educators will provide intensive training on all aspects of HIV—transmission, prevention, treatment, and care—to service staff of selected senior centers in neighborhoods with high rates of infection. We will provide ongoing technical assistance to the centers and their staff as they integrate HIV into the services they provide and work with both HIV-positive and HIV-negative seniors.

The *Update* has reported earlier on our Research Department's groundbreaking *Research on Older Adults with HIV* (ROAH) study and the interest it has generated, resulting in our partnering with Gay Men's Health Crisis (GMHC), the New York City Council, and others to develop new programming for this growing population.

Project SEE is the first fruit of these efforts, and we are grateful to M·A·C AIDS and CSCS for helping us to make it happen.

RTC Partners

ACRIA's HIV Health Literacy Program (HHLP) is entering its second cycle as a Regional Training Center for the New York City region under a contract with the New York State Department of Health AIDS Institute.

Under this initiative, HHLP educators train nonmedical HIV/AIDS service providers across the city to help them develop the knowledge and practical skills they need to help people with HIV. During the first cycle, from September through December 2006, HHLP provided training to 280 staff members of 55 agencies, from all five boroughs of New York City.

For this second cycle, we decided to take as many trainings as possible to the outer boroughs. We have been successful in this, thanks to the host agencies that have provided us with space to hold the trainings and the staff time to help us with outreach and organization in their neighborhoods.

Special thanks Linda Dianto and Lillian Agbeyegbe from St. Elizabeth Ann's Day Care and Staten Island Health Action, and also to Caroline Numa from FACES NY in Central Harlem; Sarah Frei and Christine Mastin from Jacobi Hospital, George Smith from Lincoln Hospital, Carrie Taft from United Bronx Parents, and Margaret Rivers from Beth Abraham Health Services for helping us bring trainings to the Bronx. In Brooklyn, we thank Audria Russell from Women in Need.

We are still looking for partners to help us bring our trainings to the agencies that need them. If you would like to become a host agency in New York City, please call Luis Scaccabarrozzi at (212) 924-3934, ext. 111.

ACRIA Researchers Present Findings

Members of ACRIA's Research Department continue to publicize the findings of its *Research on Older Adults and HIV* (ROAH), the first comprehensive study ever conducted of HIV-positive adults over the age of 50.

Stephen Karpiak, Ph.D., presented an overview of the study in a lecture at NDRI in February. He also presented at the Council on Senior Centers Services (CSCS) about the basis for the M·A·C AIDS-funded Project SEE (see above).

Andrew Shippy spoke about ROAH at a March symposium at the Pennsylvania/ Mid-Atlantic AIDS Education and Training Center, focusing on depression, stigma, and social networks.. The symposium, sponsored by The Johns Hopkins University School of Medicine, was entitled "The Graying of HIV: An Aging and Growing Population."

New ACRIA Staff

Please join us in welcoming these new staff members:

Mervin Otero, Research Enrollment Coordinator, is ACRIA's new clinical trials recruiter, responsible for educating potential participants, case mangers, and providers on our enrolling and planned clinical trials. During Mr. Otero's fifteen years in HIV/AIDS services, he has been involved with the development of HIV/AIDS education and counseling programs for incarcerated men in the New York State Department of Correctional Services and assistance with the Osborne Association's anonymous HIV testing program.

Rafael Madrid is the HIV Health Literacy Program's new Local Technical Assistance Manager, succeeding Carlos Santiago. Mr. Madrid earned a Ph.D. in psychology in his native Chile and since then has been working in the HIV field. He has been a case manager at Aid for AIDS and Saint Vincent's Catholic Medical Center and has worked in an infectious diseases clinic as a health educator.

Benjamin Bashein is ACRIA's new Development Director, bringing with him ten years of experience leading fundraising and communications for not-for-profit organizations. Among the organizations with which he has worked are the Grand Street Settlement on the Lower East Side, Doctors of the World, and Amnesty International.

generous contributions

The following persons, corporations and organizations made major donations between December 21, 2006 and March 30, 2007 to support ACRIA's research and education efforts:

Boehringer Ingelheim Pharmaceuticals
The Elton John AIDS Foundation
GlaxoSmithKline
Kern McNeil International
Mizuho USA Foundation, Inc.
New York State Dept. of Health AIDS Institute
Paul Rykoff Coleman Foundation
Pfizer Foundation Volunteer Program
RMF Foundation
Schechter & Brucker, P.C.
The Long Island Community Foundation
The Olive Bridge Fund
UPS Capital Insurance Agency
Gail Alcalay and Mark Goldstein
Doris Ammann
Michael J. Atmore
Sara D. Back
Joseph P. Barri
Kim Bates
Michael Beatty
Alexander Beck
Dr. Kenneth Berger
Arlene and Jerry Binkowitz
Mark B. Black
Shirley and Max Boman
Watson F. Bosler
Jeffrey J. Bright
Larry T. Broughton
Alexis Bryan
Don Buchanan
Richard Buckheit and David W. Bell
William Byrnes
Marisa Cardinale
Rita and Michael Carey
Amy Chan
Thomas Cherry
Kendell J. Cronstrom
Scott Dainton
Grazia D'Annunzio
Anthony J. De Mare
Anthony Depersia
Alan Dlugash
Randall G. Drain
Glenn Dranoff
Frederick and Isabel Eberstadt
Melanie Ecung
Dennis W. Emerling and Glenn D. Bundy
Jamison Ernest
Gerald and Reba Faigeles and Mrs. Mitchell Fleiss
John-Andrew L. Forde and Alvaro Martinez-Fonts
Gabriella Forte Glantz
Eric Freeman
David J. Gale
Claudia L. Ganz
Paula E. Garzon
James Gilday
Raul Godoy
Dr. Kay E. Goldberg
Mark E. Goldberg
Caryl Goldsmith
Karen and Charles Goss
Michael L. Gowing
Paul D. Green
Jeffrey B. Green
Gary Greener
David Gross
Fredric Hanson
Pam Hassenfelt
Robert Herzenberg
Donald A. Insley
Jerry Jacobs
Simon Katz
Gary M. Killingsworth
Paul Kimball
Charles Klein
Irwin Krieger
Peter Charles Lanthier
Winston Lapham
Harison T. Lefrak
Jean-Pierre and Rachel Lehmann
Annie Leibovitz
Dean T. Lewallen
Paul J. Lobello
Jennifer J. Mach
Anthony Marzani and Harry Schroder
Stephen Matchett
Dan C. Matherly
Alison Mazzola
Edward R. McCay
Patrick McMullen
John Montgomery
Alain Montour
Henry and Rose Moskowitz
William R. Nye, Ph.D.
Frances M. Parisi
Jay P. Paul
Evan Pazol
George L. Peabody
Richard Pleak
Mark S. Quigley
David Quinn
Maurice Reder and John Nieman
Clifford Richner
David C. Rick
Kenneth Rosenbaum
Brian G. Roskam and Mike Werb
Hal R. Rubenstein
Mrs. Lily Safra
Roger E. Schechter
Eric Schumacher
David Shinder
Samuel J. Silling
Bonnie J. Slotnick
Joette Spinelli
Petter Stange
Leon Sussman and Jonathan Green
Richard S. Swenson
Jeffrey S. Tauber
Dan Tietz
Ann N. Tsubota
Dr. W. Mark Warfel
Lorin A. Wiseman
Aurelio R. Zaino
Christian Zimmermann and Richard Kielar

AIDS COMMUNITY RESEARCH INITIATIVE OF AMERICA

230 West 38th Street, 17th Floor
New York, N.Y. 10018
T 212 924-3934 F 212 924-3936
www.acria.org

Change Service Requested

NON-PROFIT ORG.
U.S. POSTAGE PAID
Red Bank, NJ
Permit No. 556

***ACRIA Update* is sponsored in part by an unrestricted educational grant from:**

GlaxoSmithKline