

**Metabolic and Nutritional Aspects of HIV Infection
in the Era of HAART**

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Metabolic and Nutritional Aspects of HIV Infection in the Era of HAART

By Marshall J. Glesby, MD, PhD

With the advent of highly active antiretroviral therapy (HAART), AIDS-related wasting has become a less prevalent problem. However, issues related to nutrition and body composition have clearly not disappeared. In recent months, researchers and clinicians have reported a variety of metabolic abnormalities in persons on HAART. At first came reports of diabetes in persons on protease inhibitor therapy. This was followed by reports of abnormal accumulations of fatty tissue at the back of the neck, termed buffalo humps. Persons living with HIV infection and their care providers also began to note changes in body fat distribution manifested by skinny arms, legs, buttocks, and cheeks with prominent fat accumulation in the abdomen and breast enlargement. This syndrome has been termed lipodystrophy (also known as "crix belly" or "protease paunch"). Attention has also turned recently to elevations in blood lipid levels in persons on HAART.

Much remains unknown about the prevalence of these metabolic abnormalities and their cause. Even less is known about how these problems should be managed medically. The long term consequences of abnormal fat distribution, high blood sugars, and elevated lipid levels are of concern because of the potential increased risk of atherosclerosis (hardening of the arteries) which could lead to heart attacks and strokes.

Clearly more research into these metabolic problems is of tremendous importance. Having recognized this need and not being encumbered with a bureaucracy, ACRIA has quickly launched two studies that should provide important insights into the mechanism and management of two of these problems. Our study of glucose tolerance in persons initiating protease inhibitor therapy is well under way and has recently expanded to sites in Baltimore, Boston, and

Philadelphia. We have also initiated one of the first studies of a possible treatment of lipodystrophy -- a 24 week trial of human growth hormone.

In fact, body composition and nutrition have been a focus of ACRIA's research efforts for the past few years. This focus has been driven largely by the expertise provided by three members of our Board of Directors who are internationally renowned authorities in the field: Drs. Douglas Dieterich, Donald Kotler, and Judith Rabkin. When little emphasis was being placed on testing interventions for wasting, ACRIA initiated and sponsored two studies, one comparing two nutritional supplements to prevent weight loss, and another looking at testosterone and/or Met-Rx- to treat weight loss. Results of the former study were presented at the 12th International Conference on AIDS in Geneva, and the latter study is still enrolling. Furthermore, ACRIA has played a major role in studying oxandrolone, an anabolic steroid as a treatment for wasting in both men and women.

This issue of ACRIA Update is devoted to metabolic and nutritional aspects of HIV infection in the era of highly active antiretroviral therapy (HAART). We have assembled a group of writers to contribute their expertise in this field. Tim Horn, co-author of Treatment Action Groups (TAG) Wasting Report, has summarized the available data on body composition changes and current treatments for wasting. Since anabolic steroids are in wide use, they are the subject of a separate article by Nelson Vergel, who is a widely respected expert in the field and Director of Program for Wellness Restoration (PoWeR). Edwin Krales, MS, CDN, a nutritionist and Outreach Coordinator at the Momentum AIDS Project in New York, has contributed his talents in the area of practical dietary considerations for persons on combination antiretroviral therapy. We would also like to thank Dr. Donald Kotler who served as guest editor for this issue of ACRIA Update. While there are many unanswered questions posed in this issue, we hope that our research efforts and those of our colleagues elsewhere will shed further light on the complicated metabolic picture that is emerging in persons with HIV infection.

Wasting and Metabolic Changes in the Era of HAART

By Tim Horn

At first glance, wasting syndrome - an often chronic and sometimes life-threatening complication experienced by many people living with HIV and AIDS - appears to be a thing of the past. Numerous reports from both clinical trials and large cohort studies have yielded some incredibly impressive news: HIV-infected patients on highly active antiretroviral therapy (HAART), especially those in the advanced stages of disease, are getting a second chance at life and good health. Undetectable viral loads and soaring T-cell counts aside, HIV-infected people are living longer, getting fewer opportunistic infections (OIs), and are experiencing robust increases in body weight. But do these much heralded reports of weight gain necessarily mean that wasting is no longer a problem? Wasting Syndrome: A Primer All too often, wasting syndrome is assumed to mean only one thing: weight loss. While the term wasting syndrome certainly does embody profound weight loss, it also means progressive loss of muscle mass with associated fatigue. Although the Centers for Disease Control has not altered its official definition of wasting to include decreases in muscle mass, numerous researchers and healthcare providers firmly believe that changes in muscle mass are equally, if not more, important than those seen in body weight. Unfortunately, much of the research generated thus far regarding the possible causes of and treatments for wasting have only used body weight as a measurement. Clinical trials are beginning to incorporate body mass measurements - tests to measure body composition - such as bio-electrical impedance analysis (BIA; see page 8) and dual-energy x-ray absorptiometry (DEXA).

There are, essentially, two different types of wasting. The first type reflects periods of rapid weight loss and muscle wasting. This type is most commonly found in people experiencing particular

OIs, such as Mycobacterium avium complex (MAC) and tuberculosis. Given the proven benefits of HAART and prophylaxis, people living with HIV now stand a much better chance of either avoiding or recovering faster from an OI. This is certainly good news in terms of preventing one of the most common types of wasting (also referred to as cachexia). Patients who experience profound wasting as a result of an OI have an extremely difficult time regaining weight and muscle mass.

The second type reflects more gradual losses in both weight and muscle. Unlike the first type, which most often applies to patients with advanced HIV disease, gradual wasting can occur at any time and for any number of reasons and may be due to HIV infection itself. For starters, many people with HIV are simply not eating the right amounts or kinds of food, such as those high in protein and micronutrients (ie., certain vitamins and minerals). Some of the documented causes of this include: lack of nutritional knowledge; depression; economic hardship; impaired taste; nausea or vomiting (usually caused by adverse drug effects); and dietary restrictions, especially those surrounding multiple daily doses of certain antiretroviral drugs.

It is essential that people with HIV consume enough of the right kinds of food. Some studies have shown that, because HIV is a chronic infection, the body requires greater amounts of energy to consistently fuel itself. Even if viral load is being kept in check by HAART, additional energy is still required by the immune system to help build new cells and repair damaged tissues. Certain organs, such as the liver and kidneys, also require greater amounts of energy and certain micronutrients to efficiently process the relatively high levels of toxic therapies being consumed on a daily basis.

Malabsorption, a problem not uncommon among people with HIV, is another cause of gradual wasting. Foods that are swallowed require a great deal of processing by the gastrointestinal system (the gut) so that they can effectively be broken down into their most basic forms - either protein (amino acids), fat (triglycerides and cholesterol), or sugar (glucose) - and adequately absorbed by the intestine. Drug side effects, such as diarrhea and vomiting, can prevent food from staying in the gut long enough to be properly digested and absorbed. Diarrhea and vomiting may also be signs of an underlying infection or complication. Infections such as cryptosporidiosis and microsporidiosis can both cause diarrhea and drastically impair the intestine's ability to absorb essential nutrients. Other infections and complications of the gut include CMV, lymphoma, and KS, all of which can impair digestive function and absorption without causing overt symptoms (ie., severe diarrhea).

There have been numerous reports of people on HAART who are experiencing significant improvements in their overall immune status and, as a result, are much less likely to develop an OI. Yet, it has not been adequately determined if, for example, 400 T-cells post-HAART are much better than 100 T-cells pre-HAART. It is still too early to throw caution to the wind; drug- or infection-induced symptoms such as diarrhea and weight loss should be brought to the attention of a healthcare provider immediately.

In recent years, a significant amount of research has focused on metabolic problems that can cause wasting. Metabolism - an intricate system by which nutrients are either broken down (catabolism) for energy purposes or stored (anabolism) for later use - has been shown to become highly irregular in people with HIV. More simply, metabolism is the body's utilization of energy from foods. To fuel its energy needs, the body first catabolizes glucose and lipids circulating in the blood ('free floating' nutrients); amino acids are spared so that they can be used to build muscle mass and other substances such as enzymes and antibodies. If free-floating nutrients are used up and not adequately replaced, the body will then begin breaking down stored nutrients - usually lipid and cholesterol deposits (fat mass) - to keep up with its energy needs; stored amino acids, such as those in muscle, are spared during prolonged fasting and used as energy only as a last resort. In people with HIV, this entire process is often reversed. We know this because people with HIV often have elevated glucose levels and fat levels (hyperlipidemia) and, especially

during an OI, have a negative nitrogen balance (a marker of muscle loss). While negative nitrogen balances are certainly a sign that muscle wasting is occurring, the connections between elevated glucose levels, lipid levels and muscle loss have not yet been fully determined. However they are characteristic of cachexia.

Like many other chronic diseases, HIV and AIDS-related opportunistic infections put a tremendous amount of pressure on the body to rapidly expend energy. Because amino acids are much easier to convert into energy than lipids, the body begins catabolizing both free-floating and stored amino acids to fuel itself. In turn, muscle mass slowly becomes depleted while fat mass continues to accumulate. This is potentially dangerous, considering that muscle mass is necessary for survival.

How nutrient metabolism becomes altered in HIV-infected people is not entirely understood. While a number of studies have demonstrated a strong association between the severity of immune suppression and the likelihood of developing wasting, it is still not entirely clear whether or not immune system damage is an underlying cause of wasting. In its response to HIV and OIs, an abundance of hormone-like substances called cytokines are produced by cells to more effectively communicate with each other. While these cytokines play an important role in bolstering the immune response against an infection, prolonged and excessive amounts have been shown to result in significant problems. The cytokines interleukin-1 (IL-1), interferons (alpha, beta, and gamma), and tumor necrosis factor (TNF) have all been shown to induce the classic symptoms experienced during an illness. These include some that are prominent in HIV disease: fever, nausea, decreased appetite, fatigue, diarrhea, anemia, and confusion. Still it is not entirely clear whether or not hyperactivity of the immune system directly causes wasting or, more specifically, muscle loss.

Numerous studies have, however, implicated hormones and the immune system as likely culprits. Many people with HIV experience significant endocrine (hormonal) problems such as decreased production of both insulin-like growth factor (a precursor of growth hormone) and testosterone. Anabolic hormones such as these play a large role in promoting protein anabolism and muscle growth. Hypogonadism, or decreased testosterone production, is frequently reported in HIV-infected people; rates vary from 25% to 45%, depending on the stage of HIV disease. Possible causes of hypogonadism include testicular infections, drug side effects (particularly from ketoconazole, ganciclovir, and megestrol acetate), and elevations in cortisol levels (a hormone produced by the adrenal glands). No matter what the cause, low testosterone levels have been directly associated with fatigue, depression, decreased sex drive, and weight and muscle loss.

As the name syndrome implies, wasting is a multifactorial problem. One or all of the above mentioned problems can contribute to HIV-related wasting, sometimes gradually throughout the course of disease or sometimes rapidly in the presence of an OI. How each of these complications relate to each other and wasting is not entirely understood and are not likely to be worked out completely in the near future.

Treatment

Given the numerous possible causes of wasting syndrome, it should come as no surprise that treatments for wasting are equally complex and, unfortunately, cannot be universally prescribed. No "standard of care" for wasting exists; in fact, there is little consensus regarding the best way to prevent and treat wasting, especially muscle loss. Yet, there are a number of treatment strategies that have been proven effective in terms of weight gain and, in some cases, muscle growth and maintenance.

First and foremost, dietary intervention is crucial for virtually all HIV-infected individuals suffering from mild to severe forms of weight loss. Forms of dietary interventions include nutritional

counseling and oral nutritional supplementation. In terms of counseling, a registered dietitian can help identify weaknesses in an existing diet and make suggestions regarding dietary needs and how best to tailor them to meet individual tastes, schedules (ie., drug dosing schedules), and tolerances. Nutritional supplementation can also be extremely useful. A number of oral supplements - including Ensure, Sustacal, Citrisource, Resouce, Jevity, and Replete - are widely available, but can be expensive. To meet individual dietary needs and/or restrictions, some are free of wheat, dairy (lactose), or other components that are frequently difficult to digest. Very few clinical trials of oral supplements have focused on whether or not they can sustain weight in HIV-infected individuals (see ACRIA News).

There are a number of treatments available to control symptoms, including drug side effects, that make eating undesirable. Drugs to control nausea and vomiting (antiemetics), diarrhea (antidiarrheals), and decreased appetite (appetite stimulants) are widely available. Treatments such as Marinol» (gel-caps containing THC, the active ingredient in marijuana) and megestrol acetate (Megace») have been shown to significantly increase appetite. However, as is the case with megestrol acetate, patients who do manage to achieve weight gain often do so in the form of fat, not muscle. In fact, megestrol acetate - a synthetic form of the female hormone progesterone - has been shown to decrease testosterone production in men.

Treating an active opportunistic infection, especially one that causes malabsorption, can halt and possibly reverse weight loss. Treatments for conditions such as MAC, TB, and intestinal diseases such as CMV and KS have been shown to be extremely effective and are often associated with increased weight. Unfortunately, there are no effective treatments for intestinal diseases such as cryptosporidiosis and microsporidiosis, however a number of recent reports have suggested that HAART may be extremely helpful in terms of boosting the immune response against these chronic infections and ultimately increasing weight. But, like appetite stimulants, treatments for OIs associated with weight gain usually contribute to fat accumulation, not muscle.

Treating metabolic disorders associated with wasting has been a large focus of research over the past few years. In particular, results from clinical trials of anabolic therapies have suggested that certain agents - including testosterone, growth hormone, oxandrolone, nandrolone, and oxymethalone - can significantly increase muscle mass in HIV-infected people with wasting. Interestingly, weight gain as opposed to muscle mass does not appear to be a significant benefit of anabolic steroids and might be best used in combination with appetite stimulants and/or nutritional supplements to boost weight.

In terms of treating immune system disorders, promising results have been seen using the drug thalidomide - once banned because of its ability to cause birth defects in pregnant women taking the drug - which apparently reduces levels of the inflammatory cytokine tumor necrosis factor. Yet, the most promising therapy in terms of stabilizing the immune system has been HAART. By drastically reducing the amount of virus circulating in the body, HAART allows the immune system to recover from the onslaught of HIV. In fact, a large number of studies have demonstrated that patients on HAART, especially those with wasting, are gaining weight while on therapy. At first, this weight gain was heralded as a significant triumph. As of recent, however, many researchers, healthcare providers, and patients have begun to wonder what much of the weight gain is really all about.

Lipodystrophy: A New Type of Wasting?

Little less than a year ago, reports began to surface that people on HAART were experiencing significant increases in weight... and waist size. Over time, the number of reports increased and were classified as a distinct syndrome associated with HAART. Along with fat mass accumulation around the waist, the syndrome was also characterized by the loss of the layer of fat under the skin, making veins seem to protrude; wasting of the face and limbs; narrowing thighs; breast enlargement in women; and the accumulation of fat between the shoulder blades. The syndrome,

now dubbed lipodystrophy, has become one of the most closely watched manifestations in people with HIV. While numerous researchers and clinicians have directly associated the lipodystrophy with protease inhibitor therapy, some experts argue that the syndrome is associated with the biological consequences of HAART, not the drugs themselves.

Cases of lipodystrophy have now been reported among people taking any of the four approved protease inhibitors. Although lipodystrophy's early nickname was "Crix belly" (after Crixivan®), it is now clear that it is not specific to one drug. In fact, there have been a number of reports of lipodystrophy occurring among HIV-infected patients taking non-protease inhibitor-based HAART combinations.

Estimates of the proportion of people who develop lipodystrophy while on HAART have ranged from 11% to 64%. While the obvious discrepancy in this range is highly suspect, it is important to note that some researchers only reported cases in which body changes were physically apparent, while others used scans (ie., MRI, DEXA, CT scan) to measure very subtle body changes. In light of these varying study methods and results, further research into the epidemiology of this syndrome is warranted.

Many people on HAART are also experiencing metabolic complications such as elevated glucose levels and glucose intolerance, hyperlipidemia, hypertension, along with mild elevations in cortisol secretion and hypogonadism, all of which have been associated with body composition changes in HIV-infected patients. Yet, many people on HAART have only specific metabolic complications sometimes in the presence of body composition changes and sometimes without. In turn, there is not even consensus on exactly what HIV-related lipodystrophy includes; a case definition of the syndrome does not exist.

Research into the this syndrome is still in its infancy. Preliminary results from one study have demonstrated that protease inhibitors can have a direct effect on fat metabolism. However, some researchers are not convinced that protease inhibitors are necessarily to blame. According to Dr. Donald Kotler, ACRIA Vice President and a researcher at St. Luke's Roosevelt Hospital, the major weaknesses in the protease inhibitor argument are that: 1) Some HIV-infected patients with lipodystrophy are not taking protease inhibitors; 2) A similar syndrome was seen in the past - although more rarely; and 3) A similar syndrome exists in HIV-uninfected subjects. Lipodystrophy has been found in patients with diabetes mellitus, Cushing's syndrome, and other chronic diseases. As with these other diseases, HIV-related lipodystrophy is associated with body composition changes in both men and women, glucose intolerance, hyperlipidemia, hypertension, elevations in cortisol secretion, and decreased testosterone levels. A common thread in the syndromes seen in both HIV-positive patients on HAART and HIV-negative patients with other diseases, may be the presence of a 'chronic stress response'; even in the presence of therapy intended to control certain aspects of the disease, the metabolic system remains highly dysfunctional. The similarities in syndromes are worrisome, since the syndrome in HIV negative patients is associated with accelerated cardiovascular disease, stroke, and osteoporosis.

To date, virtually no anti-wasting/weight loss therapy has shown to be effective in terms of halting or reversing lipodystrophy. Clinical trials are currently being conducted to study possible treatments (ig., growth hormone) for lipodystrophy, including one at ACRIA. Anecdotal reports regarding the efficacy of anabolic compounds, anti-inflammatory drugs (ie., prednisone), and various alternative treatments (non-pharmaceutical compounds such as alpha-lipoic acid) have suggested that therapeutic intervention may be helpful.

Blood Lipid Levels

By Marshall J. Glesby, MD, PhD

Lipids (fats) are needed by the body to build cell membranes, make certain hormones, and store energy. Cholesterol and triglycerides are the main types of lipids measured in routine blood chemistry tests. Because lipids do not dissolve in water, they are carried in the blood by special proteins made in the liver. The two main forms of protein-bound cholesterol are called LDL and HDL cholesterol, which are sometimes referred to as "bad" and "good" cholesterol respectively. These terms come from the fact that high LDL levels increase the risk of heart attacks and stroke, while high HDL levels are associated with a decreased risk of these conditions. Measurements of LDL and HDL are usually not a part of routine blood work but may be ordered as part of a special lipid panel. Very high triglycerides can be a concern in the short term because of the risk of pancreatitis (inflammation of the pancreas), and there may be a longer term increased risk of heart attack and stroke associated with high triglycerides.

Many persons on combination therapy are developing abnormally high blood lipid levels, particularly triglycerides. High LDL and low HDL cholesterol levels also seem to be relatively common in patients on protease inhibitors, and may increase the risk of heart attack and stroke. A recent report of two men ages 26 and 37 with high blood lipid levels who developed coronary artery disease while on protease inhibitor therapy highlights the potential risk of lipid elevations.

It is not known if and how protease inhibitors cause lipid elevations. Some researchers have suggested that the drugs act to inhibit the function of human protease enzymes and thereby affect the function of other proteins involved in lipid metabolism.

Protease inhibitors are also known to affect the function of liver enzymes called cytochrome P450, which are involved in the metabolism of many compounds. These effects on cytochrome P450 are why many drugs interact with protease inhibitors. Researchers have also theorized that the effects of protease inhibitors on cytochrome P450 may affect the body's metabolism of lipids leading to elevations. Further research is ongoing in an attempt to sort this out.

In the mean time, what should persons taking protease inhibitors do? Many physicians are now testing blood lipid levels on a regular basis (for example, every 3 to 6 months) in their patients on protease inhibitors. These blood tests are optimally done in the fasting state, since food elevates lipid levels, especially triglycerides. Dietary management of elevated lipids may be tried, but many persons ultimately need medication to lower lipid levels. Doctors prescribing cholesterol-lowering drugs must be aware of all of the other medications that the patient is taking because of the potential for drug interactions with protease inhibitors.

Diabetes and HAART

By Marshall J. Glesby, MD, PhD

Diabetes mellitus is a group of diseases which are characterized by elevated levels of blood glucose (sugar). In the spring of 1997, reports began to surface about a possible association between protease inhibitor use and the development of diabetes mellitus, or worsening of glucose control in persons already diagnosed with diabetes. Cases have been seen in association with all four marketed protease inhibitors, and the average time to onset was 101 days after starting protease inhibitor therapy. Although 190 new cases of diabetes in patients on protease inhibitors were reported to the Food and Drug Administration (FDA) as of November 1997, the true incidence of the problem is difficult to determine from these reports, since the exact number of persons taking the drugs and for how long is not available. Furthermore, it is unlikely that all cases of diabetes were actually reported by physicians to the FDA. A recent study from the Johns Hopkins Hospital, however, suggests that new onset diabetes is relatively uncommon in persons taking protease inhibitors.

How protease inhibitors may cause diabetes or worsening of blood sugar control in diabetics is not known definitively. Some researchers have reported elevated levels of insulin in persons on protease inhibitors. Insulin is a hormone made by the pancreas which acts to lower blood glucose levels. Diabetes may result from inadequate secretion of insulin from the pancreas or from defects that make cells in the body less sensitive to the effects of insulin (insulin resistance). Elevated insulin levels suggest that insulin resistance is present. The body tries to compensate for this resistance by producing more insulin, and if it fails to compensate sufficiently, high glucose levels (hyperglycemia) or actual diabetes may result.

Further research is ongoing to determine the frequency of diabetes, risk factors for its development, and why it occurs. Included in this research effort is an ongoing ACRIA study of responses to the oral glucose tolerance test in persons initiating protease inhibitor therapy (see [Currently Enrolling Trials](#)).

Should all persons on protease inhibitors be monitored for diabetes? There are no definitive guidelines, but it makes sense to have blood glucose levels checked periodically. Glucose levels are usually included in routine blood chemistry tests. Persons on protease inhibitors should be aware of the usual symptoms of diabetes which include: increased thirst and appetite, increased frequency of urination, unexplained weight loss, and blurry vision.

Anabolic Steroids: A Practical Guide

By Nelson Vergel

For those who need to regain their lost lean body mass (LBM), anabolic steroids are a possible answer. These compounds are being prescribed increasingly by some physicians to treat their HIV-infected patients. Androgenic/anabolic steroids are synthetic analogs of the natural androgenic "male" hormone called testosterone that is produced primarily in the testes in males and in the ovaries in females. Many of them were originally synthesized in the 1930's and 40's in an effort to deliver a more optimal protein tissue building (anabolic) effect with less of the potential for masculinizing (androgenic) side-effects that are characteristic of testosterone itself. Although they are not part of the "standard of care" for HIV disease, anabolic steroids have gained acceptance in reversing the loss of LBM, strength, sexual function, appetite, and general sense of well being in HIV positive patients. However, they have received a lot of bad press due to their abuse in the bodybuilding and sports world and were banned for general public use with the Anabolic Steroid Control Act enacted by the U.S. Government in 1990. This act made anabolic steroids Class III regulated drugs, available by prescription only to people with justifiable health problems. All anabolic steroids but one have been approved to treat anemia related to renal insufficiency and other non-wasting related disorders. So physicians who prescribe these compounds to treat LBM loss are doing so under an "off-label", yet legal, application.

Women and Children Often Forgotten

Women and children are often ignored when it comes to wasting. Physicians may be afraid to prescribe anabolics to women because of the potential to masculinize them. Women also have the added pressure from society (and sometimes their physicians) to be thin, so wasting may go unreported and untreated in this population. Most anabolics will stunt growth in children (children with HIV also have slow growth problems). Some anabolics agents like human growth hormone (Serostim »), and the oral anabolic steroid oxandrolone (Oxandrin») appear to be safe and effective for women and children with HIV. However, they are both very expensive, so many HIV-positive people have to turn to pharmaceutical compassionate use programs, which can be difficult to access. Furthermore, no State AIDS Drug Assistance Program (ADAP) includes these compounds in their list of approved drugs for those who are uninsured.

How do Anabolics Work?

The anabolic effect of anabolic steroids is elicited by the action of the steroid on androgen receptors in muscle tissue. The steroid binds to the receptor and is carried to the nucleus of the cell where it instructs the cell to increase protein synthesis. This results in hypertrophy (growth) of the cells and the muscle tissue itself.

The different molecular configurations of the various anabolic steroids cause significantly different responses, and even a subtle change of one atom can elicit a unique response for a specific steroid.

Potential Side-Effects

Testosterone, being the most androgenic of all compounds soon to be discussed, is responsible for most of the side effects cited in the literature. Long term use of moderate to high doses (greater than 200 mg/week) may cause side effects which can include acne in the back and shoulders, hair loss, testicular atrophy (reduced size of testicles), mood changes, prostate enlargement, facial hair growth in women, and water retention. Other anabolic compounds are more benign than testosterone and still very effective in their anabolic action.

Oral steroids may cause liver toxicity which manifests as increases in liver function tests in the blood. Dr. Patricia Salvato from Houston has found that common injectable steroids have not caused this kind of liver burden in over 200 of her patients using anabolic steroids. Some people prefer injectables to oral steroids for this reason. Injectable steroids, however, may appear to cause elevated liver function tests during increased exercise and other stress in the body. Liver test elevations usually reverse with cessation of the steroids.

INJECTABLE ANABOLIC STEROIDS

Testosterone

Testosterone is the primary androgenic/anabolic hormone in the body of men and women. The forms of injectable testosterone available in the U.S. are testosterone cypionate and testosterone enanthate, both of which maintain blood levels of testosterone for a number of days. Without the cypionate or enanthate "carriers," testosterone is cycled through the body in several hours, so these carriers are important for ease of use, as they allow weekly rather than several times per day administrations. Both products come in a 10-ml bottle with 200 mg/ml. Many physicians prescribe anywhere from 200 mg/every other week to 100 mg/week.

The first controlled study on high dose testosterone enanthate with normal HIV negative men was published in the New England Journal of Medicine on July 4, 1996. This study involved the use of 600 mg per week of testosterone enanthate for ten weeks, and was controlled for weight training. Four different combinations were evaluated; testosterone with exercise, testosterone without exercise, exercise without testosterone and no exercise with no testosterone. Those who were given testosterone plus exercise had the greatest increase in muscle strength and greater increases in body weight compared to the other groups.

Nandrolone Decanoate (Deca Durabolin®)

Nandrolone decanoate is felt to be one of the best anabolic steroids for men because it has much less potential for side effects than testosterone, yet it still has basically as much or more anabolic potential as testosterone. The decanoate "carrier" delivers nandrolone over a slightly longer period of time than a cypionate carrier, but weekly injections are still preferred. The package

insert administration recommendations of the manufacturers of nandrolone decanoate have recently been changed from bi-weekly injections to weekly injections. Keep in mind that nandrolone decanoate is the generic version of Deca Durabolin» and can be purchased for about one third the cost per vial.

Nandrolone does not produce as much androgenic activity in the body as testosterone, so there is considerably less potential for hair loss or prostatitis (inflammation of the prostate).

Dr. Julian Gold in Australia published two studies in 1996 and 1997 showing that 100 mg of nandrolone decanoate produced significant increases in lean body mass and quality of life for HIV positive male patients. At the XI International Conference on AIDS, in July 1996, Dr. Gary Bucher of Chicago's Center for Special Immunology, presented the first placebo controlled study of the anabolic steroid nandrolone decanoate with 73 HIV patients over 12 weeks. There was a significant increase in lean body mass, even though there was no specific weight training protocol, and we know that steroids exert their greatest effect on gaining LBM when weight training is performed. Hematocrit increased significantly.

There are several points that should be noted. First, the dosage used in this study is rather low at 100 mg of nandrolone decanoate per week. For instance, a study underway at University of Southern California at Los Angeles that was being directed by Dr. Fred Sattler, is using 600 milligrams of nandrolone per week. This higher dose is being studied because there is good reason to believe that it will be much more effective for increasing lean body mass yet still be safe. There are several other studies in progress using these higher dose.

ORAL ANABOLIC STEROIDS

Stanozolol (Winstrol»)

A study that reviewed patient charts of HIV-positive men given stanozolol showed that it may be valuable for lean body mass improvement at doses of only 6-12 mg per day. stanozolol is priced much lower than oxandrolone at about \$80 per 100 two-milligram tablets. So, this makes it much more accessible than oxandrolone, which costs about \$300 per 100 2.5 milligram tablets. Stanozolol is an unusual compound that is considered to be relatively free from side effects, even for women, because like oxandrolone, it has a very low androgenic potential. While the previously mentioned study on HIV-positive men using stanozolol showed significant bodyweight improvements from doses as low as 6 and 12 milligrams per day, anecdotal information suggests that stanozolol exerts its greatest effects when combined with anabolic steroids like nandrolone or testosterone. An appropriate dose for stanozolol used in combination with either nandrolone or testosterone appears to be between 6-18 mg/per day for men, and 4-12 mg per day for women. Stanozolol, for unknown reasons, also appears to have a positive effect on libido, and much more so than oxandrolone. Watch for liver enzyme increases if taking protease inhibitors and stanozolol.

Oxandrolone (Oxandrin»)

Unlike all the other anabolic steroids, oxandrolone is an oral steroid specifically approved for the treatment of weight loss due to trauma, sepsis, surgery, and other conditions. Oxandrolone is also very mild and, according to the manufacturer, not liver toxic. However, there have been reports of people on ritonavir or other protease inhibitors who have experienced increases in their liver enzymes, which made them stop taking oxandrolone.

Oxandrolone does not virilize women in low to moderate doses and it has been used in children also. It is an expensive drug, and the manufacturer has created an expanded use program which is probably the most accessible in the AIDS industry. Dosages of 20-60 mg/day for men, and 5-20

mg/day for women have been used successfully. ACRIA is participating in a multicenter study of oxandrolone for women with unintentional weight loss and recently completed a similar study in men.

Oxymetholone (Anadrol®)

Oxymetholone is an oral anabolic which was recently reintroduced in the US market last year. It used to be called the "gorilla" steroid by bodybuilders in the 1980's.

A study published in 1996 in the British Journal of Nutrition showed that this powerful oral anabolic steroid improves body weight with what appeared to be no significant side effects in HIV-positive men and women. Oxymetholone was given for thirty weeks at a dose of 150 mg per day. Weight gain averaged 14.5% of bodyweight, which is significant because there was no exercise program instituted, and it is known that anabolic steroids exert their greatest effect when weightlifting is used. Notably, even the subset of patients burdened with AIDS-related infections continued to gain weight on oxymetholone.

While oxymetholone is considered to be a harsh steroid with a high potential for side-effects, the subjects were reported to have no significant problems with liver function, water retention, virilization, and several side-effects thought to be associated with its use. The dose was three times what many bodybuilders would use and the treatment period was considerably longer. Since oxymetholone was brought back to the U.S. early in 1998, we will see how effective it is and also see whether there actually are side-effects in real world situations with HIV positive people.

Optimum Nutrition and LBM

Anabolic steroid therapy is much more effective when a high-protein (one or more grams of protein per pound of bodyweight per day) slightly hyper-caloric diet is maintained consistently, along with resistance weight training (one hour, three to four times a week) and an adequate micronutrient program. Whey protein, a byproduct of cheese manufacturing, is the most bioavailable protein known (eggs and meats follow). One small but interesting study showed that over a three month period HIV patients using whey protein gained between 4 and 15 pounds (without anabolic steroids). This type of new "high-tech" protein has also been shown to increase tissue glutathione levels and glutathione content in blood mononuclear cells, which no other commonly available protein supplement seems to do. It also does not seem to cause GI disturbance, like gas, bloating and diarrhea, commonly seen with other protein supplements.

Steroid	Anabolic*	Androgenic*	Reported Doses*	Side Effects
Nandrolone Decanoate Deca Durabolin (injections) Available in the U.S.	High	Low to Medium	Men 100-200 mg/wk Women 25	Some water retention
Methenolone Primobolan Depot (injections) Available in Europe & Mexico	Low to Medium	Very Low	Men 100-600 mg/wk Women 25-100 mg/wk	No information available
Methenolone/Primobolan (Oral - tablets) Available in Europe & Mexico	Low to Medium	Very Low	Men 50-200 mg/day Women 100 mg/day	No information available
Stanozolol Winstrol (injections) Not available in the U.S. Can be	Low to Medium	Very Low	Men 100-200 mg/wk Women 25 mg/wk	Slight chance of virilizing for women. Pyrogenic (fever-causing), watch liver function.

obtained overseas.				
Stanozolol Winstrol (Oral) Available in the U.S.	Low	Very Low	Men 6-18 mg/day Women 4-12 mg/day	Slight chance of virilizing for women. Watch liver function.
Oxandrolone Oxandrin (Oral) Available in the U.S.	Low to Medium	Very Low	Men 15-20 mg/day Women 10-40 mg/wk Children 2.5-5 mg/day	Slight chance of virilizing for women. Patients on protease inhibitors should watch liver function. Women report water retention.
Oxymetholone Anadrol 50 (Oral) Available in the U.S.	Very High	Very High	Men 150 mg/day Women 150 mg/day	Balding in men, high blood pressure, water retention, body hair growth in women and breast enlargement in men. Watch liver function.
Testosterone Cypionate or Enanthate (injections) Available in the U.S.	High	Medium to High	Men 100-200 mg/wk Women 25 mg/wk	Water retention, balding in men, acne, breast enlargement in men, may virilize women.

* Many of the above dosages are not based on clinical data. Any individual considering using anabolic steroids should consult their physician. "Anabolic" characteristics are desirable for wasting therapy because it means increased lean body mass (LBM), which correlates with survival in AIDS. "Androgenic" means having a masculinizing effect, which is generally undesirable for women. Generally speaking, the less androgenic a steroid is, the fewer side effects there will be. The upper dosage listed for women is usually for severe wasting only. Women's systems do not tolerate anabolic steroids as well as men in general; caution is advised, and high dose is usually reserved for severe wasting.

Resistance Weight Training

Resistance exercise with weights and machines has been shown to increase muscle hypertrophy (growth) with or without the use of anabolic steroids. As previously mentioned, Dr. Shalender Bhasin in Los Angeles determined that HIV negative men receiving injections of 600 mg per week of testosterone and who exercised with weights had more LBM gains than those receiving testosterone but no exercise. Dr. Marc Hellerstein in San Francisco just finished a controlled study using oxandrolone and exercise in HIV positive men. He also found that men who exercised and took oxandrolone were the best responders to therapy.

All exercises should be performed to one's best ability to finish 8-12 repetitions in 3 sets per body part. Splitting the body in three areas (chest + shoulders + triceps, back + biceps + abs, legs) gives all body parts enough time to recover. The most common and effective exercises are: barbell flat bench press, overhead cable front pulldowns, barbell biceps curl, triceps pushdowns, abdominal crunches, and leg press. Working out with a partner and keeping a workout logbook are also great ways to ensure success.

The use of anabolic steroids for HIV therapy is a complex yet successful way to increase LBM and strength. Without proper nutrition and exercise, this therapy is only marginal in its effectiveness. Anyone who is considering the use of this therapy should become knowledgeable and empowered with information about these compounds, and the optimal nutritional and exercise programs.

Nelson Vergel is the Executive Director of Program for Wellness Restoration (PoWeR), which disseminates information to enhance LBM, quality of life and survival in HIV.

Bio-electrical Impedance Analysis

By David Pieribone

Bio-electrical Impedance Analysis (BIA) is a simple painless procedure which enables a doctor or healthcare provider to analyze the amounts of fat, muscle and water in the body. Not all healthcare providers perform BIA tests, but more and more are becoming aware of its importance. It costs around \$35-\$65 and is sometimes reimbursable through standard insurance.

If you have HIV disease your worst enemy can be the loss of weight specifically of lean body mass (LBM), which is also known as fat free mass (FFM). FFM is muscle as well as the metabolically active tissue in your organs. The loss of LBM may be an indication of wasting. Weight measurements alone may not detect the presence of wasting. Without the proper amount of LBM, the body does not function properly, and with the loss of 1/3 or more, death can occur. If the loss of lean body mass is significant, measures to reverse the loss may be necessary. Using anabolic agents like steroid hormones, and human growth hormone, in conjunction with resistance exercise and good nutrition can be beneficial. In addition to telling how much LBM an individual has, BIA can also give information about hydration status. Hydration, or how much water is in the body, is very important for overall health. Someone with diarrhea or vomiting who is not getting enough liquids runs the risk of becoming dehydrated.

BIA is a test which can be given in a doctor's office and takes only a few minutes. The test is preformed lying down. Electrodes are placed on the wrist and the ankle on one side of the body. Then a small electrical current is passed through the body and measurements are made. The electrical current is so small that it can not be felt at all. After the information is collected, it is put into a computer which calculates the percentages of fat, muscle and water in the body according to height, weight, sex and age. A single BIA measurement is not as important as tracking BIA over time which can show trends in a person's body composition.

The BIA analysis is accurate to within 5%, and is considered to be as good as any test to measure body composition. Most experts prefer the RJL BIA machine which uses equations validated by wasting expert and ACRIA Vice President, Donald Kotler, MD.

Dr. Norma Muurahainen, a well known expert on wasting and HIV infection, recommends that persons with T-cell counts above 300 should have a BIA every four to six months. Individuals with under 300 T-cells should have measurements every three months. There are some considerations you should keep in mind when having a BIA done. Firstly, be careful of alcohol and caffeine intake 24 to 48 hours prior to the test since they can cause dehydration and alter tests results to show an increase of body fat. Second, try and have the BIA done first thing in the morning before you eat, exercise or have your morning coffee or tea. This will give you more accurate test results.

Dietary Considerations and Combination Therapy

By Edwin Krales, MS, CDN

Diet is an important part of the battle against HIV infection. In general, a good diet of whole foods provides the body with the right nutrients it needs to perform its many functions. Diet is especially important when taking combination therapy for HIV infection. In many instances it can be the difference between success and failure with these medications, since many HIV medications have special dietary needs for their absorption in the body. Dietary management can also help alleviate some of the side effects of these medications.

The hardest part is setting up a system that is right for you. You must be realistic about your daily schedule and your available time. Are you an early riser with time to spare? Do you have time to eat in the morning, or do you jump out of bed at the last minute and rush out the door. Do you have to get kids ready for school? Do they eat before they leave? Is it important to eat with them?

Do other duties or habits have priority? The more complex your daily life is, the more important it is to set up a realistic medication /eating schedule. Make sure you discuss these issues with your healthcare provider.

In order for medications to get into the body they must be absorbed by the gastrointestinal tract (through the stomach and intestines). Some drugs require stomach acid (with no food in the stomach) to be absorbed while others need to be absorbed in the presence of food. So what you eat or don't eat can directly affect whether your HIV medications get into your body and thus are able to suppress the virus.

When you start sorting out your HIV medications, particularly your antiretroviral medications, you find that they can be divided into three "eating requirement categories." The first and easiest category is those medications that have no specific eating requirements. These medications can be taken on a full or empty stomach, with or without food. These medications include the non-nucleoside reverse transcriptase inhibitors nevirapine (Viramune) and delavirdine (Rescriptor) , and the nucleoside analogues AZT + 3TC (Combivir), 3TC (Eпивir), d4T(Zerit), ddC(Hivid) and AZT (Retrovir).

The second category is medications that should be taken on an empty stomach. They are the nucleoside analogue didanosine (Videx®) and the protease inhibitor indinavir (Crixivan). Taking indinavir on an empty stomach may be a problem for some people because of stomach upset. If you need to , you can take indinavir with a light snack. The manufacturer Merck says that a low fat, low protein, low calorie snack will not interfere significantly with absorption. According to Merck's guidelines a "snack" has no more than 301 calories, with no more than 23 calories from fat, 23 from protein and the remainder of the 255 calories from carbohydrates. (See Table 1 for a list of snacks you can eat with Crixivan.)

Table 1

Light Snacks that can be taken with Crixivan

Food Items	Calories	Fat Grams	Protein Grams	Carbo. Grams
1 cup instant oatmeal, regular and 1/2 banana	197	2.6	2.5	38.5
1 cup Cheerios, 1/2 cup skin milk, 1/2 banana	184.5	1.7	7.5	35.5
1/2 bagel, 1 oz nonfat cream cheese, 1 TBSP jam	146	1.4	5.7	33
1 egg white, 1	135	1.2	7	21.2

slice wheat toast, 1/2 grapefruit				
1 english muffin, 1 TBSP jam, 1 orange	244	1.4	5.7	33
1 pkg cream of wheat (mix & eat), 1 peeled apple	165	2.2	3.2	37
1 cup white rice (instant), 1/2 cup vegetables	199	.4	5	43
1 cup white rice (instant), 1/4 cup black beans	218	.4	7	45
1 baked potato, 1 TBSP low fat sour cream, 1/2 cup corn kernels (can or frozen)	241	1.9	5.2	54
1/2 cup macaroni, 1/3 cup tomato sauce, 1 TBSP parmesan cheese (grated)	147	2	6.5	26.2
1 cup vegetarian vegetable soup, 2 rice cakes	210	4	4	40
1/2 cup spaghetti, 1/2 cup	127	2.2	6.6	30

mushrooms (sliced), 1/2 cup tomatoes (chopped)				
1 bagel	92	1	5.5	6
1 bagel with 1 oz nonfat cream cheese	187	1.2	7	19
1 cup white rice (steamed)	267	1	6	58
2/3 cup mashed potatoes & gravy (KFC)	124	1	4	210
1/3 cup baked beans (KFC)	105	1	5	18
1 banana	60	0	0	15

[Another list of snacks](#)

The third category is medications that should be taken with food. They are the protease inhibitors Invirase, Fortovase, Norvir and Viracept. The amounts and types of food vary from drug to drug. Invirase and Fortovase should be taken within two hours of a meal. A "meal" is considered to be about one third of the calories you need each day if you eat three meals a day. The definition of a meal changes if you eat more or fewer than three meals a day. The total daily caloric intake usually is between 1500 and 2500 calories depending on your size, age, sex and activity level. The average meal is considered to be 600-900 calories with 25-30 grams of fat. Norvir should be taken with food if possible and is best absorbed with a full meal. This means the more food you eat the better absorbed the drug will be. Viracept should also be taken with food, preferably a substantial snack or a light meal. The manufacturer of Viracept, Agouron, says that the more food you take with your medication the better it is absorbed since it stays in your small intestine longer. They also say that the more food you eat, the less diarrhea you may experience, although there are no studies to prove this.

It is important to define some terms that on first appearance may seem very simple. When you need to take your medications on an empty stomach, this doesn't mean that five minutes after you take your medications you can eat - one hour is more appropriate. You must allow your body to digest the pills without anything else in your stomach, or you will not let the medications get absorbed. On the other hand as described above, if you have to take your medicine with food, eating a tangerine or a banana on the run won't give you enough food in your stomach to absorb the medication. It is also important to drink plenty of pure water with your medications to get proper absorption, and in the case of Crixivan to avoid kidney stones.

In addition to antiretroviral therapy for HIV infection, additional drugs used to treat other aspects of HIV infection (especially antibiotics) may also have dietary restrictions or requirements. Poor medication absorption due to faulty eating habits did not start with the HIV epidemic. It has been around for as long as people have been taking medication. For example, if you were prescribed the antibiotic tetracycline for a specific infection and you succeeded in completing the regimen 100%, but you took the pills with a glass of milk or with meals, you may have neutralized the antibacterial activity of the drug. You probably did not get good results. Tetracycline needs to be taken on an empty stomach one hour before or two hours after eating. Always ask your doctor or pharmacist for instructions on how to best take your medication. The pharmacist has over 50 instruction labels that can be put on your medication containers to help remind you how your medications should be taken.

MANAGING SIDE EFFECTS WITH DIET

Diet is not only an important consideration when taking combination therapy for proper absorption, but diet can also be helpful in managing some gastrointestinal side effects of therapy.

Diarrhea

Many HIV medications, especially the protease inhibitors, can cause diarrhea. If diarrhea continues for more than two weeks or begins after you have been on medications for some time, it may be caused by something other than the medications. If this is the case your doctor should do a complete GI work up to check for parasitic or bacterial infection. Besides prescription medications that can relieve diarrhea, diet can be helpful to manage diarrhea.

Many individuals can not tolerate milk or milk products because of a sugar called lactose which can be hard to digest. This condition is known as lactose intolerance, which has symptoms that include diarrhea, cramping, abdominal pain, gas and bloating. People who are lactose intolerant do not produce enough lactase - the enzyme which breaks down lactose so that it can be absorbed.

For people who are lactose intolerant, avoiding milk products is the best bet, but if you can not do without milk, there is a supplement called lactase which provides the necessary enzyme to digest the lactose in milk. Lactase can be purchased at your local pharmacy.

Try and avoid foods with lots of fat, especially deep fried foods; these can cause diarrhea all by themselves and can aggravate an already sensitive intestine. Avoid synthetic fats like Olestra, which is known to cause diarrhea. Beverages or foods with caffeine like coffee, tea, soda, hot chocolate, or foods with chocolate should also be avoided since caffeine stimulates the intestine. Don't drink anything with alcohol, including over the counter medications like cough syrup with alcohol. Raw fruits and vegetables and other foods high in insoluble fiber can irritate the intestine, causing or aggravating diarrhea. Sometimes the diarrhea may have several causes so you may have to experiment with a few things to get relief. You can also try the BRAT diet listed at the end of this article.

Nausea and vomiting

Many HIV positive individuals experience nausea and vomiting as a result of certain medications or opportunistic infections. Most people don't even want to think about eating or drinking when they feel nauseated. But not eating with certain medications can reduce the effectiveness of the medication, leading to possible drug resistance. To help relieve nausea, eat small meals

throughout the day. Choose cold foods rather than hot foods. Try foods like clear soups or broth, rice, noodles, oatmeal or cream of wheat without butter or sauce, mashed potatoes, plain eggs, cottage cheese, cheese or yogurt, pudding or Jell-O, plain crackers, pretzels, unbuttered popcorn, canned fruit, fruit ices or a chilled nutritional supplement. Avoid greasy foods, foods with strong odors and sweet or spicy foods. Instead, try foods that are salty or bland.

Loss of appetite (Anorexia)

Many people with HIV suffer from anorexia from time to time, but since not eating can reduce the absorption of medications and therefore their effectiveness, it is important to deal with this problem as soon as possible. Instead of trying to eat three large meals, eat more smaller meals throughout the day. Remember that the meals must be large enough to meet the minimum guidelines necessary for absorbing medication. Try eating while watching a video or listening to music. Eat with friends. We usually eat more when we eat with friends. Don't drink anything that may fill you up right before you eat. Ask your doctor for an appetite stimulant such as Megace® or Marinol®.

You should keep in mind that taking the current HIV medications on a daily basis is something you have to do until better medications are developed. So having a diet that you can live with will make all the difference. Ask others how they are managing. Go to congregational meal programs to give yourself a break from cooking everyday. At first this may all seem so complicated, but with time it will eventually fit into your daily routine.

BRAT Diet for Diarrhea

The BRAT diet is used to help slow down or stop diarrhea. It is not meant to be used for more than a couple of days at a time, because it does not contain all the nutrients you need to stay healthy. If you are allergic to any food on this list, don't eat it. All foods are to be eaten plain.

- B - bananas, boiled potatoes without skin, baked sweet potatoes without skin.
- R - rice (steamed)*, cream of rice cereal, rice water.
- A - apple sauce, baked apple without the peel.
- T - tea without caffeine and white bread toast, unsalted plain crackers.

While on this diet, don't eat or drink anything with caffeine like chocolate, cola, coffee, tea, hot chocolate or chocolate soda. Don't eat synthetic fats like olestra or Olean at any time. *Cooked, plain white rice is very easy to find when you are out in the world making your rounds. Any Chinese restaurant has it for take-out. Small containers are very cheap. *Rice water is made by cooking white rice with more water than it needs. For example, four cups of water to 1/2 cup of rice. When the rice is soft, pour the extra water into a container that can be covered, and put it into the refrigerator until it cools off. Refrigerate the rice in a closed container until you need it. Drink the water and eat the rice. Rice water is easier to drink when cold.

Edwin Krales is a nutritionist and the coordinator of Nutritional Services at the Momentum AIDS Project in NYC.

CRIA NEWS

Growth Hormone Therapy for Fat Accumulation

In conjunction with Dr. Donald Kotler and St. Luke's-Roosevelt Hospital, ACRIA has launched the first pilot study of the effect of recombinant human growth hormone (Serostim») in the treatment of truncal obesity associated with HIV infection. The study is known as the Fat Accumulation in the Belly (FAB) study. As detailed elsewhere in this issue (see page 12), redistribution of fat into the abdominal region is being seen in HIV-infected persons, many of whom are on protease inhibitor therapy. There is no known effective treatment for this condition. This study will test the safety of self-administering growth hormone, by injection under the skin, daily for 24 weeks.

To be eligible, persons must be at least 18 years old, HIV-infected, on stable antiretroviral treatment, and have noticed increasing abdominal size. Further eligibility will be confirmed in the clinic by body measurements to determine the abnormal distribution of abdominal fat. The study involves 8 visits to ACRIA and 3 visits to St. Luke's-Roosevelt Hospital, where special tests to measure body fat - including magnetic resonance imaging (MRI) and other scans - will be performed. The growth hormone needed for this study is being donated by Serono Laboratories. All visits, tests, and study medication are free. For more information, call Dr. D. Mendez at 212-924-3934.

ACRIA's Treatment Education Program Presented in Geneva ACRIA's Executive Director, J Daniel Stricker presented his abstract entitled "Providing HIV/AIDS Treatment Education to an Ethnically Diverse Population in a Large Urban Setting", detailing ACRIA's Treatment Education Program at the 12th World AIDS Conference in Geneva, on July 2, 1998. We are pleased that the Conference organizers through their acceptance of the abstract acknowledged the innovative nature of ACRIA's program.

The initiative is a unique model for the dissemination of treatment information to underserved populations, especially women and ethnic minorities. The program delivers culturally and linguistically appropriate treatment information to people living with HIV/AIDS, and technical assistance to staff members of AIDS service organizations in all five boroughs of NYC. The program has been a success reaching over 1500 individuals since its creation over one year ago.

Nutrition Supplement Study

At the 12th World AIDS Conference in Geneva, Dr. Donald Kotler presented data from ACRIA's recently completed study comparing Sustacal Plus» and Lipisorb», two commercial liquid nutritional supplements. Sustacal Plus» contains long chain triglycerides (large fat molecules) while Lipisorb» contains medium chain triglycerides (smaller fat molecules).

The study examined the impact of the two treatments on body weight and body composition in HIV positive individuals without wasting and T-cells under 100. Each participant was given three cans of supplement a day for six months.

The rationale for the study was that the medium chain triglycerides would be easier for the individual's body to absorb, due to the size of fat molecule, than long chain triglycerides and thus would result in better weight gain. However, while the results showed both groups gained weight, those who used Sustacal Plus» gained significantly more weight than individuals who used Lipisorb». More information will be available after further analyses of the data are completed.

ACRIA Board Elections

ACRIA is pleased to announce the election of Reinaldo Herrera to its Board of Directors at the June 17 board meeting. Mr. Herrera and his wife Carolina have actively supported ACRIA's research and treatment education agenda since 1995, and Mr. Herrera has become increasingly involved in advising the agency on diversifying and strengthening its fundraising activities.

Mr. Herrera is Special Projects Editor at Vanity Fair magazine and serves as a Director of Revlon Inc. ACRIA's staff and Board look forward to the guidance Mr. Herrera will provide on all aspects of agency operations during the years to come.

Charles Franchino, DC was elected Treasurer of ACRIA's Board of Directors at the June board meeting. Dr. Franchino, who has been on ACRIA's Board since 1994, and currently serves as Chair of the Nominating Committee, has the depth of understanding of ACRIA's operations to assume the pivotal role of Treasurer. Dr. Franchino was formerly the President of the Treatment Action Group's (TAG) Board of Directors. The position of Treasurer became vacant upon the death of George N. Stathakis in April of this year.

CRIA Joins the MRAA

CRIA is proud to announce its recent selection to become a member of the Medical Research Agencies of American (MRAA). Among other things, this affiliation makes ACRIA eligible for participation in the Combined Federal Campaign (CFC) for federal employees and armed services personnel in all 50 states and overseas.

We are excited about our membership in the MRAA because it will better enable a far broader audience to learn about and support our critical clinical research and treatment education programs for people living with HIV and AIDS. Look for ACRIA in the 1998/99 CFC brochure if you are a federal employee or in any branch of the United States Armed Services. We would like to give special thanks to the staff at MRAA for their invaluable assistance.

In Memory

CRIA's Board and staff are extremely sad to report on the recent death from AIDS of our Treasurer, George N. Stathakis. George joined ACRIA's Board of Directors in 1995, and was a forceful advocate of our clinical research and treatment education mission. He had been a Senior Vice President at both L. F. Rothschild & Co. and Tucker Anthony, Inc. and was instrumental in the packaging and sales of fixed income securities at both firms. George was a unique and extremely caring individual, and his thoughtful direction was instrumental to the rapid improvement in our agency's fiscal stability during his tenure on the Board. Today, as a result of his contributions, ACRIA is in a better position to provide critically needed services to people living with AIDS. George was only 39 when he died. His fight against AIDS was a model of quiet courage and an inspiration to everyone at ACRIA to rededicate ourselves to discovering more effective treatments. Both his unflinching support of ACRIA's research and treatment education efforts and his warm, kind spirit will be deeply missed.

Trials

Adefovir Dipivoxil for Antiretroviral Naive Patients

CRIA is participating in a 48 week study of Gilead Sciences' nucleotide analog drug adefovir dipivoxil (Preveon®). Adefovir is a new type of drug that is active against HIV as well as some other viruses such as CMV, hepatitis B virus, and herpes viruses. The study is of HIV+ persons with more than 100 T-cells and HIV viral load of greater than 5,000 who have not taken other anti-HIV drugs in the past. Participants will be assigned to one of three treatments, all of which include

the protease inhibitor indinavir (Crixivan®). Participants will be reimbursed \$15 per scheduled visit after enrollment.

Adefovir Dipivoxil for Protease Inhibitor Naive Patients

ACRIA is also participating in a 48 week study of adefovir dipivoxil for HIV+ persons who have taken nucleoside analog drugs (e.g., AZT, 3TC, ddI, d4T, ddC) for at least four weeks. Participants will be switched to one of three possible combinations, all of which include adefovir dipivoxil and one or two protease inhibitors. To be eligible, participants must have more than 100 T-cells and a viral load greater than 5,000. Participants will be reimbursed \$15 per scheduled visit after enrollment.

Fat Accumulation in the Belly (FAB)

Study Fat buildup in the abdomen may be a complication of protease inhibitor use. ACRIA is studying the safety of daily human growth hormone injections as a possible treatment for this complication. To be eligible for this 24-week study, you must be HIV-infected, on stable antiretroviral therapy, and have noticed increasing abdominal size.

Twice a Day Crixivan® Study

In this 24 week study, persons already taking Crixivan® (indinavir) three times a day will be randomly assigned to continue this dose or change to 1200mg twice a day. To be eligible, you must be taking Crixivan® plus two nucleoside drugs for the past 6 months, have undetectable viral load (less than 400 copies/ml), and have more than 100 T-cells. Participants will be reimbursed \$15 per scheduled visit after enrollment.

DMP 266 (Sustiva®)

Study DMP 266 is DuPont Merck's new non-nucleoside reverse transcriptase inhibitor (NNRTI) that appears to be quite active against HIV in early clinical studies when used in combination with other drugs. ACRIA is participating in a study of DMP 266 for people with more than 50 T-cells and HIV viral loads greater than 10,000 who have not taken a protease inhibitor drug, 3TC, nevirapine, or delavirdine. Participants will be assigned to one of three combinations: AZT + 3TC + indinavir (Crixivan®), AZT + 3TC + DMP 266, or indinavir + DMP 266. The study will last 60 weeks and participants will be reimbursed \$15 per scheduled study visit after enrollment.

Oxandrolone for Women with Weight Loss

Oxandrolone is BTG's anabolic steroid hormone which has shown promise as a treatment for AIDS-related wasting in small, preliminary studies and, unlike testosterone, can be taken as a pill. ACRIA is participating in a multicenter study of oxandrolone for AIDS-related wasting in women. In this study, different doses of oxandrolone will be compared with inactive pills (placebo) for 12 weeks, followed by a 24 week period during which all participants will receive oxandrolone. Participants must be HIV+ with unintentional weight loss of 10-20% of their usual body weight. Participants will be reimbursed \$15 per scheduled study visit after enrollment.

Protease Inhibitor and Blood Sugar Study

ACRIA is conducting a study to examine the effects of protease inhibitor use on responses to the oral glucose tolerance test (measurement of blood sugar levels after taking a drink with a high sugar content). To be eligible, participants must be about to start treatment with a protease

inhibitor drug for the first time. Participants will be reimbursed \$30 for each of the first two visits and \$50 for the final visit.

SMART/EST Women's Project

CRIA is participating in a multicenter study to test a 10 week stress management program to teach women how to cope more effectively with their illness and everyday problems. Two approaches -individual and group relaxation training- are being compared. Women 18 years of age and older with a diagnosis of AIDS may be eligible. Participants will be reimbursed \$25 per visit after enrollment (up to \$575). Free child care and refreshments will be provided. For more information, call Debra Munger at 212- 924-3934.

Testosterone and MET-Rx TM

CRIA is sponsoring a study of testosterone and MET-Rx TM, a high protein nutritional supplement for treatment of AIDS-related wasting. Participants will receive testosterone or placebo injections in combination with MET-Rx» or standard nutritional supplement. Participants must be HIV+ men with T-cell counts of less than 400, low testosterone levels, and weight loss or loss of lean body mass. For information, call Dr. Judith Rabkin 212-543-5762.

FOR MORE INFORMATION ON ANY OF THESE STUDIES, PLEASE CALL DR. AVINASH DESAI OR DR. DOUGLAS MENDEZ AT (212) 924-3934, OR VISIT OUR TRIALS PAGES.

Forum Update

CRIA co-sponsors monthly educational forums on AIDS research and treatment issues. Upcoming forums:

- Wednesday, July 15th Update from the 12th World AIDS Conference, Geneva
- August - No Forum
- Wednesday, September 9th Women and HIV

The forums are held at 7PM in the Cronin Auditorium, 10th Floor of St. Vincent's Hospital at 11th Street and 7th Avenue, Manhattan.