The New AIDS Paradigm: Living With Metabolic Complications

(Richard S. Ferri, PhD, ANP, ACRN, FAAN)

The treatment paradigm for people living with human immunodeficiency virus (HIV) infection has radically changed since the advent of protease inhibitors (PI) drugs in 1995, which essentially transformed HIV from a life threatening disease to a chronic illness. Despite advances in treatment regimes there are many evolving unknowns in relationship to the long-term effects of HIV infection and its consequential treatment. Over the course of the last two years as the newer and even more familiar AIDS therapies have been used for longer periods of time it has become increasingly clear that we are only beginning to discover new “long-term” clinical complications. The emerging complications of the long-term use of PI and other antiretrovirals are yet at a level of infantile understanding for their complexity and impact on people living with HIV disease.

Emerging Clinical Conditions/Long Term Complications

There appears to be a clinical phenomenon developing that includes changes in body fat and another clinical condition known as lipodystrophy. The components of body fat redistribution and lipodystrophy include body shape changes, insulin resistance, and hyperlipidemia. Although the cause of fat redistribution and insulin resistance remains unclear at this time, investigators believe that hyperlipidemia is closely related to PI use.

Factors that appear to increase the prevalence of these metabolic changes include age, duration of antiretroviral therapy, and a history of severe immune compromise.

Body fat changes and lipodystrophy syndrome can significantly impact the physical and mental health of people living with HIV. In light of this fact it is vital that we understand how these clinical phenomena effect the patient’s self-esteem, personal/social relationships, and adherence to antiretroviral therapy.

Each component of HIV related fat redistribution and lipodystrophy have distinct clinical features, yet it remains impossible to categorically predict which patients will experience these phenomena. The first is body shape changes. The change in body habitus can present as:

- **Extremity Thinning:** The wasting of the muscle of the upper extremities is often associated with symmetric accumulation of subcutaneous fat such as confluent lipomas. It may also be associated with increased triglyceride levels.

- **Buffalo Hump:** Fat deposits on the cervical region and in the abdomen. Fat appears to accumulate in the dorsocervical region similar to what is seen in patients on long term steroid therapy or in Cushing’s syndrome. Typically patients do not have any of the endocrine associated abnormalities classically seen with Cushing’s syndrome.

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This report summarizes the results of some small studies that are now shedding light on how some anti-HIV therapies may play a role in the syndromes, but these findings are by NO MEANS CONCLUSIVE. Early results from some studies demonstrate that people with fat loss in the face; arms or legs (called lipoatrophy) had decreased number of mitochondria in their cells. This reduction in mitochondria was only seen among people dating d4T (Stavudine, Zerit) and was not seen among people taking other nucleoside analogue reverse transcriptase inhibitors (NRTIs). The average number of mitochondria in cells decreased by 44% among people on d4T.

Another study compared the number of mitochondria in cells from people living with HIV who had never taken any anti-HIV therapies, those with no signs of fat redistribution, those who had never taken any anti-HIV therapies, and those who had HIV-negative people. The study found that people in group A had fewer mitochondria in cells than those in group B who in turn had fewer mitochondria in cells than those in group D. There were no differences in the number of mitochondria found in cells between people in groups C or D. This clearly suggests that the reduced level of mitochondria is a result of anti-HIV therapies rather than HIV disease itself.

Two other studies looked at the effect of protease inhibitors on body composition. A group in Seattle found that when ritonavir (Norvir) was given to HIV-negative people for two-weeks, they experienced a significant rise in cholesterol and triglycerides levels. Another group in San Francisco gave indinavir (Crixivan) to HIV-negative individuals for four weeks, and while there was no significant rise in cholesterol or triglycerides people had a marked decrease in insulin sensitivity (a marker associated with diabetes). Changes in these markers associated with the way the body uses fats and sugars are believed to be part of the lipodystrophy syndrome.

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A French study looked at cosmetic surgery for facial wasting with a product called New Fill (polylactic acid). The study showed that New-Fill may help increase the thickness of the cheek fat pad and other places where fat may have been lost. However, New-Fill does not directly fill the spaces left empty by lipoatrophy, which is claimed to build or grow a matrix under the skin which is then filled in by the body’s own collagen. This product is not currently FDA approved. A major problem is that the supplier is a small company that does not have the resources to conduct clinical trials. This product would certainly prove helpful in decreasing some of the added psychological burden of facial lipoatrophy, for people with HIV infection.

A small study of five people has shown that human growth hormone (Serostim) can decrease triglyceride and cholesterol levels (decrease in LDL or bad cholesterol and increase HDL). It was, however, associated with the development of insulin resistance and led to increased glucose production. The dose used in this study was 3mg/day. Future studies using lower doses are planned.

If you would like to read the Lipodystrophy Updates in their entirety or find out more information about Lipodystrophy syndromes or mitochondrial toxicity go Project Inform website at www.projectinform.org.

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Self-care is never a selfish act -- it is simply good stewardship of the only gift we have, the gift I was put on earth to offer others. Anytime we can listen to true self, and give it the care it requires, we do so not only for ourselves, but for the many others whose lives we touch.

-Parker Palmer

Recommended Readings

I Will Not Die an Unlived Life: Reclaiming Purpose and Passion (Dawana Markova)
The Art of Effortless Living: Simple Techniques for Healing Mind, Body, and Spirit (Ingrid Bacci)

The Four Levels of Healing: A Guide to Balancing the Spiritual, Mental, Emotional, and Physical Aspects of Life (Shakti Gawain)
The Secret of the Shadow: The Power of Owning Your Whole Story (Debbie Ford)
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The etiology remains unclear. HIV clinicians have noticed this event in people taking antiretroviral drugs with a marked increase since the introduction of PI’s into treatment regimens.

- Increased Abdominal Girth: Increased abdominal girth or “protease paunch” is often associated with bloating, heartburn, and feeling of fullness. The increase in the size of the abdomen can be significant enough to impair respiration.

- Breast Enlargement: Both men and women may experience breast enlargement. Women in PI therapy have experienced breast enlargement, which is often associated with the increased abdominal girth. In men the enlargement can be seen as true gynecomastia (an increase in the glandular tissue) or as lipomatous deposits. The etiology remains unclear.

- Lipodystrophy Syndrome: Patients will present with a loss of subcutaneous fat. Veins become extremely prominent and pronounced in appearance. Subcutaneous fat loss can also be seen in the face, giving the person a very gaunt appearance (the new “stigma of AIDS”).

- Insulin Resistance: Insulin resistance has also been seen in people on PI therapy and can lead to the development of treatment related diabetes that may require insulin management. Accompanying insulin resistance is the associated condition of cardiovascular disease.

Treatment of Metabolic Complications of Anti-HIV Therapy

The treatment issues surrounding the metabolic complications of anti-HIV therapy are complex. First, one of the major issues facing people on antiretroviral therapy is drug adherence. Many people find it difficult to adhere to the often-complex medication regimens with rigid dosing schedules and food and fluid requirements. Second, the side effects of many of these agents affect quality of life (nausea, fatigue, joint pain, peripheral neuropathy, and mental status changes). Basic adherence to therapy, which is considered to be life long, can be a significant challenge even for the most motivated patient. When metabolic problems further complicate the clinical picture issues may become more pronounced.

In addition to the constitutional side effects of AIDs therapy there is now the additional burden of taking even more medications. Some of the treatment issues to resolve far re-distribution and lipodystrophy have their own complexities that impact care and treatment. For instance, consider the “recovering” injection drug user who must inject insulin to control drug induced diabetes – the metabolic complication/treatment can significantly impact recovery from injection drug use (IDU). The treatment stages for the metabolic complications of AIDs therapy now focus on introducing disease specific agents and lifestyle changes. Hyperglycemia is generally treated with insulin or oral agents. However, troglitazone is generally contraindicated in people with HIV because of the drug’s potential for hepatic toxicity. Although statin drugs can be used to manage hyperlipidemia and hypercholesterolemia, lovastatin and simvastatin should be avoided due to their competition with the CYP oxidase system of the liver. Niacin should also be avoided since it can increase insulin resistance. However, it needs to be pointed out that even the best lipid-lowering agent may only do “marginally” well in the case of increased triglycerides from anti-HIV therapy because many people experience dramatically high levels. So if the patient’s triglyceride level is 2000 (normal range under 200) then drugs that site a 50% reduction will only have the ability to reduce the level to 1000. While certainly an improvement, by no means a cure.

The body habitus changes associated with lipodystrophy are being studied by introducing human growth hormone. Some studies suggest that administering human growth hormone three times per week, via injection, reduced some abdominal obesity and positively impacted other metabolic changes. However, this agent is very expensive, needs to be injected, and has not been approved for treatment of body habitus changes secondary to lipodystrophy. Some have argued that switching therapies may reduce metabolic complications, yet this remains controversial. Recently, there have been numerous published studies that suggest switching the patient from a PI to another agent, such as a non-nucleoside reverse transcriptase inhibitor (NNRTI) may produce beneficial results for the patient experiencing metabolic complications. However, many of these studies were small and uncontrolled and the data is still preliminary.

Living with HIV has always been a hard and now it appears even more challenging. The proverbial case of the cure is worse than the disease. Nurses need to take a very proactive role in the health and well being of their patients with HIV. It is time to reinforce the basics of health living. Diet, exercise, limited (or no) alcohol/drug use, and smoking cessation are paramount in the new age of AIDS. Nurses have a renewed role as treatment partners in HIV disease. Nurses have always been expert educators and counselors, now it more critical than ever for nurses to take that role and help people live with HIV long term.

2. Lipodystrophy and Metabolic Disorders in 646 HIV-1 Infected Patients Previously Treated with or without a Protease Inhibitor (PfU BOUSSA1, A DULLOUST2, AS LASCACUS, L BODRATA, C GOUGARD1, and the Lipodystrophy Study Group. 1INSERM U292, Hop, Bichat; 2TNF&T Cell Producers after HAART; 3Béclère; 4Inst. Montsouris; and 5Hosp. Bicêtre. Assistance Publique Hôpitaux des Paris, France.
3. Alteration of Homeostasis of Naive and Memory IL-2- and TNF&+T Cell Producers after HAART. Consequences on Lipodystrophy. LEDRU, N. CHRISTEFFI, O. PAEZY2, J. C. MELCHORS, and M. L. GOGUEER1. 1INSERM U292, Hop, Bichat. Paris; 2Villeneuve-St. Georges Hop; and 3R. Poincare Hop., Garches, France

- Ingrid Bacci

Hints for Staying Healthy

(David J. Sterken MN, CNS, CPNP)

The emerging clinical phenomena (fat redistribution, elevated cholesterol/ triglycerides, and lipoatrophy) related to metabolic complications of HIV therapy can add significant psychological burden to those of us infected with HIV. There are some very specific things that we can do to decrease, slow and maybe even avoid the effects of lipodystrophy.

- Avoid foods that are fried, high in fat, and high in sugar. Eat a balanced diet that is rich in protein, vegetables, fruits, and high in grains.

- Exercise regularly. Although studies have indicated that weight training may help to maintain lean muscle, aerobic exercise is necessary if your triglycerides or cholesterol levels are elevated. Aerobic exercise does not require that you have a gym membership. Lycra work out garb, or own “Sweating to the Oldies” – aerobic exercise can be as simple as walking around your neighborhood. The key to aerobic exercise is to increase your heart rate for at least 30 minutes and to do this at least three times per week. *Check with your physician before beginning any exercise program.

- Drink lots of water. Pop/soda tends to dehydrate because of the high soda content and many also have some long-term effect on the bones. Juices generally have a high sugar content (sucrose, fructose) and may only add to problems related to elevated blood glucose levels. Good old H2O flushes the system of toxins and ensures adequate hydration.

- Know your body and report changes to your health care provider. You know your body the best because you live in it 24 hours a day, 7 days a week, 12 months out of the year. Realize that the changes that occur over time. It could be a simple as pants that are sagging in the buttocks, an increase in bra cup size or bra size in general.

- Know about the side effects of your medications. Ask your health care provider about what the latest research is showing in regard to lipodystrophy. Realize, however, that some of the burden of being “up to date” may fall on you. Bring in articles etc. that you have read to discuss with you health care provider. Be your own advocate.

- Debbie Ford

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The only way we can find the pathway to satisfaction is by lessening our obsessive grip on doing and focusing more on being.

- Ingrid Bacci

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Our lack of faith in ourselves limits our ability to challenge ourselves. We are more greatly endowed with character in others, yet often assume that we cannot develop this greatness in ourselves.

- Ingrid Bacci

... the core of healing is self-forgiveness.

- Debbie Ford
Lipodystrophy - Is There A Spiritual Perspective?

(David J. Stehen, MN, CNS, CPNP)

When one of the other editors suggested that we look at lipodystrophy from a physical and spiritual perspective quite frankly I had to ask myself, “Is there a spiritual perspective on lipodystrophy?”

Previously we discussed the psychological burden related to the bodily changes (e.g. buffalo hump, protease paunch, breast enlargement, thinning of the extremities) that seem to occur in conjunction with lipodystrophy. We live in a culture that is very body conscious, idealized by models we see in the pages of Vogue or Men’s Health. As a result we have created an atmosphere which promotes eating disorders and exercise behavior that no longer “fun but feeds into our addiction to perfection. So to answer my own question, — “Yes, there is a spiritual perspective to lipodystrophy!”

As I gave some serious consideration to the “challenge” of this article almost immediately realized that I was allowing myself to get mired down in terminology. A “spiritual perspective” to a particular clinical issue is devoid of religious overtones, if “spiritality” is defined in terms of the individual’s journey toward self-actualization, or the discovery of purpose. Personally, I believe that each one of us is created to fulfill a specific task in this world. When one of the other editors suggested that we look at lipodystrophy from a physical and spiritual perspective quite frankly I had to ask myself, “Is there a spiritual perspective on lipodystrophy?”

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Let me be very clear about the fact that I am not minimizing the psychological impact of body habitus changes on the individual with HIV infection. My concern is that we do not let the symptoms of a disease or the side effects of the treatment define who we are as a person. I am not HIV, nor am I lipodystrophy! I am a “being” who exists in a world of limitation, but the only limits I have are the limits I place on myself.

I sometimes wonder if we “fear” the side effects of our disease so much that we create an “energetic state” of susceptibility that deeply effects us on a cellular level. The implications of this would extend to every disease process and treatment regime. Do we in fact create the “potential” for someone to experience treatment side effects by listing all the potential complications? We are only beginning to understand the intricacies of the mind-body connection on health. Knowing that I have a purpose to fulfill in this life means that I live a conscious life. Therefore, I eat right, exercise, spend quiet time alone, adhere to my therapeutic regime, and seek to maintain balance in all areas of life.

As I look at myself in the mirror each morning I affirm, “I am not my body.” Some days this is easier than others as I can see the physical effects of the disease on my body. Yet, to realize that my “worth” goes deeper than my outer shell helps me remain focused on fulfilling my purpose.

Life is structured according to what we think needs to be done, not according to sensitively to a natural rhythm. - Shakti Gawain