

Available on the World Wide Web at  
<http://www.catie.ca/tu.nsf>

## Table of Contents

### SIDE EFFECTS

A. The usual suspects	1
B. A brief history of HIV drug therapy	2
C. Strange side effects	3
<i>Selected highlights from the 4<sup>th</sup> International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV</i>	
D. Focus on fat	4
E. Lots of volunteers needed	5
F. Lactic acid and nuke damage	5
G. No nukes please	6
H. Fat wasting — AZT vs. d4T	6
I. Sugar blues	6
J. Predicting body shape changes	7
K. Niacin for high triglycerides	7
L. Supplement fix for nelfinavir- related diarrhea	8

## SIDE EFFECTS

### A. The usual suspects

In this special “Side Effects” issue, we focus on reports from the 4<sup>th</sup> International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV, held in San Diego, 22-25 September 2002. Before describing the interesting findings from this workshop, we will provide a list of commonly used anti-HIV drugs and briefly review how therapy for HIV infection was introduced. This review is important because it should give some insight into a group of side effects now called the “HIV lipodystrophy syndrome.”

Commonly used anti-HIV drugs in high-income countries:

#### Nucleoside analogues (nukes or NRTIs)

- AZT (zidovudine, Retrovir)
- abacavir (ABC, Ziagen)
- ddI (didanosine, Videx EC)
- d4T (stavudine, Zerit)
- 3TC (lamivudine, Epivir)

#### Nucleotide analogue

- tenofovir (Viread)

#### Non-nukes (NNRTIs)

- delavirdine (Rescriptor)
- efavirenz (Sustiva)
- nevirapine (Viramune)

#### Protease inhibitors

- amprenavir (Agenerase)
- atazanavir (Zrivada) - not yet approved in Canada
- indinavir (Crixivan)
- lopinavir (Kaletra)
- nelfinavir (Viracept)
- ritonavir (Norvir)
- saquinavir (Fortovase, Invirase)

produced by



Canadian AIDS Treatment  
Information Exchange

Réseau canadien  
d'info-traitements sida

555 Richmond Street West, Suite 505  
Box 1104  
Toronto, Ontario M5V 3B1 Canada  
phone: 416.203.7122  
toll-free: 1.800.263.1638  
fax: 416.203.8284  
<http://www.catie.ca>  
charitable registration number:  
13225 8740 RR

A term that's commonly used in North America is HAART — highly active antiretroviral therapy. Historically, this has meant a combination of anti-HIV drugs that can include a protease inhibitor and/or a non-nuke and one or more nukes. For more in-depth information about HAART, see CATIE's *Practical Guide to HAART*, available at [www.catie.ca](http://www.catie.ca).

---

## B. A brief history of HIV drug therapy

At the beginning of the 1990s, therapy for HIV usually consisted of one anti-HIV drug taken several times a day. This drug was one of several nukes — generally AZT, ddI or ddC. (The latter drug is hardly ever used in North America in 2002.) In the early to mid-1990s, as more nukes became available, doctors increasingly began to prescribe combinations of these drugs. Not considered potent today, combinations of two nukes were, for a time, able to increase or maintain CD4+ cell counts in some people with HIV/AIDS (PHAs). Up to the mid-1990s, the side effects generally associated with nukes included the following:

- damage to the nerves in the hands/feet — peripheral neuropathy
- bone marrow damage
- painfully swollen pancreas gland — pancreatitis
- muscle weakness

### New drugs, new hope

By 1996, a new class of drugs called protease inhibitors (PIs) became available in high-income countries. When used in combination with nukes or non-nukes, PI-based therapy has powerful anti-HIV effects and raised CD4+ cell counts to very high levels in people with AIDS. A benefit of PI-based therapy was that many PHAs began to recover from previously hard-to-treat complications of AIDS. As a result, fewer PHAs were dying. As more and more PHAs heard about or experienced the dramatic results of PIs, a new optimism emerged. Complaints about PI-based regimens at that time were generally limited to nausea and diarrhea with the odd report of kidney stones in indinavir (Crixivan) users.

In 1997, a number of reports appeared about unusual side effects in PHAs using combination therapy. First, there was a report of higher-than-normal levels of blood sugar that developed in people who did not have diabetes. More troubling was a report from Atlanta about strange changes

in body shape. The report involved a man who had developed pads of fat on and around his shoulders — a feature commonly called a “buffalo hump.” He had been using AZT for three years, 3TC for eight months and the PI indinavir for six months when the buffalo hump developed. The doctors were puzzled — buffalo hump was not commonly reported to occur in HIV/AIDS. It has been known to happen in “male alcoholics” and in others with a hormonal disorder called Cushing's syndrome. However, tests revealed no obvious hormonal disorders and the man did not drink alcohol. The doctors suspected that his problem was caused by the use of indinavir.

The published report of the buffalo hump was followed by similar reports on the Internet written by PHAs on an e-mail list called “Crix list.” Because buffalo humps had not been previously associated with HIV or therapy for HIV and because PIs were relatively new on the scene, people assumed that PIs were the cause of the “new” problem. But, in 1998, doctors in San Francisco published a report on eight PHAs (all male) who developed buffalo humps while on anti-HIV therapy. What was interesting about this report is that four of the subjects were taking only one or two nukes and no PIs.

The treatments used by the 8 PHAs were as follows:

1. AZT and ddI
2. AZT and ddC
3. AZT
4. ddI
5. AZT, 3TC and indinavir
6. AZT, ddI and indinavir
7. 3TC, delavirdine and nelfinavir
8. 3TC, ddI and indinavir

Below are some key points about these 8 PHAs:

- The average age was 46 years.
  - They had been living with HIV for about 10 years.
  - The first four PHAs had never been exposed to a PI.
  - Extensive blood tests determined that none of the men had any obvious serious hormonal imbalances that could have caused the buffalo humps.
  - Of note, on average, the level of a blood fat called “triglycerides” was twice as high in these men as it normally should be.
  - Three years before any of the humps developed, only one of the men used oral/
-

---

injected corticosteroids and none used testosterone.

The researchers were stumped as to why the buffalo humps developed. What is clear from this study is that buffalo humps (fat deposits) can occur in PHAs who are taking nukes without PIs. Into the late 1990s, other aspects of body shape changes appeared, which are detailed in our next report.

#### REFERENCES

1. Lo JC, Mulligan K, Tai VW, et al. "Buffalo hump" in men with HIV-1 infection. *Lancet* 1998;351:867-870.
  2. Hengel RL, Watts NB and Lennox JL. Benign symmetric lipomatosis associated with protease inhibitors. *Lancet* 1997; 350:1596.
- 

### C. Strange side effects

By the end of 1998, doctors around the world had began to collect reports of strange changes in body shape, blood fats and hormones in their patients on HAART. Collectively, they called these side effects the "HIV lipodystrophy syndrome." While there is not consensus about a definition for the syndrome, features that have been associated with lipodystrophy can include the following:

#### Changes in body fat

- Loss of fat (fat wasting) just under the skin (subcutaneous fat), particularly in the face, arms and legs. This results in sunken cheeks and more prominent veins in the arms and legs.
- Fat gain or accumulation, mainly deep in the belly and in the breasts (mostly in women). Note that sometimes breast enlargement is due to breast tissue (glands, ducts) that grows inappropriately. Although fat gain is a common feature of lipodystrophy, buffalo humps are not. Sometimes small lumps of fat appear on the abdomen or back.

#### Changes in insulin and blood sugar

- The hormone insulin helps to maintain blood sugar levels within a normal range by allowing cells to take in sugar (glucose). In PHAs with lipodystrophy, higher-than-normal levels of blood sugar can occur. This problem arises because insulin does not have the same effect that it used to — cells have become less sensitive to this hormone's action. This state is called "insulin resistance." To compensate for reduced sensitivity to insulin, the body pumps more of this hormone into the blood. Not surprisingly, some PHAs with lipo-

dystrophy have higher-than-normal levels of insulin. Over time, serious cases of insulin resistance can lead to diabetes.

#### Lipids — cholesterol and triglycerides

- Another common feature seen in lipodystrophy is higher-than-normal levels of cholesterol and triglycerides. Prolonged elevation of lipid levels — a condition called "dyslipidemia" — increases the risk of cardiovascular disease and diabetes. Poor dietary habits, tobacco smoking and lack of regular exercise also increase this risk.

While we have listed three groups of side effects associated with lipodystrophy, it is important to remember that not all of them occur at the same time in the same person. For instance, some people may have fat accumulation without fat loss, or vice versa. Moreover, if caught early on, insulin resistance and high lipid levels may, in some cases, be managed — depending on the severity of the side effect — with a number of interventions, including improvement in diet, use of certain supplements, exercise and various lipid-lowering drugs.

Exactly why these side effects occur is not clear. However, what is clear is that lipodystrophy was not reported before 1996 and it is probably caused by the following factors:

- drugs used to treat HIV
- the body's response to these drugs

In this issue of *TreatmentUpdate*, we review recent findings that may help explain some aspects of the lipodystrophy syndrome. CATIE has recently published *A Practical Guide to HIV Drug Side Effects*, which is chock-full of many helpful hints and suggestions for dealing with drug-related side effects. It is available in print and on our website at [www.catie.ca](http://www.catie.ca).

#### REFERENCES

1. Chen D, Misra A and Garg A. Lipodystrophy in human immunodeficiency virus-infected patients. *Journal of Clinical Endocrinology and Metabolism* 2002;87(11):4845-4856.
  2. Behrens GMN, Boerner A-R, Weber K, et al. Impaired glucose phosphorylation and transport in skeletal muscle cause insulin resistance in HIV-1-infected patients with lipodystrophy. *Journal of Clinical Investigation* 2002; 110(9):1319-1327.
  3. Bastard J-P, Caron M, Vidal H, et al. Association between altered expression of adipogenic factor SREBP1 in lipoatrophic adipose tissue from HIV-1-infected patients and abnormal adipocyte differentiation and insulin resistance. *Lancet* 2002;359:1026-1031.
-

*Selected highlights from the  
4<sup>th</sup> International Workshop on Adverse Drug  
Reactions and Lipodystrophy in HIV*

#### **D. Focus on fat**

Some attendees at the above conference noticed that at previous lipodystrophy workshops there seemed to be excessive focus on describing and documenting the lipodystrophy syndrome. At the most recent workshop more effort was made to try to understand the cause(s) of lipodystrophy. One workshop attendee said (with tongue in cheek):

*“There seemed to be a lot of presentations by older male scientists who showed slides of mice and told the audience about how they interfered with the animals’ immune systems. When asked about the relevance of their findings to people, the scientists replied they only knew about mice.”*

While there was some truth to this description, there were also reports from studies in people presented at the workshop. But before we get to those, we will highlight some important test-tube research. The results of this research provide insight into some aspects of the lipodystrophy syndrome. Note that all references, unless otherwise noted, are from the workshop.

#### **Fat and indinavir**

Because changes in fat have a large and visible impact on body shape, much research is taking place on fat cells (adipocytes). Researchers want to know how anti-HIV drugs affect the growth of these cells.

One team in Paris, France, led by Dr. Jacqueline Capeau, grew fat cells in the test-tube. There they were exposed to the protease inhibitor indinavir (Crixivan) at levels found in people who take the drug. The team found that indinavir affected the ability of young fat cells to mature. Indeed, this protease inhibitor impaired the growth and development of about 50% of fat cells. This occurred because indinavir appears to damage certain key proteins that fat cells need in order to mature.

#### **Therapy is more than one drug**

The experiments with indinavir are useful, however, because PHAs take combination therapy consisting of several drugs, studies of different drugs would also be of interest. To this end, another team of scientists, in Liverpool, UK, conducted test-tube studies on fat cells, exposing them to combinations of nukes (AZT, d4T, ddI,

3TC) as well as protease inhibitors (indinavir, nelfinavir, ritonavir and saquinavir).

This team found that, in general, nukes do not appear to be toxic to fat cells. Moreover, nukes did not appear to affect the growth or development of fat cells. Protease inhibitors, however, had a different effect. PIs appeared to decrease the build-up of triglycerides (TG) inside cells (thus possibly pushing TG into the blood). PIs also increased the breakdown of fat cells, which release their contents into the blood, again adding to the load of fat that builds up there.

When AZT or d4T was combined with indinavir, suppression of the growth of fat cells greatly increased. For instance, with d4T alone, only about 1% of fat cells had reduced growth. However, when a combination of d4T and indinavir was used, technicians detected a 28% reduction in the growth and development of fat cells.

In addition to reducing the growth and development of fat cells, PIs also impaired the ability of insulin to help cells absorb sugar. In the body, this affects the ability of cells to get energy, and excess sugar gets turned into fat. Based on these experiments, the PI with the strongest anti-insulin effect is listed first, followed in descending order by the others:

- indinavir
- saquinavir
- ritonavir
- nelfinavir

Bear in mind that these results are from test-tube studies. They could, however, serve as a guide when conducting studies in people.

#### REFERENCES

1. Caron M, Auclair M, Kornprobst M, et al. Indinavir-induced nuclear lamina alterations are correlated with adipocyte dysfunctions in cultured adipocytes. Abstract 1.
  2. Janneh O, Hoggard PG, Sales SD, et al. Intracellular disposition of zidovudine, stavudine and protease inhibitors and their metabolic effects in cultured adipocytes. Abstract 2.
  3. Jones SP, Janneh O, Maher B, et al. Altered TNF-alpha and IL-6 levels and the antiadipogenic effects of antiretrovirals on cultured adipocytes: possible mechanisms for their role in lipodystrophy in HIV-infected patients. Abstract 3.
-

---

## E. Lots of volunteers needed

Drug safety is an important issue for manufacturers, regulatory agencies and, most of all, the user. One of the problems with HIV clinical trials, according to researcher Andrew Hill from the UK, is that there may not be enough volunteers or research subjects enrolled in studies. When there are relatively low numbers of subjects in a study, certain side effects may not be judged to be significant. This can lead to incorrect conclusions about the safety of a drug. Below are some numbers of subjects calculated by Dr. Hill that are needed for certain measurements or events.

### Cholesterol

To detect significant changes when comparing two treatment groups in a study, at least 435 subjects in each group (for a total of at least 870) would be needed to detect a 5% vs. 10% incidence of severe or life-threatening increases in cholesterol levels.

### Rare events — pancreatitis, hypersensitivity reactions and lactic acidosis

These side effects, though dangerous, are not common. To detect a doubling of the risk of these events, the number of subjects needed for meaningful statistical evaluation would be as follows:

- 1,826 subjects for an incidence of 1% to 2%
- 1,141 subjects for an incidence of 2% to 4%
- 749 subjects for an incidence of 3% to 6%
- 553 subjects for an incidence of 4% to 8%

Dr. Hill concluded that most HIV clinical trials are too small to detect differences between two treatment groups when it comes to severe or life-threatening side effects. This is something to bear in mind when reading results from clinical trials, particularly those of new anti-HIV drugs.

### REFERENCE

Hill A, James I, McKinnon E and Law M. Statistical power to detect drug toxicity in HIV clinical trials. Abstract 20.

---

## F. Lactic acid and nuke damage

Nucleoside analogues (nukes or NRTIs) such as AZT, d4T and ddI may be associated with a number of side effects, including the following:

- wasting of muscle tissue, including the heart
- malfunctioning kidneys
- swollen pancreas gland — pancreatitis

- type 2 diabetes (non-insulin dependent)
- thyroid hormone abnormalities
- swollen livers due to excess fat deposits
- nerve damage — peripheral neuropathy
- loss of fat just under the skin (subcutaneous fat)

Some researchers think that these problems occur because nukes damage the energy-producing parts of cells called “mitochondria” (Mt). Large numbers of damaged or malfunctioning Mt produce lactic acid (lactate). When high levels of lactic acid in the blood occur, this is known as “lactic acidosis.” Generally, this condition is uncommon in PHAs. People with hepatitis B or C are at increased risk for developing lactic acidosis. Symptoms of lactic acidosis include the following:

- unexpected tiredness
- abdominal pain
- shortness of breath
- nausea and/or vomiting

The following blood tests help identify lactic acidosis:

- lactate levels of 5 mmol/L or greater
- bicarbonate levels of 20 mmol/L or lower

If left untreated, lactic acidosis can be deadly.

Reseachers in San Diego, California, conducted a study to find out if switching nukes (more about this later) in a combination could help PHAs with one or both of the following:

- fat wasting
- symptoms of high levels of lactic acid

All 118 HIV positive subjects had suppressed viral loads and had been using d4T as part of HIV combination therapy for at least six months when they entered the study. All subjects were switched from the nuke d4T to either AZT or abacavir.

Sixteen subjects had high lactic acid levels (more than 2.2 mmol/L) and took a temporary drug holiday (for about a month) until lactic acid levels returned to normal. Once this happened, they resumed therapy, with the d4T in their combination replaced by either AZT or abacavir.

### Results — lactic acid

About 93% of all subjects continued to achieve low viral loads up to one year after the switch. No further cases of high lactic acid levels developed, although eight cases of abacavir hypersensitivity occurred.

---

Special X-ray scans, called DEXA, taken of the legs and trunks of some subjects detected increased subcutaneous fat levels one year after the d4T switch. However, these increases were generally not obvious to the naked eye.

#### REFERENCE

Lonergan T, McComsey G, Hessenthaler S, et al. Lack of recurrence of symptomatic and asymptomatic hyperlactatemia when stavudine is replaced by either abacavir or zidovudine: 48-week data. Abstract 21.

---

### G. No nukes please

Because nukes have been suspected of damaging mitochondria, the use of some of these drugs may be linked to fat wasting. This is why some doctors and their patients are interested in testing combination therapy that does not include nukes (nuke-sparing). Researchers in Canada (Vancouver and Toronto) have been studying combinations of nuke-sparing regimens, such as the protease inhibitor Kaletra with the non-nuke nevirapine, to assess this combination's effect on the lipodystrophy syndrome. Similarly, researchers in Ottawa have been testing another combination — ritonavir-boosted saquinavir (PIs) with the non-nuke efavirenz. Complete details from these studies have not been released.

Meanwhile, researchers in the Netherlands have reported preliminary, six-month data from their study of another nuke-sparing regimen: ritonavir-boosted indinavir (PIs) and efavirenz. In this study, all subjects received the following regimen:

- ritonavir 100 mg twice daily
- indinavir 800 mg twice daily
- efavirenz 600 mg once daily

Some subjects also received standard doses of d4T.

The researchers analysed data on 36 subjects, none of whom had previously been exposed to anti-HIV therapy before entering the study. In measuring the level of DNA in mitochondria within white blood cells, they found some surprising results. After six months, levels of mitochondrial DNA doubled in both study groups. The researchers speculate that this increase was due to suppression of HIV, because HIV can damage mitochondria. However, only six months' worth of data were analysed. Long-term follow-up is needed to find out if there are differences between the two study groups. As well, it would have been interesting if researchers had presented data about changes (or not) in fat levels just under

the skin (subcutaneous fat) as well as in the belly. Information on any damage to mitochondria in fat cells would have also been useful.

#### REFERENCE

Casula M, de Baar MP, van Gemen B, et al. Therapy with efavirenz+ ritonavir-boosted indinavir, with or without stavudine after 24 weeks does not decrease mtDNA and mtRNA content of PBMC assessed by single tube duplex real-time NASBA. Abstract 25.

---

### H. Fat wasting — AZT vs. d4T

Researchers in Australia conducted a two-year study of HIV positive subjects who were using their first HAART regimen. Before starting therapy, DEXA scans of their legs were taken to assess fat levels. Doctors recruited 53 subjects, all of whom were male. Twenty-seven subjects received the nuke d4T and 26 received the nuke AZT, both in addition to other anti-HIV drugs. Thirty-three subjects received protease inhibitors.

#### Results

At the start of the study, subjects had about 22% leg fat. Two years later, among d4T users the proportion of leg fat fell to 13%. In the group of AZT users, the proportion of leg fat had decreased to only 19%. This difference between the d4T and AZT groups was statistically significant; that is, not likely due to chance alone.

The researchers found that protease inhibitors did not have a significant impact on changes in leg fat, at least over a period of two years. No mention was made of fat gain in the belly. This study is one of many to confirm the negative impact of d4T on the loss of subcutaneous fat. However, there are other parts of the body rich in fat, such as the arms, belly, buttocks and face, where the impact of nukes needs to be assessed.

#### REFERENCE

Nolan D, James I, McKinnon E and Mallal S, et al. Effect of stavudine, zidovudine and HIV protease inhibitor therapy on subcutaneous leg fat wasting in HIV-infected males — a longitudinal study. Abstract 28.

---

### I. Sugar blues

Having higher-than-normal levels of blood sugar (glucose) is a problem that can occur in HAART users, particularly in those PHAs who take protease inhibitors. To find out just how common this problem is, researchers in Milan, Italy,

---

conducted a large study with 1,481 subjects who had the following profile:

- 28% female, 72% male
- average age — 37 years
- average CD4+ count — 265 cells

Subjects were monitored for almost two years while they took anti-HIV therapy.

### **Results**

Regular blood testing found that only a relatively small number of subjects (32 out of 1,481) developed abnormal blood sugar readings. Eight of the 32 subjects had to temporarily stop taking HAART because of severe blood sugar problems. In each year of the study, the following proportion of the 32 subjects developed this complication:

- in the first year — 53%
- in the second year — 34%
- in the third year — 9 %

Thus, high blood sugar levels developed in 43% of subjects after their first year on anti-HIV therapy. The researchers, noting the delayed development of this problem in some subjects, suggest that PHAs who have risk factors for high blood sugar (a family history of diabetes, high lipid levels) need close monitoring to catch blood sugar problems early on before they become serious and lead to complications and interruptions in therapy.

#### REFERENCE

Quirino T, Bonfanti P, Faggion I, et al. Glucose metabolism abnormalities associated with highly active antiretroviral therapy: a cohort study. Abstract 35.

---

## **J. Predicting body shape changes**

It may be useful for PHAs to know their risk of developing lipodystrophy, particularly early in the course of therapy. That way, those who are at high risk for this complication could perhaps take preventive measures to minimize its impact. Researchers in Italy suggest that a simple blood test — triglyceride (TG) measurements — may be useful in this regard.

### **Study details**

Researchers recruited 837 HIV positive subjects between September 1999 and March 2000. Every six months, researchers assessed subjects for the presence and extent of lipodystrophy. At the start of the study, subjects had the following profile:

- 28% female, 72% male
- average age — 36 years
- average CD4+ count — 332 cells
- average viral load — 50,000 copies

Anti-HIV combinations used were as follows:

- 35% of subjects started with one or two drugs
- 64% of subjects started with three drugs
- 1% of subjects started with four or more drugs

Researchers monitored subjects for up to three years.

### **Results**

After three years, the risk of developing specific body shape changes were as follows:

- 16% — fat loss
- 15% — fat gain
- 8% — both

Analysis of many different blood tests revealed that those subjects who developed high TG levels were at greatest risk for body shape changes. For instance, for TG readings every 100 mg/dL above normal, the risk of developing fat wasting doubled. Cholesterol and glucose levels were not as closely linked to developing body shape changes as were TG levels.

#### REFERENCE

Gallim, Cozzi-Lepri A, Gervasoni C, et al. Triglyceridaemia, but not cholesterolaemia and glycaemia, is a predictor of lipodystrophy: the results of LipoICONA longitudinal study. Abstract 41.

---

## **K. Niacin for high triglycerides**

High levels of blood fats such as triglycerides (TG) increase the risk for cardiovascular disease as well as diabetes. Unfortunately, in some HAART users, TG levels soar over time. Although changes to diet, an exercise program and lipid-lowering medication can lower TG levels, supplements of the B vitamin niacin can also do the same. In HIV negative people, high doses of niacin (between one and three grams daily) have been used to lower TG levels. Because of concern that high-dose niacin may pose a risk to the liver and increase the chance of developing type 2 diabetes, researchers at the University of Hawaii tested this supplement in a clinical trial of eight HIV positive subjects.

### Study details

All subjects had higher-than-normal TG levels, averaging nearly 500 mg/dL. They made changes to their diet and began an exercise program. If after eight weeks their TG levels did not improve, doctors gave them extended-release niacin (Niaspan) 500 mg/day. This dose was increased each month until subjects were taking 1,500 mg/day. The reason for gradually increasing the dose is that high doses of niacin can sometimes cause skin flushing, redness and itching.

### Results

After six months of niacin therapy, all subjects were able to take the 1,500 mg/day dose. No significant changes in blood sugar or liver enzyme levels were detected. TG levels fell significantly, on average by over 300 mg/dL. One subject developed low phosphorus levels and had to receive a supplement of this metal. Niaspan was safe, effective and well tolerated in this small study.

People should not be discouraged that changes to diet and exercise did not improve TG levels because in this study these interventions were only carried out for two months.

#### REFERENCE

Souza S, Chow D, Walsh E, et al. A 36-week safety and tolerability study of extended-release niacin for the treatment of hypertriglyceridemia in subjects with HIV. Abstract 49.

---

### L. Supplement fix for nelfinavir-related diarrhea

One of the side effects of protease inhibitor-based therapy can be diarrhea. If left untreated, diarrhea could, in theory, lead to wasting, tiredness and reduced quality of life. For protease inhibitor-related diarrhea, sometimes supplements of calcium (500 mg twice daily) or soluble fibre, such as Metamucil, have been reported to be helpful. For more details about this, see *TreatmentUpdate 108*.

However, calcium supplements may not always work, so researchers in Chicago and Indiana tried a novel approach for treating diarrhea caused by the protease inhibitor nelfinavir (Viracept).

Researchers recruited 20 HIV positive men who used nelfinavir who had more than two liquid stools daily. They observed four while giving the remaining 16 the following:

First four weeks:

- supplement of 1.2 grams/day of friendly bacteria (*L. acidophilus* and *L. bifidus*) taken each morning on an empty stomach
- soluble fibre — 11 grams taken two hours after subjects took a dose of nelfinavir

If after four weeks these products did not work, subjects could add the amino acid L-glutamine, starting at a dose of 10 grams/day to a maximum of 30 grams/day. L-glutamine soothes the intestines and helps them heal from inflammation. It is also used by the body to make the antioxidant glutathione, which is often deficient in PHAs. This supplement helps to increase muscle mass when used in conjunction with exercise. So perhaps it was not surprising that the study protocol included supervised exercise for 16 subjects.

### Results

Among the 16 subjects who received supplements, nine reported that their diarrhea cleared up within the first four weeks of the study, and six reported that gradually increasing the dose of L-glutamine helped reduce diarrhea from 2 ½ episodes daily to one episode daily. Diarrhea in one subject was unaffected by the supplements. Among the four control subjects who were not given any supplements, diarrhea continued.

#### REFERENCE

Heiser CR, French N, Russert MM, et al. Dietary supplementation and exercise reduces diarrhoea, increases muscular strength, and improves quality of life in HIV-positive men receiving nelfinavir. Abstract 59.

---

### Disclaimer

**Decisions about particular medical treatments should *always* be made in consultation with a qualified medical practitioner knowledgeable about HIV-related illness and the treatments in question.**

The Canadian AIDS Treatment Information Exchange (CATIE) in good faith provides information resources to help people living with HIV/AIDS who wish to manage their own health care in partnership with their care providers. Information accessed through or published or provided by CATIE, however, is not to be considered medical advice. We do not recommend or advocate particular treatments and we urge users to consult as broad a range of sources as possible. We strongly urge users to consult with a qualified medical practitioner prior to undertaking any decision, use or action of a medical nature.

We do not guarantee the accuracy or completeness of any information accessed through or published or provided by CATIE. Users relying on this information do so entirely at their own risk. Neither CATIE nor Health Canada nor any of their employees, directors, officers or volunteers may be held liable for damages of any kind that may result from the use or misuse of any such information. The views expressed herein or in any article or publication accessed or published or provided by CATIE are solely those of the authors and do not reflect the policies or opinions of CATIE or the official policy of the Minister of Health Canada.

### Permission to Reproduce

This document is copyrighted. It may be reprinted and distributed in its entirety for non-commercial purposes without prior permission, but permission must be obtained to edit its content. The following credit must appear on any reprint: *This information was provided by the Canadian AIDS Treatment Information Exchange (CATIE). For more information, contact CATIE at 1.800.263.1638.*

### Credits

**Writer** Sean Hosein  
**Research assistant** Tim Rogers  
**Editor** RonniLyn Pustil

© CATIE, Vol. 14, No. 8  
 November 2002



Funding has been provided by Health Canada, under the Canadian Strategy on HIV/AIDS.

### What CATIE Does

The Canadian AIDS Treatment Information Exchange (CATIE) enables people living with HIV/AIDS (PHAs) to make informed choices about their health care, to optimize their quality of life, to prevent the progression of disease and opportunistic infections and to reduce the impact of side effects. CATIE provides such information through a comprehensive Web site, a bilingual toll-free phone service, electronic and print publications, a national reference library and workshops and exhibits at conferences across Canada.

### Other CATIE Publications

#### A Practical Guide to HAART

The latest on what is known about the various aspects of treatment, including a description of the virus and the immune system, the stages of HIV disease, the tests used to assess health status, and anti-HIV medications.

#### A Practical Guide to HIV Drug Side Effects

The latest on what is known about various side effects related to treatment, from appetite loss to sexual difficulties, and tips for countering or preventing them.

*The Practical Guide series also includes:*

- **A Practical Guide to Nutrition**
- **A Practical Guide to Complementary Therapies**
- **A Practical Guide to Herbal Therapies**

#### Fact Sheets & Supplement Sheets

Concise overviews of conditions, symptoms, medications, side effects, complementary therapies, vitamins, herbs and other treatment issues.

#### Plain & Simple Fact Sheets

The basics of HIV/AIDS treatment.

#### Managing Your Health, 1999 edition

A must-read guide for PHAs which addresses social, legal, health-related and practical issues comprehensively and from a national perspective.

#### The Positive Side magazine

Holistic health, information and views for PHAs.

#### pre\*fix

A harm reduction booklet for HIV+ drug users.

### Contact CATIE

**by e-mail:** info@catie.ca

**on the Web:** http://www.catie.ca

**by telephone:** 416.203.7122  
 1.800.263.1638 (toll-free)

**by fax:** 416.203.8284

**by post:** 555 Richmond Street W., Suite 505  
 Box 1104  
 Toronto, Ontario  
 M5V 3B1  
 Canada