A Practical Guide to
HIV DRUG SIDE EFFECTS
for people living with HIV/AIDS
A Practical Guide to HIV Drug Side Effects

first edition

Canadian AIDS Treatment Information Exchange
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mission statement The Canadian AIDS Treatment Information Exchange (CATIE) is committed to improving the health and quality of life of all people living with HIV/AIDS (PHAs) in Canada. CATIE provides HIV/AIDS treatment information to PHAs, caregivers, health care providers and AIDS service organizations who are encouraged to be active partners in achieving informed decision-making and optimal health care.

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helpful tips for
countering or preventing
HIV drug side effects
and other symptoms
The availability of HAART (Highly Active AntiRetroviral Therapy) — also referred to as a drug cocktail or combination therapy — has extended the lives of many people with HIV/AIDS (PHAs) and greatly reduced deaths due to AIDS and related complications. However, HAART medications (meds) can cause problems for your body that will create troubling symptoms. They’re called drug side effects, and they can range from mild to annoying to life-threatening. Many, but not all, PHAs who take HAART will experience side effects from these drugs. For some people, the side effects are temporary and disappear after a few days or weeks. For others, they can last as long as the drugs are continued and, in some cases, will remain even after drugs are discontinued.

A few tips may help you handle side effects. First and foremost, you must be in touch with your body (so you’re really clear on what it’s experiencing and can describe it) and with your doctor (so a medical decision concerning your symptom can be made). This leads us to the two most important rules:

I Rule #1: Tell your doctor everything, from beginning to end — if a symptom appears, changes, disappears, reappears...tell your doc what’s up (and write it down so you do not forget).

I Rule #2: Always apply Rule #1.

If you talk to your doctor about possible side effects before starting treatment, you’ll be better prepared to deal with many of the minor problems. If there is a side effect that might be severe or life-threatening, you’ll know what to watch for. If it’s likely that this or that side effect will improve over time, it will be easier to convince yourself to stick with a particular drug if you know that the problem it’s causing may soon improve.

Know that while your body adjusts to any new med, you may experience headaches, nausea, muscle pain, diarrhea or dizziness — all of which may disappear in two to six weeks. The same may hold true for other, more drug-specific symptoms. In general, as your body adjusts to a drug, many symptoms may diminish or become more manageable.

It’s important to remember that you are not alone. Countless others are feeling the same thing. So even if your symptom seems too awful to handle long-term, talk to your co-sufferers, ask what has worked for them, soak a few shoulders if you must, and try to hang in there for at least six to eight weeks after a med is introduced, if you possibly can.
You should also know that new side effects may appear at any time. Repeat, any time. Never say to yourself: “I’ve been on this drug combination for three years now so what I’m feeling couldn’t possibly be tied to the medications.” It could. And refer to Rules #1 and #2.

Regardless of the specific symptom, always seek a full diagnosis from your doctor on all possible contributing causes. Yes, what you’re feeling may be from the med, but it could also be a hormone problem, a nutrient deficiency, an infection, depression, HIV itself or any of the countless other contributors to symptoms that are discussed in this guide. The approach that’s most likely to eliminate your symptoms will address all of these and perhaps may make switching or stopping medicines unnecessary.

Changing drugs is your final option. The possibilities will, of course, depend on your treatment history and current needs. But be sure to ask your doctor. If you don’t, you may not find out that there is a good alternative. Your doctor may not have mentioned this because you haven’t reported how troubling your symptoms are. See Rule #1.

The goal here is simple: to allow you to have your cake and eat it, too. In other words, to create an integrated approach that will allow you to gain the benefits that your drugs can give you, while avoiding the side effects that can make taking them so difficult. In the end, there are two potentially huge benefits to this approach:

First, it can help prevent treatment failure, since you are much more likely to properly adhere to your drug regimen — which means sticking to your pill-popping schedule and taking your drugs exactly as prescribed and directed — when your meds aren’t making you feel sick or causing symptoms that you hate. And the result of always taking your drugs as directed — instead of skipping the Saturday night dose because you don’t want smelly gas at the party, or the Sunday morning pills because you’ve been invited to brunch and don’t want to be sick to your stomach — is that you’re much less likely to experience drug resistance. That means that your medicines — and their ability to save your life — may remain effective for years instead of months.

And last, but most assuredly not least, your quality of life can be immensely improved when life-degrading symptoms are eliminated or, at least, lessened. It’s all about living well with HIV, not just longer.

Now to the nitty gritty. The most common HIV drug side effects are listed in this guide, with tips on how to handle them. Wherever possible, information on natural and herbal products that are available in health food stores or pharmacies has been included. Your local AIDS service organization may be able to suggest a health food store in your area where you can shop for some of the supplements listed in this guide. At the back of the guide we’ve listed a few that provide mail-order service.

Don’t forget that treatments taken to relieve side effects — even natural or herbal treatments — can have side effects of their own. Always ask your physician, pharmacist or naturopathic doctor to check for possible interactions with other drugs or treatments you may be using.
Loss of interest in eating can come from many different medications, whether they directly suppress your appetite or create changes in your sense of smell and/or taste. It can also occur when medicines are causing nausea that makes the very thought of eating impossible (see “Nausea and Vomiting”). Although discontinuing the offending drug will usually quickly solve the problem, this is often not a possibility, so other approaches are needed.

**Tips for handling appetite loss**
First, consider the causes other than meds that might also be contributing to appetite loss:

- infections and fever — treat ’em
- abnormally low levels of hormones (especially testosterone, which can be replaced if testing determines that your levels are low)
- abnormally high levels of certain chemicals (called cytokines) produced by the immune system — they can be partially suppressed with meds or the nutrients N-acetyl-cysteine, or NAC, 500 mg, 3 times per day, and L-carnitine, 1,000 mg, 3 times per day (or acetyl-L-carnitine, 500 mg, twice daily)
- depression — get the treatment you need; many people lose interest in eating when they’re depressed, so feeling better is a must
- nutrient deficiencies (particularly of zinc, so try 75 mg daily; but always take it along with a potent multivitamin/mineral for overall micronutrient support) — nutrient deficiencies are one of those vicious circles: the appetite loss has caused inadequate nutrient intake, and now the lack of nutrients is causing appetite loss. The solution that’s needed is usually a combination of appetite boosters, high-nutrient foods and supplementation.

When the appetite’s still not there, you may have to change your eating habits or patterns. Try to eat on a schedule and substitute multiple smaller snacks for three big meals. Even if you don’t feel hunger pangs by the next scheduled intake, just sit down and do the best you can to eat as much as possible. Chow down on healthful snacks whenever you have the urge. Make the most of those times you do feel hungry and make every bite count. Anything that helps spark your interest in food should be tried, such as:

- new seasonings or substitutes for food that tastes odd
- sauces to cover metallic-tasting protein foods
- serving food after it has cooled in order to lessen objectionable smells
- keeping lots of tasty snacks around so that any moment of appetite can be used to your advantage

When sitting down to a whole meal seems impossible, supplemental drinks can be an excellent source of additional calories. Drinking a meal may seem a lot easier than eating one. Try a blended soup or a high-calorie blender drink, such as the following:
Combine regular milk (if there’s no problem with lactose intolerance) or rice milk (such as Rice Dream) with half a banana, half an apple and a tablespoon of Knudsen Coconut/Pineapple Nectar (for the medium-chain triglycerides, or MCTs, and, of course, the piña colada taste). Instead of or in addition to the coconut milk as the source of MCTs, you can add a lot of calories with a tablespoon or two of coconut cream or oil or MCT oil, available in most health food stores. You can also add other fruits (fresh or frozen) and vanilla or other flavorings to this blender drink; just avoid anything with concentrated sugar. If you prefer the iciness of a smoothie, add ice when you blend this drink.

If you’re not reaching the desired level of daily protein intake with the foods you’re eating, it may also be useful to add high-quality protein powder to the blender drink. Among the best of the available protein powders are the whey protein products. In addition to weight gain, whey protein may contribute to increasing the antioxidant glutathione (GSH) in the body, an important additional benefit, as PHAs tend to have less-than-normal levels of glutathione. Another possible benefit is that some of the whey protein products are rich in immunoglobulins, the proteins that act as antibodies and may actually help in the body’s defense against some infections. Don’t overdo it when you use protein powders. Remember that too much protein can actually strain the kidneys. Large amounts of such protein powders can also cause diarrhea because they are water-seeking. A moderate amount to increase the protein content of your diet if you’re not otherwise getting enough is reasonable.

If you don’t want to create your own supplement, it may be helpful to use supplemental drinks made from powdered or liquid formulas that are low in sugar and fat (or that use predominantly MCTs), moderately high in good-quality protein and high in calories overall.

And, finally, some substances can act as appetite boosters, such as the following:

- Medicinal marijuana, or its synthetic cousin Marinol (dronabinol), is a powerful appetite stimulant. Smoking marijuana can be hard on your lungs (especially if you have asthma), so some people prefer to bake it into brownies or cookies. The major problem encountered with Marinol is that it can be difficult to absorb and its effectiveness seems to vary between individuals. Both marijuana and Marinol can leave people feeling “stoned.” For people who have problems with the mental effects (such as drowsiness and dizziness), with Marinol at least these can be lessened by taking the drug before bedtime, because the appetite stimulation often carries over into the next day.

- Megace (megestrol acetate), a female sex hormone, was prescribed in the past for appetite stimulation but it has several serious drawbacks. First, it can suppress testosterone production, which is clearly an unwanted side effect because testosterone deficiency can actually contribute to appetite loss. Megace can also sometimes cause breast enlargement in males. Further, the use of Megace has recently been tied to avascular necrosis, the death of bone tissue (see “Bone Death and Destruction”).

- The antihistamine cyproheptadine (Periactin), usually prescribed for allergies, can be an effective appetite booster in some, especially children.

For more info on medicinal marijuana, see “Green Acres” in the Spring/Summer 2002 issue of CATIE’s Positive Side magazine, available at www.positiveside.ca or by calling 1.800.263.1638.
Lipodystrophy syndrome is the term used to describe a range of symptoms that include changes in body shape and metabolic changes (for the latter, see “Cardiac Concerns” and “Insulin Resistance and Diabetes”). Lipodystrophy-associated body changes — loss of fat in the face, arms, buttocks and legs, and, at the other extreme, enlarged breasts and bellies, along with buffalo humps (fat at the base of the neck) and fatty tumours (lipomas) — are at the top of many PHAs’ don’t-want-to-have-it lists. The causes are not yet fully understood but many think that they may include some combination of drug side effects, changes in the body that occur when HAART leads to immune restoration, HIV disease itself, and possibly other factors that are as yet unknown. Unfortunately, discontinuing medications doesn’t always reverse the problems, although there have been reports of gradual improvements over time in at least some people.

Although many people think of this as a “cosmetic” issue, it certainly isn’t when:

- the buffalo hump creates difficulty sleeping, headaches and neck pain, which may obstruct side vision
- the abdominal fat causes difficulty breathing, digestive problems and back pain
- the facial fat loss and overall body distortion cause serious emotional distress (involved in the development of anxiety and depression), an unwillingness to pursue life activities and non-adherence to medications

**Tips for handling body distortions**

Research is underway to attempt to determine exactly why lipodystrophy occurs and how to prevent or treat it so in the future there may be much better solutions. For now, therapies differ depending on the area affected and whether the problem is fat excess or fat loss (lipoatrophy).

Numerous studies and anecdotal reports have shown that human growth hormone (Serostim) often effectively shrinks big bellies, buffalo humps and lipomas by decreasing the abnormal fat deposits, although full results may not be seen for a period of time. Because many people have a mixture of fat accumulation in some areas of the body and fat loss in others, concerns have been expressed that Serostim’s stimulation of fat burning might actually worsen fat loss in the face, arms and legs. However, this has not been reported in the studies done to date. Clearly, it will not return lost fat to the face, arms or legs, but some people have actually reported that it appears to stimulate enough muscle growth for their limbs to look better.

The standard Serostim dose of the past was 6 mg injected daily, but treatment activists have found that lower doses (1–3 mg), taken either daily or every other day, may work just as well and have the advantage of reducing or preventing the drug’s possible side effects — swollen joints, carpal tunnel syndrome (numbness and pain in the wrist and hand) and higher-than-normal blood sugar levels. Although these lower doses, taken daily, are now being studied for lipodystrophy treatment by the manufacturer (Serono, Inc.),
Serostim is currently only approved for standard wasting, making coverage of the expensive drug dependent on the PHA and his or her doctor reporting a weight loss of at least 10% — the justification for a diagnosis of traditional wasting.

**Anabolic steroids combined with exercise** can help boost “lean tissue,” including muscle size, but have not been found to significantly improve the fat loss/accumulation process. In studies done to date, muscle size has increased but there have been no reductions in accumulated fat, and there have been worrisome decreases in HDL cholesterol (the good or healthy kind of cholesterol) in those using the steroids oxymetholone or nandrolone. In those on oxymetholone, there were also troubling increases in liver enzymes, indicating toxicity to the liver.

Studies of exercise alone have generally shown either no benefit in terms of losing accumulated fat associated with lipodystrophy (in one study, four months of serious weight-lifting four times weekly resulted in no fat loss) or only very small improvements (in another study, there was only 2% fat loss after four months of intensive exercise, including both strength-training and aerobics). But exercise does have many other benefits, including boosting cardiovascular fitness, mental well-being and self-esteem.

In some areas of the body, excess fat can be removed via **liposuction** (of buffalo humps or lipomas) or **standard surgery** (for breast reduction), though the fat sometimes returns over time, and neither approach is possible in the belly because of high hemorrhage risk.

Research is underway into the possibility that some drugs used to control diabetes (metformin and the glitazone drugs, all of which help improve insulin sensitivity) may prevent or reverse the development of fat accumulation. However, the studies done to date with metformin have been relatively discouraging, with only small or no decreases in visceral fat (the fat deep inside your body) in the abdomen. And it is important to note that metformin also resulted in significant losses in subcutaneous fat (the fat just under the skin), which is a big negative for those who have already lost fat in their face or limbs. Rosiglitazone has not been shown to either decrease abdominal fat or restore lost subcutaneous fat. Anyone considering metformin should be aware that it can cause lactic acidosis, a rare but potentially lethal side effect of nucleoside analogues (nukes). Whether combining multiple agents (metformin and nukes) that have the potential to cause this problem would increase the overall risk of developing lactic acidosis is not clear, but be forewarned of the possibility.

The drugs d4T and AZT (called “thymidine analogues”) have been linked to loss of subcutaneous fat, particularly in the face, arms and legs. Switching these drugs, or avoiding them altogether, may help minimize this side effect.

**Mitochondrial toxicity**

Preventing body-shape changes will require a better understanding of causes. Researchers theorize that nuke-induced damage to the mitochondria (your cells’ energy factories) may contribute to not only lipodystrophy but also to neuropathy, muscle aches (myopathy), pancreatitis (a painful inflammation of the pancreas gland) and lactic acidosis (a potentially lethal build-up of lactic acid in the body). Although the latter is rare, it can be fatal, so experts urge anyone experiencing any of the symptoms that can indicate lactic acidosis to see their
Increased blood lactate can cause a wide range of symptoms including:

- fatigue
- nausea
- vomiting
- abdominal pain
- sudden unexplained weight loss
- shortness of breath or difficulty breathing (respiratory symptoms)
- neurologic symptoms (including difficulty moving)

Experts urge anyone who appears to be experiencing lactic acidosis to immediately stop antiretroviral therapy.

Although researchers say that much more research is needed to confirm possible ways to counter mitochondrial toxicity, some have suggested that in the meantime it would be reasonable to try the following:

- antioxidants (vitamin C, vitamin E, carotenoids, selenium, alpha-lipoic acid, co-enzyme Q<sub>10</sub> and others)
- B vitamins
- the amino acid L-carnitine (or its other form, acetyl-L-carnitine)

In one of the studies, the following combination reversed lactic acidosis when given intravenously twice daily:

- L-carnitine (1,000 mg) and
- B-complex vitamins (in the following doses: 100 mg thiamine, 20 mg riboflavin, 100 mg niacinamide, 10 mg pyridoxine and 10 mg dexpanthenol).

**For facial restoration** (to help fill out sunken cheeks), injections of a synthetic compound of polylactic acid (New-Fill) have worked wonders. The New-Fill procedure requires several injections into each cheek, repeated three to six times (three weeks apart). In one study, 22 out of 26 people said their faces returned to normal. The change in facial appearance usually lasts for around one year to 18 months, after which another treatment is required to maintain the results.

When done by a skilled plastic surgeon, the use of fat injected into areas of lipoatrophy (fat wasting/loss) can also be effective in restoring facial appearance. The initial facial restoration usually requires only one or two treatments, but later treatments will be required to maintain the benefits. The length of time that the facial restoration remains seems to vary between individuals, with results lasting for as short as three months in some and as long as a year or more in others. Some plastic surgeons say that the best overall results might come with a combination of fat and New-Fill injections but there has been little experience with this so far.

Other therapies may also be available—ask your doctor for a referral to a plastic surgeon. Reconstructive surgery for lipodystrophy is not covered by provincial formularies. Any plastic surgery may result in scarring.
Avascular necrosis: The thigh bone’s (no longer) connected to the hip bone. That could be your problem if you develop the tongue-trippingly named *avascular necrosis* (AVN) of the femoral head, a bone disease in which a lack of blood flow results in tissue death in the top end of the thigh bone, the section that creates part of your hip. Studies have indicated that protease inhibitors may contribute to this hip-destroying problem. Researchers theorize that elevated blood fats — particularly the high triglyceride levels often caused by these drugs — might be blocking the blood supply to the bones, thus leading to tissue death, but note that this is definitely still theory, not a proven fact. Even in PHAs not on HAART, triglycerides are often too high and might be a factor in the development of bone problems.

The following are additional risk factors because each of these can contribute to decreased blood supply to the bone:

- long-term use of corticosteroid drugs
- alcohol abuse
- bone injury (such as fractures)
- bone infections
- scuba diving
- Addison’s disease — an adrenal gland condition that some PHAs develop, which results in reduced production of the steroid hormone called cortisol. It is usually treated with low doses of hydrocortisone (30 mg or so daily), a dosage level that is not usually thought to cause AVN but might contribute (via the same process as any chronic corticosteroid use).

The hip is usually the first place where avascular necrosis of the bone shows up, but it may also develop in the shoulder, knee or hand. Common early symptoms include:

- pain in the hip joint or groin area, which may radiate down the leg to the knee, and may in some cases be quite excruciating
- stiffness in the hip area (often particularly noticeable upon awakening)
- occasional aching (especially after long periods of walking or standing)
- a decreased range of motion

With any such symptoms, getting a comprehensive physical exam is a must, followed, if appropriate, by an MRI (magnetic resonance imaging) scan of the bone.


**Tips for handling avascular necrosis (AVN)**

If detected early on, small holes can sometimes be drilled in the bone to increase blood flow and allow new blood vessels to grow (a process called core decompression surgery), thus helping to slow worsening and reduce pain. However, there are no known curative measures that will permanently prevent a downhill slide toward bone death. If it has progressed too far in the hip bone, the only thing that works is hip replacement. It may be useful for PHAs who are concerned about AVN to avoid the following activities that could increase the pressure on the hip joint:

- some weight-lifting exercises
- squats
- running on concrete
- carrying heavy weight on the shoulders

**Osteopenia and osteoporosis**

The other bone problem being seen in PHAs is osteopenia, or its more advanced stage, osteoporosis. These are the gradual loss of bone tissue that occurs when the body's normal constant loss of bone cells is not equaled by constant replacement, resulting in gradually thinning and weaker bones that may become brittle and break easily. Postmenopausal women are inherently at greater risk than men for osteopenia and osteoporosis. As with AVN, it is not fully understood what all the causes may be, although it appears that protease inhibitors may be contributing, as well as HIV disease itself, hepatitis co-infection, nutritional deficiencies, smoking and lowered sex hormone levels. It is theoretically possible that the osteoporosis in some PHAs might actually be contributing to the development of AVN, a known complication of severe osteoporosis, although studies to date have not shown this.

A DEXA scan is the best way to diagnose bone mineral loss, whether it is still at the stage of osteopenia or has developed into the more severe osteoporosis. A baseline scan (done before starting HAART) can be compared to later readings. Without a baseline scan, doctors can compare the current results with standard values based on the person’s age, weight and build, thus estimating the probable bone loss.

**Tips for handling osteoporosis**

Until all the causes are well defined, advice on specific curative or preventive measures will be lacking. However, in the meantime, what we do know to help prevent or reverse osteoporosis in general may certainly help, including:

- weight-bearing exercise
- cutting down or quitting smoking
- a nutrient-rich diet
- additional supplementation with calcium (1,000 mg daily for men, and 1,000–1,500 mg for women)
- magnesium (500–600 mg daily; excess magnesium can cause loose stools so watch for this)
- vitamin D₃ (400-800 IU daily). Vitamin D has been shown to be deficient in many PHAs and is important to ensure good uptake and use of your calcium.
Addressing the blood fat problems — sky-high triglycerides, often combined with increased total cholesterol, increased LDL cholesterol (the bad or lousy kind of cholesterol) and decreased HDL cholesterol (the good or healthy kind) — that many people on HAART are developing is crucially important to help provide long-term protection against artery damage and heart disease. There have been many reports from clinicians on serious arterial blockage and resulting angina (pain around the heart) in patients on HAART.

Thus, it is highly advisable for PHAs to do everything they can to lower their risk for heart disease by:

- quitting smoking
- keeping blood pressure and stress under control
- eating healthful diets
- exercising appropriately
- working at lowering elevated blood fats
- for those who are seriously overweight, working to lose the excess pounds

It is definitely time to be concerned if:

- Your total cholesterol is greater than 250 mg/dl or 5.2 mmol/litre (SI units) on repeated measures, and
- you have an unfavourable cholesterol/HDL ratio (which is variable, depending on age and sex; age above 40 and being male are greater risks).

Factors that would add to the concern include the following:

- Your triglycerides are elevated.
- You have a family history of cholesterol problems or heart disease.
- You have diabetes (see “Insulin Resistance and Diabetes”).
- You smoke.
- Your blood pressure is constantly elevated.
- You are overweight.

Tips for handling cardiac concerns
The standard medical advice for high blood fats (lipids) would usually begin with advising dietary changes to lower fat intake, but the experience of most clinicians, as well as the findings from a couple of small studies, indicate that changing what people eat is unlikely to be of substantial benefit when HAART meds are the main cause of the problem. On the other hand, if someone is on a French fry/milk-shake/cheeseburger meal plan, then this could certainly be contributing to the high blood fats. In such cases, aiming for less fat intake, along with increases in fruits, vegetables and whole grains (especially oats) — all of which contribute soluble fibre that can block cholesterol absorption — could help. Soluble fibre sources like psyllium seed (Metamucil) may also be useful. You may want to consult with a nutritionist who can help you with healthy eating.
On the topic of overall cardiovascular protection, it is very important to reduce your total fat intake and eliminate partially hydrogenated fats/oils from your diet. These are chemically modified fats that are found in most margarines, vegetable shortening and a large percentage of commercial ready-to-eat baked goods and snack foods. Everyone who cares about protecting their cardiovascular system needs to read labels and try to avoid these artery-damaging fats to the greatest extent possible. Instead, stick with the fats Mother Nature made, especially the monounsaturated fats like olive oil.

Several switch studies have shown that blood fats that were elevated during protease inhibitor therapy fell after people switched from the protease inhibitor (PI) to either the non-nuke nevirapine (Viramune) or the nuke abacavir (Ziagen, ABC). Switching to the non-nuke efavirenz (Sustiva) has not been shown to consistently improve blood fat levels. Thus, some “PI-sparing” regimens may work better than others, although much more research will be required to determine what really may be best in this regard. It will be very important to take into account the treatment history for anyone considering switching drugs, since some people may really need the PI(s) to maintain viral control.

With high cholesterol readings, drugs that act as cholesterol-lowering agents — commonly called statins — are often recommended. There have been a number of reports on the successful use of such drugs, but the specific agents need to be chosen carefully because of the potential for drug interactions with protease inhibitors. Statin drugs help prevent the chemical conversion of fats into cholesterol, but some of these drugs use the same liver enzyme pathway used by protease inhibitors (CYP 3A4) while others do not. Thus, the risk of negative interactions with PIs varies considerably between the different drugs. Currently, it is thought that the most acceptable choices are pravastatin or atorvastatin, with fluvastatin considered a secondary possibility. Rosuvastatin is another option. Lovastatin and simvastatin should not be taken with PIs. It is also important to be careful about interactions with herbs. The heavily promoted cholesterol-lowering herbal compound called Cholestin works similarly to the statins and may cause similar interaction problems. All statin drugs severely deplete co-enzyme Q_{10}; supplementation with 100–400 mg daily is needed with these drugs.

Fibrates are another class of lipid-lowering drugs which may help with blood fat abnormalities. They are considered the best choice for those who have only elevated triglycerides (and no cholesterol problems). Some believe that of the available fibrate drugs, fenofibrate may be preferable to gemfibrozil because it is easier to take and may do a better job lowering elevated LDL cholesterol. Sometimes the two classes of lipid-lowering drugs (statins and fibrates) are used together to improve effectiveness, but it is important to know that this increases the risk of muscle toxicity, a side effect of statins. Some fibrates, including gemfibrozil, deplete both vitamin E and co-enzyme Q_{10}. Supplementation with vitamin E (800 IU daily) and co-enzyme Q_{10} (100–400 mg daily) is needed with these drugs.

Because of drug interaction problems, when it comes to lowering blood fats some doctors prefer the B vitamin niacin (1,000 mg daily), which can lower overall cholesterol, LDL cholesterol and triglycerides. Niacin actually works
better than the statin drugs to raise HDL cholesterol, although the statins do work well to lower LDL cholesterol. However, there are several potential problems with niacin. First, a lot of people get flushing, redness, warmth and, in some people, painful stinging and itching for a period of a half-hour or more after it’s taken. A sustained-release, no-flush form is much less likely to cause these problems, especially if combined with a baby aspirin taken 30 minutes before the niacin. Taking it in the middle of a meal will also help. Niaspan (500 mg per tablet) can be taken with breakfast and dinner, and the tablet can be cut in half if even that dose causes problems. If the dose is tolerable but insufficient for normalizing blood fats, it can be increased until good results are seen, but this increases the risk of niacin’s second important potential problem: liver toxicity. Liver enzyme tests should be done to watch for such toxicity. Blood glucose (sugar) levels should also be monitored because niacin has the potential to affect blood sugar levels. Some experts say that niacin’s potential to increase insulin resistance makes it inadvisable for HAART takers (since many people on HAART will develop insulin problems), and that is particularly true for anyone already showing signs of blood sugar problems.

Another important possibility for lowering triglycerides is the amino acid L-carnitine (the prescription form of which is Carnitor). Not yet studied for HAART-caused problems, it was shown in the past to be effective in normalizing HIV-elevated triglycerides when used in doses of 6,000 mg per day. Some doctors have found that using a combined approach with Carnitor or acetyl-L-carnitine and one of the lipid-lowering drugs can result in normalization of blood fats when drugs alone do not do the job, so that may be an approach worth considering.

Omega 3 fatty acids, found in fish oil and flaxseed oil, can help to lower triglyceride levels. Eating fatty fish (such as salmon, mackerel, sardines, tuna, cod and halibut) is a tasty way to get those fatty acids, and studies of the general population (not HIV-specific) have shown reduced incidence of heart disease in those who consume several helpings of such fish weekly. However, the use of fish oils has not been studied in those with PI-caused high triglycerides, so it is not known if they would work as well in this population.

It is important to remember that even when blood fats can’t be completely normalized, you can lower your overall heart disease risk by combining regular exercise (as little as 30 minutes of cardiovascular training three times a week is great), nutrient supplementation and meditation and other stress reduction therapies.

The following nutrients may help prevent arterial damage and protect the heart:

- Magnesium (500–600 mg doses daily), which has been found to be deficient in some PHAs, can help prevent arterial damage and protect the heart. Be reminded that too much magnesium can cause diarrhea.

- Antioxidants (including vitamin E, vitamin C, bioflavonoids, selenium, co-enzyme Q10, N-acetyl-cysteine and alpha-lipoic acid) and B vitamins help prevent the chemical changes in the blood vessels and blood fats that are required for fat to be deposited into the lining of the blood vessels, thus helping to prevent damage to the arteries. So even if you can’t fully normalize your cholesterol readings, you can help keep it from being deposited in the blood vessels by having a plentiful supply of all these nutrients in the body.
Heart attack warning signs:
- uncomfortable pressure, fullness, squeezing or pain in the centre of the chest lasting more than a few minutes
- pain or numbness spreading to the shoulders, neck, jaw or arms
- chest discomfort with light-headedness, fainting, sweating, nausea or shortness of breath

Stroke warning signs:
- sudden weakness or numbness of the face, arm or leg on one side of the body
- sudden dimness or loss of vision, particularly in one eye
- loss of speech or trouble talking or understanding speech
- sudden, severe headaches with no apparent cause

If you experience any of these symptoms, call your doctor or go the emergency room right away.
Diarrhea — an increase in the frequency and decrease in the consistency of stools — can be caused by many antiretrovirals. This is an important side effect to keep in check, and any diarrhea that is frequent, watery or lasts for more than a couple of days should always be reported to your doctor.

The two medications most commonly reported to cause diarrhea are the protease inhibitors nelfinavir (Viracept) and ritonavir (Norvir), but many other meds may also cause this problem, including:

- indinavir (Crixivan)
- saquinavir (Fortovase)
- amprenavir (Agenerase)
- ddI (Videx EC)
- ddC (Hivid)
- d4T (Zerit)
- 3TC (alone in Epivir and also in the combination drugs Combivir and Trizivir)
- abacavir (alone in Ziagen and also in the combination drug Trizivir)
- nevirapine (Viramune)
- efavirenz (Sustiva)
- the anti-herpes drug acyclovir (Zovirax)
- many antibiotics and other meds

In other words, a large number of meds can be implicated in the problem of diarrhea. Obviously, combining these meds can make it difficult to tease out a single culprit. If the onset or sudden worsening of diarrhea is tied closely to beginning a medicine, it’s a likely suspect. In some cases, the diarrhea may diminish after a period of time on the drug, but too often it will become your daily companion.

**Tips for handling diarrhea**

If switching drugs is possible, that may be the best solution and will usually result in a quick resolution of the problem. However, since more than one cause often contributes, truly effective treatment requires aggressive diagnosis to pin down all possible factors. In addition to medicines, these can include:

- infections and parasites — check for them with aggressive diagnostic measures and treat anything found
- fat intolerance and malabsorption (very common in PHAs, even in earlier disease stages) — cut back on dietary fat and take lipase, the fat-digesting enzyme (found in the better pancreatic enzyme formulas) with meals
- lactose intolerance (very common in PHAs)— eliminate or decrease dairy products and take lactase enzyme when you do consume them
- excessive sugar or caffeine — cut back on ’em
- stress — find a way to chill out or consult with a therapist
When all causes can’t be eliminated, using standard anti-diarrheal agents, such as the following, may help relieve symptoms:

- Kaopectate
- Pepto-Bismol
- anti-motility agents (Imodium, Lomotil, tincture of opium, paregoric or opiates)
- luminal-acting agents or those that act in the intestinal passage (cholestyramine, pectin, Kaolin or fibre supplements)

Here are some other options for the runs:

- Shaman Botanicals’ SB Normal Stool Formula is a tree sap extract that many PHAs have reported helps reduce or eliminate med-induced runs.
- The amino acid L-glutamine, taken in doses of 5-30 grams daily (a powdered form is best; mix it in water or juice), can both help to heal damaged intestines and reduce the diarrhea by enhancing water and sodium (salt) absorption across the wall of the small intestine.
- Friendly bacteria, such as L. acidophilus, may also help relieve the symptom.
- Ground flax seeds (also called flaxmeal) will also sometimes help to relieve diarrhea and heal the intestines.

For diarrhea caused by protease inhibitors (PIs):

- Calcium taken in doses of 500 mg, twice per day, may work. Initially, a small study showed calcium therapy to be very effective for reducing or eliminating diarrhea caused by nelfinavir (Viracept), and since that study’s publication there have been many anecdotal reports that it also works for diarrhea caused by other PIs.
- Another small study showed that a pancreatic enzyme formula containing a high level of lipase (Digestive Care, Inc.’s Pancrecarb) taken with meals significantly improved stool consistency in those with PI-caused diarrhea.

Increasing your intake of foods that contain soluble fibre can help since they absorb water and expand, binding together the intestinal contents. This bulks up the stool and slows the passage of food, particularly when there is a lot of fluid in the stool. Examples of foods that contain soluble fibre include the following:

- peeled apples or apple sauce made from them
- other fruits such as apricots, peaches, pears, plums, grapes, melons, nectarines, bananas
- grains such as oatmeal, oat bran, white rice and barley
- soluble fibre supplements like psyllium (Metamucil) that you dissolve in a glass of water and drink

Fibre intake should be slowly increased to help limit the increase in intestinal gas that it can cause.
For as long as diarrhea continues, it is crucial to:
- Consume plenty of calories (eat more and make every bite count toward high-quality nutrition) and
- Drink plenty of healthful liquids (water, juices, herb teas, broth and fruit juice smoothies) to replace what’s being lost.

Remember that it is crucial to prevent dehydration when you are suffering from diarrhea, regardless of the cause. Drinking lots of water daily is very important. You should consume at least 1.5 litres of water every day.

With serious diarrhea, it is important to rebalance the body’s electrolytes, including sodium, potassium and chloride. Drinking vegetable and fruit juices, nectars or broths (diluted with water to enhance absorption) can help. However, more concentrated sources of electrolyte minerals may be needed. Gatorade is often recommended but it is not a very concentrated source of the minerals and is also loaded with sugar, which could actually worsen the diarrhea. Infalyte and BestLyte are better choices.

Another possibility is the use of the oral rehydration salts recommended by the World Health Organization, which are available through many pharmacies at low cost. The other inexpensive option is to mix your own solution with a teaspoon of light salt (which contains potassium mixed with sodium) and a quart of orange juice or apricot, peach or pear nectar (diluted with water); sweeten with a tablespoon of pasteurized honey, if desired. To add soluble fibre to this mix, dilute the nectar half and half with rice water (made by boiling four parts water and one part rice until the rice is tender, and then straining off the rice water). This rice water can also be drunk on its own as a source of both hydration and soluble fibre.

The following foods and liquids should be avoided because they can make diarrhea worse. Try to eliminate or at least cut back on these as much as possible:
- Coffee and other caffeinated beverages
- Alcohol
- Chocolate
- Fried and fatty foods
- Spicy foods
- High-sugar foods or liquids
Fatigue (tiredness, weakness or a lack of energy) — crawling out of bed feeling like you’ve been hit by a truck and going downhill from there — can be caused by many HAART combinations. Just taking all those drugs seems to wear some people’s bodies out. The energy loss caused by your medications will sometimes disappear after a period of time on those drugs (so you may want to consider waiting to see if the fatigue passes), and will often disappear fairly quickly if the meds are stopped. It seems to be an individual response — some meds may cause fatigue in you but not in your friends.

Fatigue can sometimes be a symptom of a more serious underlying problem, such as anemia. Anemia is a red blood cell (RBC) problem indicated by decreased hemoglobin, hematocrit and RBC count. When the medicines that can cause bone marrow (your blood cell production centre) suppression result in anemia, fatigue is highly likely. Among the meds that can cause anemia are:

- AZT (alone in Retrovir and also in the combination drugs Combivir and Trizivir)
- abacavir (alone in Ziagen and also in the combination drug Trizivir)
- valganciclovir (valgan, Valcyte)
- sulfa antibiotics (Septra/Bactrim, Dapsone)
- alpha interferon (Intron-a, Peg-intron, Pegasys)
- hydroxyurea (Hydrea)
- pyrimethamine
- pentamidine
- various anti-cancer drugs (chemotherapy)

Anyone with fatigue should have their blood cell levels checked. Anemia is experienced by more than three-fourths of those with symptoms of AIDS, and perhaps one-fourth or more of those with less advanced disease. Treating it is critical. A very large (more than 3,200 people) study found that regardless of CD4+ count, the risk of death was substantially higher for those with anemia, and that recovery from the anemia, by whatever means, significantly lowered that risk. Unfortunately, anemia too often goes untreated, and the result is:

- needless fatigue and weakness
- shortness of breath
- heart palpitations
- increased susceptibility to infections
- lowered quality of life
Meds are not the only cause of anemia. Other causes include the following:

- MAC (Mycobacterium avium complex)
- TB (tuberculosis)
- CMV colitis
- cryptococcal meningitis and other fungal infections
- parvovirus B19
- lymphoma
- KS (Kaposi’s sarcoma)
- deficiencies of the B vitamins folate (folic acid) or B₁₂ (both of which are common in PHAs)
- iron deficiency (less common in men but fairly common in women)

HIV alone can also cause anemia. And that is the Catch-22—the drugs you’re taking may cause it, but leaving HIV untreated will let the virus impair the production of red blood cells.

**Tips for handling fatigue**

The answer for many fatigued people is injections of recombinant human erythropoietin, termed Epoetin alfa (sold as Procrit, Epogen, or Eprex), usually given three times per week, to promote the production of red blood cells. It will often resolve anemia fairly quickly (within four to six weeks, the time needed for the new red blood cells to be created), and return real energy to your life.

Because many factors can contribute to energy loss, it is important to consider that you may also have the following:

- infections — treat ’em
- inadequate nutrition — eat well and often, and take nutrient supplements
- hormonal deficiencies — test and replace any that are suboptimal
- depression — get therapy and/or medication
- not enough rest — take naps and deal with insomnia
- stress — find a way to chill out or consult with a therapist
- excessive recreational drug or alcohol use — ask for help
- excessive caffeine and sugar — cut back on ’em

One of the most common causes is unsuspected vitamin B₁₂ deficiency. Blood levels may not accurately reflect the problem since it’s what’s in the tissues that counts, and the standard tests don’t show this. So simply doing a trial run of vitamin B₁₂ supplementation for at least six to eight weeks may be best. For many people, this has been a miracle cure for HIV-related fatigue.
The smelly intestinal gas and abdominal bloating that any of the protease inhibitors can cause will usually disappear quickly once the offending drugs are discontinued. But these side effects often continue unabated for as long as the drugs are taken unless you take measures to counter them.

Not all gas comes from your medications. Other causes include fat malabsorption, lactose intolerance and many intestinal infections (especially parasites).

**Tips for handling gas and bloating**

Taking **pancreatic enzymes** (one or more, taken with every meal or snack) can often eliminate the problem (unless the cause is an infection, which must be treated). Make sure to choose a brand that contains lipase, the fat-digesting enzyme, since it appears to be the key. Pancrecarb, manufactured by Digestive Care, Inc., is one such brand. There are other prescription versions, such as Ultrase MT-20 (manufactured by Axcan Scandipharm), but Pancrecarb appears to work better because it also contains ingredients that help the enzymes do their work better. (Pancrecarb is not currently approved in Canada and is only available by prescription in the U.S. However, any enteric-coated pancreatic enzyme that contains a potent amount of lipase may help.)

The **amino acid L-glutamine** (5–10 grams per day) may also help by improving absorption of fat and preventing its passing into the colon undigested where it will be acted on by bacteria and create — you guessed it — stinky, smelly gas.

**Conservative dietary modifications** can sometimes resolve a lot of “passed gas” and bloating. Try to identify which food products cause you the most problems and moderate or eliminate them. Some of the worst culprits are broccoli, beans, garlic, onions, cabbage and tough-to-digest vegetable skins. Over-the-counter products such as Beano (a vegetable enzyme) can help by improving the digestion of such foods.

If lactose intolerance is a problem, try to avoid dairy products and/or take a lactose-containing product (such as Lactaid) any time such foods are consumed.
Hair loss (alopecia) is a common experience, particularly in men as they age. When hair loss is new, rapid or severe, it is considered abnormal. There are many medical treatments that can cause disturbing hair loss, including cancer drugs and some arthritis drugs.

Hair loss can also be caused by many HAART meds, but for PHAs the most common cause is the nucleoside analogue 3TC (alone in Epivir and also in the combination drugs Combivir and Trizivir). The protease inhibitor indinavir (Crixivan) has also been implicated in some instances of accelerated hair loss. Unfortunately, no one seems to have found a perfect solution other than switching or discontinuing the problematic drug. Even then, the return of the lost hair may be slow and incomplete.

Other causes of hair loss include:
- malnutrition, particularly low protein intake
- thyroid problems
- B complex vitamin deficiency

It is important to note that androgenic steroids, such as testosterone, are often implicated in rapid or new-onset hair loss, particularly when too-high doses are used. An evaluation of the pros and cons of testosterone for you should be considered with your doctor. In general, doses that simply replace normal levels of testosterone using through-the-skin delivery (via gels or patches) are considered best; too-high doses, especially via injections, should be avoided. For some people, minoxidil products (Rogaine) may help with hair loss, but as with all medications, check to make sure there are no possible interactions with your other drugs before taking such products.
Some people develop headaches as a result of drug side effects. In some cases, these will only occur during the beginning of drug therapy and will gradually disappear over the next few weeks. In others, they may remain long-term, and the only solution may be a drug switch. Medications should be particularly suspected as a headache cause when a new drug treatment has recently been started, but note that such reactions can occur even after months of using a particular drug.

Headaches can also be a symptom of many different infections and conditions, some of which could be fatal if undiagnosed. Among the possible causes of headaches are:
- cryptococcal meningitis
- endocarditis (heart infection)
- syphilis
- candidiasis (yeast infection)
- toxoplasmosis
- herpes outbreaks
- progressive multifocal leukoencephalopathy (PML)
- CMV encephalitis
- primary central nervous system (CNS) lymphoma

All headaches that are at all severe or that last for more than a few hours or that recur should be taken very seriously. If you are suffering from such headaches, run (do not walk!) to your best available neurologist or HIV specialist for a comprehensive diagnosis. It is best to not treat such headaches until your doctor has diagnosed the problem and told you what treatment is best. If you cover up this symptom with pain medications, you might mask what would otherwise point the way to a diagnosis of something serious. So this is a case where you should always call your doctor.

When a diagnosis is being sought, it is important to remember the old rule that you only find what you seek. There have been cases in which, because the person is HIV positive, the diagnostic procedures were too exclusively focused on opportunistic infections (OIs) and conditions, forgetting that PHAs are certainly also susceptible to other infections and malignancies. In some of these cases, when none of the common OIs or conditions were discovered, the headache was then attributed to HIV disease itself and no further attempts were made at diagnosis. Then, down the line, and usually when other symptoms appeared that gave better indications of a probable diagnosis, the person was finally discovered to be suffering from something unrelated to HIV disease. Unfortunately, by that time, the condition or infection was often much more advanced and more difficult to successfully treat. In these situations, if the person had been HIV negative, the diagnosis might actually have been made sooner because the non-HIV-related possibilities would have been considered more quickly. Never forget this possibility.
Tips for handling headaches

One cause of headaches that is rarely suspected by doctors is magnesium deficiency, a problem that Canadian researchers have found is relatively common in PHAs. In those who are HIV negative, it has been found that even in people who have suffered from severe headaches for many years, supplementing with magnesium may eliminate the problem. Supplementation with magnesium is not something that should be substituted for immediate medical attention to severe or recurrent headaches. However, if no other cause is found, keep the possibility of a deficiency in mind. Magnesium in doses of 500–600 mg per day may be required for some.

It is important to remember that if you are treating your headache, your choice of drugs should be made in the context of all the other factors currently affecting you, including:

- other drugs you are taking — because of possible interactions
- medical conditions such as liver problems — which would weigh against Tylenol because Tylenol (acetaminophen) can be hard on the liver
- other medical conditions such as ulcers, gastrointestinal bleeding problems, intestinal Kaposi’s sarcoma, low platelets, kidney dysfunction or low serum albumin levels (common in those with wasting) — which would weigh against aspirin and other non-steroidal anti-inflammatory drugs (NSAIDS)

In general, unless any such issues make it problematic, aspirin or buffered aspirin is probably the best choice. Tylenol (acetaminophen) lowers levels of the antioxidant glutathione (GSH) in the body. Since glutathione levels are already too low in PHAs, worsening this is not a good idea. In addition, the lowered levels of glutathione already present may significantly increase the chance for acetaminophen toxicity. Even in doses considered to be in the routine therapeutic range, acetaminophen can cause liver or kidney injury in certain populations with a tendency for glutathione deficiency, such as PHAs. Aspirin also lowers glutathione, but to a much lesser extent.

If you are taking either aspirin or Tylenol, the use of the following agents to help normalize glutathione levels is very important:

- N-acetyl-cysteine (NAC)
- alpha-lipoic acid
- the amino acid L-glutamine (this is also important to help keep the intestinal tract from being damaged by drugs)

Remember that long-term use of aspirin or other NSAIDs can cause damage to the intestines and gastrointestinal bleeding. In general, only use these meds when you absolutely need them to relieve headache, and avoid long-term use, if possible.

Other possibilities for treating some kinds of headaches include acupuncture or acupressure. The herb feverfew may also help. It contains parthenolide, an agent that reduces spasms in blood vessels in the head, and has been shown to work for both migraines and tension headaches.
Protease inhibitors have been tied to an increased incidence of glucose intolerance and decreased sensitivity to insulin, the hormone that is needed for the uptake of glucose (sugar) into the body’s cells. When that process isn’t working properly, glucose remains in the bloodstream, creating the high blood sugar that can cause damage to the blood vessels, and, ultimately, diabetes, with its list of possible complications, including:

- kidney failure
- blindness
- cardiovascular problems from top (strokes) to bottom (amputations) and in between (heart attacks)

So far, the rate of development of diabetes in PHAs is relatively low, but researchers fear it will increase over time. It is important to watch for the classic warning signs of diabetes:

- excessive thirst
- abnormal hunger
- increased urination

With any of these, call your doctor immediately so that diagnostic tests can be run.

You may be at increased risk for diabetes if:

- You have a family history of diabetes.
- You are overweight.
- You live a couch-potato lifestyle.

Recent research shows that indinavir (Crixivan), amprenavir (Agenerase) and ritonavir (Norvir) — and probably all the other protease inhibitors — may have specific effects that will cause blood sugar problems. The researchers, noting that other studies have shown that insulin resistance appears prior to the appearance of lipodystrophy symptoms, predict that insulin resistance may occur much earlier than has been so far reported, may be far more widespread, and may be implicated in the development of lipodystrophy.

**Tips for handling insulin resistance**

Substituting a non-nucleoside analogue or a nucleoside analogue for a protease inhibitor (PI) has been suggested as a possible way to improve insulin sensitivity. The switch studies done to date have been somewhat conflicting, but there is some evidence that switching from a PI to either the non-nuke nevirapine (Viramune) or the nuke abacavir (Ziagen, ABC) may improve insulin sensitivity and lower glucose. Results with a switch to the non-nuke efavirenz (Sustiva) have been less clear, with one study showing improvement and another not. Much more research will be required to determine what may be best in this regard. It will be very important to take into account the treatment
history for anyone considering switching drugs, since some people may really need the PI(s) to maintain viral control.

For anyone with elevated insulin levels (indicating insulin resistance) or elevated blood sugar levels, it definitely couldn’t hurt to do the things that normally help to increase insulin sensitivity, including the following:

- progressive resistance exercise (like weight-training) and a cardio workout
- weight loss in those who are significantly overweight — obesity alone is a serious risk factor for adult-onset diabetes
- limiting sugar and refined carbohydrate intake (white starchy foods, white sugar and flour and all the foods made with them)
- eating a more nutritious diet that is higher in fibre (found in whole-grain foods and fruits and vegetables) and lower in polyunsaturated fats (found in most vegetable oils and many prepared foods; it’s best to stick with monounsaturated oils like olive oil) has been shown to be tied to improved insulin sensitivity
- testosterone replacement therapy in men, where needed
- supplementation with a potent multiple vitamin/mineral that contains the B complex vitamins (especially B6), antioxidants (especially alpha-lipoic acid) and minerals (especially chromium) that help maintain normal cellular insulin sensitivity

It is important to have your blood sugar monitored regularly. If it begins to rise, and lifestyle modifications or drug switches are not enough to get blood sugar under control, antidiabetic medications may be needed. Two common drugs are rosiglitazone (Avandia) and metformin (Glucophage). Studies on the use of such drugs with protease-inhibitor-caused insulin resistance are limited but have shown improvements. However, there may be substantial drawbacks related to body fat loss (for more on this, see “Body Distortions”).

Most expert groups are waiting for additional research before making official recommendations on approaches to handling insulin resistance and blood sugar problems in PHAs, but the British HIV Association now recommends the following for anyone with symptoms of glucose intolerance:

- dietary advice and exercise
- switching from a PI-based regimen to a PI-sparing regimen (in people taking their first regimen)

For more info on insulin resistance, see “La Dolce Vita” in the Spring/Summer 2005 issue of CATIE’s Positive Side magazine, available at www.positiveside.ca or by calling 1.800.263.1638.
Kidney stones can occur for many reasons and are more common in temperate climates. Part of the reason for this is that stones develop when your urine is much more concentrated in minerals or crystals, as can happen when people sweat more in warmer climates. Kidney problems can occur in people taking HAART meds, especially if they drink inadequate quantities of fluids. The protease inhibitor indinavir (Crixivan) is often a culprit in the sudden onset of kidney sludge problems (so called because it’s not really a stone). The sulfa antibiotic Septra/Bactrim has also been reported to cause kidney stones.

Symptoms of kidney trouble include:
- severe pain in the lower back and sides (called flank pain or renal colic)
- difficult and painful urination
- blood in the urine
- inability to urinate

If you develop these symptoms, notify your doctor or go to your local hospital as soon as possible.

Tips for handling kidney stones
Anyone taking indinavir or suffering from kidney stones should consume at least 1.5 litres of healthful fluids daily, including:
- water
- caffeine-free teas
- juices
- broths

Drink even more water any time you might become dehydrated — in very hot weather, when dancing or exercising, if you’ve got diarrhea or if you’ve been vomiting. And remember that alcohol and caffeine are dehydrating. That means that beverages which contain either of these not only don’t count toward that fluid amount, they actually increase your need for the good fluids. So drink up and dilute the possible harmful side effects of the medications on your kidneys.

Kidney disease is another type of kidney damage that has been associated with some antiretroviral drugs, such as tenofovir.
Liver impairment in HIV disease is common and has many possible causes, only one of which are the medications you’re taking. Many infections can result in liver damage, including:

- co-infection with hepatitis viruses
- opportunistic infections such as MAC (*Mycobacterium avium* complex), TB (tuberculosis), CMV (cytomegalovirus) or cryptosporidiosis

Other factors that may damage your liver to the point that it is operating at less-than-optimal function, even before infection with HIV, include:

- repeated use of antibiotics
- excessive alcohol or recreational drug use
- a nutrient-poor, chemically loaded diet

On top of that are the many HIV drugs which can also cause liver toxicity. The combination of all of these explains why a certain level of liver toxicity and dysfunction is a frequent occurrence in PHAs.

The liver uses enzymes to help it get rid of the waste produced in your body both by normal body processes and by the breakdown of drugs, alcohol and other toxins. When the liver is overly stressed by this waste or damaged by various infections, liver enzyme tests done on blood samples may show significantly elevated values. These liver enzyme tests include the following:

- AST, also called SGOT (aspartate amino transferase)
- ALT, also called SGPT (alanine amino transferase)
- GGPT
- AP (alkaline phosphatase)
- LDH (lactic dehydrogenase)

All PHAs on HAART should have their liver enzymes monitored on a regular basis since liver damage is rarely something that is felt until it is quite advanced. It is especially important that people who already have some liver damage — because of hepatitis, for example — get regular blood tests for liver enzymes.

Bilirubin (a waste product) is also used as an indicator of liver disease. Note that some of these tests can be elevated by problems other than liver disease, so they must be interpreted carefully. However, even without elevations in these tests, there can be a level of less obvious liver dysfunction that should be addressed. Unfortunately, many people remain unaware of liver disease until it reaches a point that causes:

- pain
- swelling (hepatomegaly, or enlarged liver)
- fever
- jaundice (when the liver dysfunction results in an inability to break down bilirubin, which then causes yellowing of the skin and/or eyes)
Tips for handling liver toxicity
Since a functional liver is critical for life, detoxifying and repairing it can be one of the most important things you do for your long-term health, especially if you want your liver to be able to handle HAART over the long-term. The most obvious first step in a liver repair program is to eliminate as many sources of toxicity as possible. You may not be able to eliminate your HAART meds, but the following steps can help a lot:

- Try to cut out recreational drugs and decrease or, preferably, eliminate alcohol.
- Make sure that you are vaccinated against hepatitis A and B.
- Avoid situations that place you at risk for hepatitis C — such as sharing needles (for drugs and tattoos) and nasal instruments used for cocaine and ketamine (sniffers, straws and bills).
- Many doctors tend to prescribe antibiotics at the drop of a hat and this is not a good idea if you want to avoid damaging your liver. You should, of course, take them if you have a real need, but they shouldn’t be used whimsically or for an infection like a cold or flu that’s obviously viral, for which an antibiotic will do nothing.
- Cut out chemically loaded junk foods and drinks, including caffeine (coffee and cola).
- Decrease the fat content of your diet.
- Check with your doctor and pharmacist to make sure that none of the supplements you are taking (particularly herbs) cause additional liver problems.

If you are taking meds that can cause liver toxicity, a careful review with your doctor should be done in order to determine if there are other meds that can be substituted for problematic ones.

A review of possible drug interactions should also be done. It is always possible that drugs that would normally cause no problems when taken alone might interact in a way that would cause significant toxicity. A “brown bag” checkup with your pharmacist to look at every single thing you’re taking, whether it’s by prescription or over-the-counter, is appropriate to check for all possible interactions.

Last, but certainly not least, any indication of liver damage should immediately prompt an assessment of the possibility of any infections or cancers that can damage the liver, including:

- viral hepatitis
- MAC
- TB
- CMV
- cryptosporidiosis
- lymphoma

When hepatitis B or C are present, treatment may be considered.

An excellent Website where you can check for drug/drug, drug/food and drug/herb interactions is www.aidsmeds.com.
In addition to removing, as much as possible, anything that might be stressing the liver, it is very important to add the therapeutic agents that can help the liver to detoxify, repair and protect itself. There are a number of potentially useful agents, listed below:

**Nutrients to Maintain Glutathione**
Glutathione (GSH) is the most important intracellular antioxidant and is crucially important for protecting the liver against toxicity when it goes about its task of breaking down drugs and other toxins. Taking the following nutrients may help to maintain or increase levels of glutathione:

- **vitamin C** (2–6 grams per day, in divided doses)
- **N-acetyl-cysteine**, or NAC (500 mg, 3 times per day; always take with food because taking it on an empty stomach can cause gastrointestinal tract irritation)
- **L-glutamine** (5 grams per day, increased up to 30–40 grams in those who also have diarrhea or wasting). Note that anyone with seriously compromised liver or kidney function should not take glutamine without a doctor’s approval since it is an amino acid that must be processed by those organs.
- **alpha-lipoic acid**, or thioctic acid (300-500 mg, twice daily; take on an empty stomach with fluids). Alpha-lipoic acid is a naturally occurring fatty acid that acts as a cellular coenzyme. It is very important to the liver cell metabolic pathways and can be rapidly depleted when the liver is under stress. It appears to help boost repair when there has been either virally induced or drug-induced liver damage. Note that alpha-lipoic acid disappears from the bloodstream very rapidly, so products made in an extended-release form will last longer and work better.

For anyone with liver dysfunction or disease, the above nutrients may be very important as part of a total treatment approach.

For people with fatty livers, another important nutrient is the **amino acid carnitine**. Researchers say that it may help prevent mitochondrial toxicity, thus helping the body to handle fat better. Early studies of its use for non-HAART-related elevated triglycerides in PHAs did, indeed, show successful lowering of the blood fat levels. Research in animals has shown its successful use in reversal of fatty livers. The usual dosage is two capsules (500 mg each) twice daily. The alternative is Carnitor, the basic form of carnitine, available by prescription only. It is usually prescribed in doses of 3,000 mg daily (three 330-mg capsules, 3 times daily). Too-high doses can cause diarrhea, so watch for this. Doses of plain carnitine need to be higher because the acetyl-L-carnitine releases four times as much free carnitine into the bloodstream, using equivalent doses.
**Silymarin and Other Herbs**

An herb called **milk thistle** (*Silybum marianum*) contains the compounds silybin, silycristin, silydianin and isosilybin, which, as a group, are commonly referred to as silymarin. Silymarin has powerful effects as both an antioxidant and protector of the liver. It protects healthy liver cells from toxic chemicals by promoting healthy cell membranes, and stimulates protein synthesis, which promotes new liver cell growth, thus repairing the liver where it is damaged. Specifically, it promotes repair and regeneration of liver cells through the anti-inflammatory silymarin flavonoids found in the plant. There are many herbal formulas available that contain silymarin in useful quantities. The suggested dosage for most of these is two capsules, three times per day, to be continued until liver enzymes return to normal; long-term use may help to continually protect and regenerate the liver. However, for those on HAART, it is important to know that silymarin may interact with some medications.

**WARNING:** Based on results of test-tube studies, milk thistle and compounds found in milk thistle, such as silymarin, may have the potential to affect levels of protease inhibitors and non-nucleoside analogues in the blood. Milk thistle and its extracts may also affect levels of other drugs that are processed by the liver. This action of milk thistle has the potential to cause side effects or weaken the activity of HIV drugs, causing them to not work effectively. One later study of milk thistle in people showed that most had only minor reductions in indinavir (Crixivan) levels. However, some caution is still required.

*For more information on the potential effect of milk thistle and sylimarin on medications, see the CATIE Supplement Sheet on milk thistle available at [www.catie.ca/supple-e.nsf](http://www.catie.ca/supple-e.nsf).*

**Glycyrrhizin**

A licorice root extract known as glycyrrhizin has been shown in studies in Japan to reduce liver inflammation. It has been used for more than 40 years in Japan as a treatment for chronic liver disease and stomach ulcers. It should definitely not be taken if you have high blood pressure, low blood potassium or a weak heart or kidney problems. It can cause water retention and blood pressure increases that could be very serious.
Symptoms that can develop in the musculoskeletal system of PHAs include:

- muscle pains (myalgias)
- joint pains (arthralgias)
- muscle damage that can result in weakness and pain (myopathy)
- muscle cramping

Some of the potential culprits that cause myopathy are:

- AZT (alone in Retrovir and also in the combination drugs Combivir and Trizivir)
- d4T (Zerit) — can cause a rapid-onset very severe problem in rare cases
- other nucleoside analogues
- lipid-lowering drugs (statins)

It is thought that damage to the mitochondria caused by nucleoside analogues may be the underlying cause of myopathy in people taking these drugs. Nutrient deficiencies (especially of magnesium, a common deficiency in PHAs) may also be a factor, especially in muscle cramping. In order to distinguish between relatively minor muscle problems and what might be a severe (and even potentially lethal) problem — like the rapidly ascending muscular weakness that may be caused (although rarely) by d4T or the problems with controlling muscles that could indicate a serious neurological problem — it is very important to always call your doctor if any muscle problems develop.

Experts, as well as the manufacturer of d4T, Bristol-Myers Squibb, urge anyone experiencing any of the symptoms that can indicate lactic acidosis who also develops ascending muscular weakness to stop antiretroviral therapy immediately and see their doctor right away. Increased blood lactate can cause a wide range of symptoms. The earliest signs that lactic acid is increasing may include:

- fatigue
- nausea
- vomiting
- abdominal pain
- sudden unexplained weight loss
- shortness of breath or difficulty breathing (respiratory symptoms)
- neurologic symptoms (including difficulty moving)

Permanent discontinuation of d4T should be considered for anyone with confirmed lactic acidosis.
Tips for handling muscle aches and pains

While discontinuing a problematic drug can often solve muscle problems, that may not be an option for those who need nucleoside analogues as part of their combinations. Although aspirin and other over-the-counter pain medicines such as Tylenol (acetaminophen) may help counter muscle aches and pains, they don’t really solve muscle problems (see the warnings about these meds in the “Headaches” section).

Luckily, research done in Italy and at the National Institutes of Health has shown that doses of the amino acid L-carnitine (3,000 mg daily) may do so. In the small studies done, the carnitine usually reversed the myopathy and left those taking it feeling substantially better, possibly via its effects on reversing the nucleoside-analogue-caused mitochondrial dysfunction (see a more complete discussion about mitochondrial toxicity in “Body Distortions”). A potentially more effective form of carnitine is acetyl-L-carnitine. The usual dosage is two capsules (500 mg each) twice daily. Doses of plain carnitine need to be higher because the acetyl-L-carnitine releases four times as much free carnitine into the bloodstream, using equivalent doses. Too high doses of carnitine can cause diarrhea, so watch for this.

Magnesium supplements (500–600 mg) can sometimes help to relieve muscle problems, especially muscle cramping. Epsom salts, which contain magnesium, may also help ease muscle pain and cramping when dissolved in a hot bath (mix about 3 cups of the Epsom salts with the water before climbing in).

Quinine sulfate taken in the evening can help some people who get night-time muscle cramps.

Acupuncture and/or massage therapy can help with some muscle problems. And chiropractic adjustments may also be useful since nerve compression in the spine could be contributing to muscle spasms and pain.

Because neuropathy (nerve damage) may actually be causing some muscle problems, using the therapies suggested for neuropathy may help with some muscle problems (see “Peripheral Neuropathy”).
Nausea — that sick-to-your-stomach feeling that makes you feel like you may vomit — is a very common side effect that many PHAs experience, especially in the first few weeks of starting HAART. It can be caused by many antiretrovirals, including the following:

- AZT (alone in Retrovir and also in the combination drugs Combivir and Trizivir)
- 3TC (alone in Epivir and also in the combination drugs Combivir and Trizivir)
- abacavir (alone in Ziagen and also in the combination drug Trizivir)
- ritonavir (Norvir)
- saquinavir (Fortovase)
- indinavir (Crixivan)
- amprenavir (Agenerase)

Many other drugs, including the sulfa antibiotic Septra/Bactrim, also cause similar problems. Nausea will almost always vanish when problematic drugs are discontinued. The exception to this can be when the liver has been damaged by the drugs, since that damage can result in persistent nausea. Supporting and protecting the liver is crucial to prevent this (see “Liver Toxicity”). Since eliminating problem drugs isn’t always possible, it is good to know that there are many things that may help reduce queasiness.

**Tips for handling nausea**

First, consult your physician or pharmacist to determine whether taking a problematic drug at a different time of day could help. Some meds need to be taken with a full meal in order to avoid nausea, while for others an empty stomach helps. If the requirements of your particular medications allow, making such adjustments can help.

Many naturopathic doctors have reported the effectiveness of ginger for countering nausea. It can be consumed as a ginger syrup (a good one is made by New Chapter), which can be put in hot, fizzy or cold water to make a sipping beverage that you can drink throughout the day or before taking meds or eating. Ginger can also be consumed via capsules of powdered ginger (two 500-mg capsules, 2 or 3 times daily with meals). You can also drink ginger ale; the whole-foods brands that contain a potent blast of ginger (usually available in health food stores) will work better than standard varieties. Or try this simple homemade recipe for ginger tea: Chop up two or three tablespoons of fresh ginger root and add to a cup or so of boiling water. Then simmer this for at least 5 to 10 minutes and drink several times daily. You can add lemon or pasteurized honey if you’d like to flavour this tea. Chopped ginger root can be added to many dishes where it will add its spicy flavor, along with its ability to counter nausea.
Taking anti-nausea (anti-emetic) drugs can often reduce or eliminate this problem. Ask your pharmacist to check for drug interactions before trying any of these over-the-counter or prescription medications:

- Gravol (dimenhydrinate)
- triethylperazine maleate (Torecan)
- prochlorperazine (Compazine; usually given in doses of 10 mg, every 6–8 hours)
- promethazine (Phenergan; given in doses of 25–50 mg, every 4–6 hours)
- trimethobenzamide hydrochloride (Tigan; usually given in doses of 100–250 mg, 3–4 times per day; can also be given via a 200-mg suppository or intramuscular injections, usually of 100–200 mg, 3–4 times per day)
- metoclopramide (Reglan; in either tablet or syrup form, usually given in doses of 10–20 mg, 3–4 times per day)
  *This should not be taken with ritonavir (Norvir).
- dronabinol (Marinol; synthetic marijuana drug usually given in doses of 2.5–10 mg, 3 times per day)
- medicinal marijuana

Since med-induced nausea is particularly problematic at mealtime, anything that helps get food down is useful. The following tips may help settle your stomach:

- Eat small, frequent meals instead of two or three large ones (a full stomach makes nausea worse).
- Munch on snacks every three hours (don’t let the stomach get too empty or your blood sugar too low).
- Crunch down on dry, salty crackers or pretzels prior to eating and taking meds (salty foods are usually better to snack on than sweets).
- Sniff grated lemon peel or drink water with lemon in it just before eating.
- Chew slowly and eat in a calm, relaxed environment.
- Substitute cool, bland, odorless foods for hot, spicy, smelly ones.
- Avoid the kitchen while food is being cooked to limit your exposure to the smells produced.

Since maintaining your food and fluid intake is crucial for health, if the nausea waxes and wanes, try to drink lots of fluids and take in lots of protein and calories when you’re feeling better, in order to make up for the times when you don’t feel like it. Try drinking supplemental drinks as an extra boost for both nutrients and fluids. If you experience recurrent vomiting, it will be very important to rebalance your electrolytes (see the suggestions in the “Diarrhea” section).
Anxiety, mental problems, depression, nervousness, dizziness, insomnia and nightmares are all possible side effects of certain HAART drugs. Specifically, the neurologic problems caused by the non-nucleoside analogue efavirenz (Sustiva) can occur both during the day (muddled or unfocused thinking, feelings of paranoia and disorientation, depression) and night (insomnia and, when you get to sleep, vivid dreams and nightmares). Some people report feeling “stoned.” In many PHAs, these side effects disappear gradually after several weeks on the drug, so waiting out the problem for at least a month is advisable, if you can stand it. For others, the problems continue and stopping the drug is the only solution for those in whom the symptoms are just not bearable. Generally speaking, it is best to avoid recreational drugs, including marijuana or alcohol, when starting efavirenz.

The following anti-HIV meds may also cause mental or sleep problems:

- indinavir (Crixivan) — in some users can cause chronic feelings of anxiety, usually low-level but sometimes more severe; the symptom normally remains until the drug is discontinued
- ddI (Videx EC) — same as above; can also cause nervousness and sleeping difficulties, although these are not very common
- abacavir (Ziagen, ABC) — can cause dizziness and trouble sleeping, problems which may or may not disappear after a period of a few weeks on the drug
- nevirapine (Viramune) and saquinavir (Fortovase) — can cause depression

As with efavirenz, all of the above side effects may diminish or disappear after a period of days, weeks or months on the problematic drug but may also remain long-term, with drug discontinuation the only solution.
**Tips for handling sleeping difficulties**

There may be approaches that will help with at least some of the problems. Certain efavirenz problems can be resolved by rescheduling the dose. If it’s causing insomnia, talk to your doctor or nurse about taking it in the morning instead of at bedtime. If daytime drowsiness is the problem, take it earlier in the evening.

With any insomnia problems, there are different approaches you can try, alone or in combination, to help improve your sleep, including:

- Try to avoid drinking or eating anything with caffeine, sugar or alcohol for 4–6 hours before bedtime.
- Try to avoid nicotine for 4–6 hours before bedtime.
- Try to avoid strenuous exercise, bright lights and television before bedtime.
- Try relaxing before bedtime by doing peace-inducing yoga or breathing exercises, indulging in a soothing bath, or sipping calming herbal teas like chamomile. Drinking a glass of warm milk may help since it provides a dose of tryptophan, a precursor to the chemical serotonin, which is involved in the induction of sleep.

For some people, medications may also help to counter certain problems:

- For sleep problems, standard sleep medications may help. There are several effective, non-addictive drugs available for short-term use. Gravol (anti-vomiting med) or Benadryl (antihistamine) can usually be used safely for the occasional bout of insomnia. With any such drugs, keep in mind this important caution: Mixing many of these meds with herbs and/or antiretrovirals can result in dangerous interactions. Always check with your doctor and pharmacist before use.

- For anxiety, the standard anti-anxiety drugs may reduce that symptom, but note that such medicines are potentially addictive. Many psychiatrists believe that antidepressants are a better choice for long-term use.

It is important to remember that other causes of depression or anxiety may be contributing, including deficiencies of certain nutrients (the entire vitamin B complex, especially B₆ and B₁₂) and testosterone (often deficient in both men and women PHAs and a major contributor to depression; if testing shows inadequate levels, replacement is crucial).

Don’t ignore the possibility that stress may be causing you symptoms of anxiety or insomnia. At times, therapy with a good mental health therapist or psychologist can work wonders, especially if you have a lot going on in your head and your life.
Pancreatitis is an inflammation of the pancreas gland, the organ that secretes enzymes (which go into the gut and help you digest food) and insulin (which regulates the use of sugar). It may or may not cause symptoms such as:

- severe nausea
- vomiting
- abdominal pain

**If left untreated, pancreatitis can be fatal. If there is any suspicion of pancreatitis, it is crucial to get immediate medical attention.**

Pancreatitis can be caused by many drugs, including the following:

- ddI (Videx EC)
- ddC (Hivid)
- 3TC (alone in Epivir and in the combination drugs Combivir and Trizivir)
- d4T (Zerit)
- hydroxyurea (Hydrea)
- the sulfa antibiotic Septra/Bactrim

As well, high levels of blood lipids, especially the sky-high triglycerides seen in many people on HAART, can place PHAs at increased risk for pancreatitis.

Elevations in the level of the enzyme amylase can indicate pancreatitis.

**Tips for handling pancreatitis**

The standard North American treatment for this potentially fatal problem usually consists of immediately stopping to take the problematic drug(s), along with bed rest, pain medication and fluids. However, based on evidence that the pancreas is damaged by free radicals (highly active compounds that damage cells much in the same way that rust damages a car) in the early stages of pancreatitis, researchers have successfully used antioxidants to counter this condition. In various trials, German researchers gave selenium (in doses of 500 mcg daily), combined with vitamin E (1,600 IUs) and sometimes other antioxidants (vitamin C and N-acetyl-cysteine) immediately after a pancreatitis diagnosis. Death rates plummeted and patients experienced faster recovery, less pain and shorter hospital stays. Although these studies were not in PHAs, the researchers showed that these improvements occurred regardless of the cause of the pancreatitis. So, long-term use of these nutrients might even help prevent the problem in the first place.

Last, but not least, because pancreatitis may be another condition tied to mitochondrial toxicity, therapies to treat the toxicity could be of value (see discussion of mitochondrial toxicity under “Body Distortions”).
Peripheral neuropathy (PN) — nerve damage that causes numbness, burning, tingling and sometimes severe pain in the toes, feet and legs, and sometimes in the hands and arms — is most often caused by the “d” drugs:

- d4T (Zerit)
- ddC (Hivid)
- ddI (Videx EC)

Other drugs, such as the following, can also cause this complication:

- Flagyl (metronidazole)
- thalidomide
- dapsone
- isoniazid
- vincristine

Less commonly, PN can also stem from the nucleoside analogue 3TC (alone in Epivir and in the combination drugs Combivir and Trizivir).

Other factors can cause or contribute to PN as well, such as:

- HIV itself
- diabetes
- cancer treatment
- alcohol
- cocaine
- amphetamines

**Let your doctor know right away if you have symptoms of PN.** When possible, it is extremely important that the drug(s) causing PN be stopped *immediately* because delaying this may result in permanent problems. When causative medicines are stopped shortly after symptoms begin, the pain and numbness usually subside over time and are eventually completely eliminated, although that may take several months. However, failure to immediately stop using the problematic drugs may greatly reduce the chances for complete reversal of symptoms. Too many people have ended up with permanent pain, numbness and burning because symptoms weren’t quickly reported to their doctors or because the doctors hesitated to take them off the drugs.

**Tips for handling peripheral neuropathy**

Large trials with diabetics, small studies with PHAs, and many anecdotal reports from PHAs have shown the usefulness of the following *nutrient supplements* for preventing or reversing PN:

- alpha-lipoic acid (in doses of 300–500 mg, 2–3 times per day; preferably using an extended-release form)
- gamma-linolenic acid (in doses of 240 mg, twice per day)
- acetyl-L-carnitine (in doses of 1,000 mg, 3 times per day)
A British study showed that PHAs on the “d” drugs (ddC, d4T, ddl) have low levels of acetyl-L-carnitine, and that 18 months of supplementation improved both symptoms and nerve biopsy results, even when the “d” drugs were continued.

Also important is replenishment of **magnesium**, often deficient in PHAs (try 500 mg daily) and B complex vitamins, in particular, the following:

- vitamin B₁₂ (1,000 mcg, 2–7 times per week; nasal gel or injections may work better than pills because of absorption problems)
- vitamin B₆ (25–50 mg daily), taken with a B complex supplement, since deficiencies of these B vitamins can cause neuropathy and are common in PHAs

In addition, the nutrient protocol proposed by Dutch researchers to help address nucleoside-analogue-caused mitochondrial dysfunction may help (see “Body Distortions”).

Anything you do that soothes and reduces pressure on hypersensitive feet or hands can help. This includes:

- limiting walking distances
- wearing loose-fitting shoes and socks
- avoiding standing for lengthy periods
- avoiding repetitive pressure on the hands
- soaking your feet or hands in ice water on a regular basis
- raising your heels or hands off the mattress with a small pillow can help prevent increased pain while sleeping
- keeping heavy covers off of painful areas
- regular exercise may help by increasing circulation to the nerves
- many swear by acupuncture or acupressure, with improvement often occurring with the first treatment, although repeated treatments may be necessary for long-term relief

The following pharmaceutical agents help some reduce pain, although they won’t eliminate numbness:

- Neurontin (gabapentin) is usually the first-line therapy since it often works better for neuropathic pain than other possible meds.
- For pain that mostly occurs at night — the standard recommendation is for oral amitriptyline (Elavil, a tricyclic antidepressant), beginning with low doses in order to minimize certain side effects (dry mouth, sedation, urinary retention and low blood pressure upon suddenly sitting up or getting out of bed — orthostatic hypotension). A starting dose of 25 mg at bedtime is gradually increased to 75 mg (or as high as 100–150 mg if needed). Elavil may be particularly useful when sleep problems accompany the neuropathy because it has sedative effects.
- For predominantly daytime pain — oral nortriptyline (Pamelor) is often advised since it is less sedating, also beginning with a low dose of 10 mg per day, and gradually increasing to 30 mg, 3 times daily.
With these drugs, effective reduction of pain may not occur for up to two or three weeks, so patience is required. When one of these is not effective, another may still be.

- For occasional pain, standard anti-inflammatories such as ibuprofen (Motrin, Advil) may help with mild neuropathic symptoms.

- For more severe pain, the World Health Organization (WHO) steps for treatment of pain should be used to ensure proper treatment (see opposite page). When pain is under-treated or not treated, it may greatly increase the risk that it will become permanent.

**WHO’s four-step approach to drug treatment of HIV-related pain:**

In general, medications should be given in the maximum tolerated doses before moving up to the next step. Where there is chronic pain, it is thought best to treat around the clock in order to prevent pain. If necessary, the usual meds can be augmented by short-acting drugs in order to treat breakthrough pain. With all these drugs, individual responses may vary and will be the best guide for proper med use.

- **Step 1:** Try acetaminophen or a non-steroidal anti-inflammatory drug (NSAID). Most effective for mild pain. Possibilities include: ibuprofen, aspirin and naproxen. When one NSAID doesn’t work, another might. Long-term use can cause gastrointestinal bleeding and should be avoided, if possible. People with low platelets, kidney dysfunction or low serum albumin levels (common in those with wasting) should not take NSAIDs. Those with gastric Kaposi’s sarcoma should take them with an antacid or avoid them.

- **Step 2:** If NSAIDs are not enough, a weak opiate derivative might help, either alone or along with a Step 1 agent. Possibilities include codeine alone, codeine with acetaminophen (Tylenol), hydrocodone with acetaminophen, or oxycodone with acetaminophen.

- **Step 3:** If the above are inadequate, talk to your doctor about switching to a stronger opiate such as hydromorphone, transdermal fentanyl patches, levorphanol, morphine sulfate (intravenous), sustained-release morphine sulfate (oral) or meperidine. The minimum daily dose that affords pain relief should be used.

- **Step 4:** At any point during the preceding steps, consider adding adjuvant therapies to boost the effectiveness of the other drugs. At the top of this list, due to good effectiveness with few side effects, is the antiseizure med gabapentine (Neurontin). Other boosters include antihistamines like hydroxyzine (Vistaril); butyrophenones like haloperidol (Haldol) and pimozide (Orap); psychostimulants like methylphenidate (Ritalin), dextroamphetamine (Dexedrine) and pemoline (Cylert); amine precursors like tryptophan; selective serotonin re-uptake inhibitors such as fluoxetine (Prozac), paroxetine (Paxil) and sertraline (Zoloft); and heterocyclic and non-cyclic antidepressants like trazadone (Desyrel) and maprotiline (Ludiomil).
Many people get a rash when they start taking antiretrovirals. Rashes can be caused by the following drugs:

- non-nucleoside analogues — nevirapine (Viramune), delavirdine (Rescriptor) and efavirenz (Sustiva)
- the nucleoside analogue abacavir (alone in Ziagen and also in the combination drug Trizivir)
- the protease inhibitor nelfinavir (Viracept)
- the sulfa antibiotic Septra/Bactrim (it’s best to avoid prolonged exposure to direct sunlight and to use sunscreen with at least 15 SPF when taking Septra/Bactrim and other antibiotics because they can cause hypersensitivity to the sun)

Most of the time, these rashes are mild and disappear after a couple of weeks. However, sometimes these rashes can be life-threatening. Any rash that appears after beginning either abacavir or any of the drugs above should prompt an immediate visit to the doctor. If he or she is not available, go to the emergency room of the nearest hospital. Although most such rashes show up within the first few weeks on a drug, they may sometimes develop later, so always pay attention. If ignored, such a rash could progress into a potentially fatal hypersensitivity reaction called Stevens-Johnson syndrome. Signs of hypersensitivity include:

- fever
- flu-like symptoms such as aches, pains, fatigue and headache
- with abacavir, there may be respiratory symptoms such as difficulty breathing, sore throat and a cough

**Abacavir hypersensitivity**

Abacavir (Ziagen) hypersensitivity is different from Stevens-Johnson-type hypersensitivity and is important to monitor for its development. You may feel as though your doctor is paranoid when describing the possible list of reactions that can occur with abacavir, however, it is important to avoid potentially fatal complications. Having said that, the number of cases of abacavir hypersensitivity is extremely low. Most cases arise in the first couple of weeks after starting the drug and rarely after six weeks of use. In addition to a possible rash, abacavir hypersensitivity may be accompanied by an increasing number of generalized symptoms that resemble the flu. These may include fatigue, fever, gastrointestinal symptoms (nausea, vomiting and diarrhea), respiratory symptoms (cough) and muscular or joint aches and pains. If your symptoms get worse with each dose you take or if a new symptom occurs — see your doctor right away. If he or she is not available, dial the 1-800 number on your pill bottle. If you must stop your meds as a result of perceived side effects, do not restart abacavir without consulting your doctor.
**Tips for handling skin problems**

In general, the only solution for severe skin reactions is to stop taking the drug that is causing it. Although some drugs can be tried again (rechallenged) after a rash, usually at lower starting doses, this is not the case with abacavir — which must never again be used. The now-standard protocols for beginning with lower doses of certain non-nucleoside analogues can help prevent the skin rashes that were once more common with those drugs.

Less serious rashes are a common occurrence that may be related to medications, although they can also be caused by many infections, so a workup by an HIV-knowledgeable dermatologist is a must. The standard medical recommendation is some sort of locally applied cream, often one of the corticosteroid variety that will suppress the inflammation, but long-term use of these is considered inadvisable because of their potential for creating immune suppression when they are absorbed.

Alternative practitioners have found that taking essential fatty acid supplements (several capsules daily of borage and flaxseed oils) can often help, both by resupplying the fatty acids that are deficient in many PHAs and are needed for skin health, and via their natural anti-inflammatory effects. Accompanying this with a potent multiple vitamin and mineral (to provide the vitamin E, vitamin A, zinc and B vitamins necessary for overall skin health) can help ensure the presence of all the nutrients necessary for the skin to be at its best. When dryness or itchiness is part of the problem, drinking plenty of fluids, especially water, and applying a non-perfumed, powerfully moisturizing cream can help. Two of the most effective are Eucerin, available over-the-counter in both cream and lotion forms, and Desitin, sold as a diaper rash cream. Oatmeal baths may also provide relief. Avoid harsh soaps that contain antibacterial chemicals and fragrances.

**Dry, cracked lips** are another painful annoyance that seems to be caused most often by the protease inhibitor indinavir (Crixivan). There have been anecdotal reports of many possible solutions including:

- vitamin E rubbed on the lips (break open a capsule)
- Micatin cream (an over-the-counter antifungal)
- Desitin (diaper-rash cream)
- bag balm (available in pharmacies)
- drinking loads of water
Loss of sexual interest (decreased libido), erectile difficulties in men, and difficulties reaching orgasm in both men and women are frequently ignored side effects of some medications. Though you may blush at the idea, it is important that you refer to Rule #1 in the introduction and discuss these difficulties with your doctor, particularly if your troubles started shortly after the introduction of a new med. Sexual difficulties have been reported in many people taking protease inhibitors, although there may be a number of other causes that contribute, including:

- many other medications
- smoking
- alcohol
- emotional issues
- stress
- many other diseases (including diabetes, heart disease and thyroid gland disease)
- a form of nerve damage called autonomic neuropathy
- hormone problems

**Tips for treating sexual difficulties**

It is important to know that sexual dysfunction is rarely simply “an age-related thing” and should not be ignored. An evaluation of your testosterone level is very important in anyone experiencing a decline in sexual interest (for both men and women), erection difficulties or inability to reach orgasm. Appropriate hormone replacement can return testosterone levels to normal and remarkably reverse sexual problems. It is very important to stick to through-the-skin testosterone therapies (gels, creams or patches) because injections can shut down your own remaining testosterone production and can actually cause sexual problems down the line.

Because many HIV positive women reach perimenopause or menopause at much younger-than-normal ages, women should also have female hormones tested. Deficiencies can contribute to sexual arousal disorder as well as vaginal thinning and dryness, which can cause difficulty with intercourse and reduced pleasure. Based on results, the pros and cons of hormone replacement therapy should be discussed with your doctor.

With autonomic neuropathy, a nerve condition that is widespread in PHAs but often undiagnosed, much less is known about possible therapies, but the nutrient therapies for peripheral neuropathy (see “Peripheral Neuropathy”) may help some people. When a physical exam and laboratory analysis of problems potentially related to sexual dysfunction appear normal, a search for other possible causes should continue.
Stress, anxiety and depression are frequently accompanied by sexual problems. These issues should be addressed and, where possible, treated through effective counselling and/or medications. If you are being treated for depression or chronic anxiety and you develop sexual problems, your antidepressant may be the cause and a change in meds may be warranted. Many antidepressants provoke sexual side effects, however, some are worse than others. The antidepressant Wellbutrin can actually increase sexual desire and function, including ability to reach orgasm in both men and women. Check into this with your doctor.

Some commonsense rules to improve your chances of sexual health:

- eat well and avoid high-fat, heavy meals before sex
- cut down or quit smoking (a potent inhibitor of the sexual reflex/erection)
- cut down your alcohol consumption (a depressant in the sexual arena)
- if you are stressed, find a way to chill out or consult with a therapist
- ensure that your body has enough rest to be able to pursue pleasure
- avoid the use of recreational drugs that diminish your sex drive

If troubles persist, a consultation with a urologist, sexologist or a trial of sildenefil (Viagra) or tadalafil (Cialis) may be an option for men with impotence.

It is very important to know that these drugs may interact with a number of other drugs, including some antiretroviral medications and certain heart disease drugs. Viagra and Cialis should not be used by anyone taking the heart drug nitroglycerin or other nitrate medications, since the combination can sharply decrease blood pressure in a way that can lead to shock or death. It is recommended that lower doses be used in anyone currently on an antiretroviral regimen that includes either a protease inhibitor or a non-nuke. The usual recommendation for such people is to limit Viagra use to one 25-mg pill in any 48-hour period. Don’t even consider using Viagra without consulting with your doctor about interaction problems.

Last but not least, don’t be embarrassed about your difficulties ... a side effect is a side effect! And, for the last time, refer to Rule #1.
We hope that the information you have found here may mean that you won’t have to experience the rather staggering list of side effects you see in the table of contents — and that for any side effects you may one day experience, you’ll have a host of options for eliminating or at least lessening them. We view this guide as a tool-kit to help prepare you to obtain the best quality care through more informed consultations with your doctor. Just remember that information in this field changes daily, so always check for the latest treatment news.

CATIE’s various publications and services are here to help. Look for “What’s New?” at www.catie.ca, call 1.800.263.1638 to speak with a treatment information service representative, sign-up for subscriptions according to your interests, and/or become a CATIE member to be kept in the treatment loop. If you thought yesterday that you couldn’t switch drugs to get away from a problematic one, today there may be a new choice that will allow you to do just that. If nobody could offer a solution for a troubling symptom you had last month, today a better understanding of the problem may provide one.

Always tell your doctor what you’re experiencing, reach out for help and knowledge, talk to other PHAs about how they handle side effects, and do the work to create the best possible total treatment plan — including not only the best available medications but all the things that can make them easier to take and far less likely to cause you problems. That’s the way to give yourself the best possible chance to live both long and well with HIV.
Shopping for Supplements

Depending on where you live, some supplements can be hard to find. The following stores offer mail-order services that provide many complementary therapies that are popular among PHAs across the country. Catalogues are also available. Please note that prices may vary.

**Supplements Plus**
2304 Bloor St. W., 2nd floor
Toronto, Ontario
phone: 416.766.2004
mail order: 416.977.3088
toll-free: 1.800.387.4761

**Ki Nature and Santé**
4279 St-Denis St.
Montreal (Quebec)
phone: 514.841.9696
www.kinat.com/index.html
e-mail: kinat@videotron.ca

**The Vitamin Shop**
1212 Broad St.
Victoria, British Columbia
phone: 250.386.1212
mail order: 250.386.1252
toll-free: 1.888.386.1211
www.canadianvitaminshop.com
e-mail: victoriavitaminshop@shawcable.com

**Global Vitamins**
60 Lombard St.
Smiths Falls, Ontario
phone: 613.284.0076
toll-free: 1.800.996.8466
e-mail: orders@globalvitamins.com

This Practical Guide is part of a series and is meant to be used in conjunction with the other guides. The other titles are:

A Practical Guide to HAART (Highly Active AntiRetroviral Therapy)
A Practical Guide to Nutrition for People Living with HIV/AIDS
A Practical Guide to Complementary Therapies for People Living with HIV/AIDS
A Practical Guide to Herbal Therapies for People Living with HIV/AIDS

All Practical Guides are available on the CATIE Website, in French and English.

To be kept up to date on the latest treatment information, become a member of CATIE by calling 1.800.263.1638 or through our Website at www.catie.ca

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