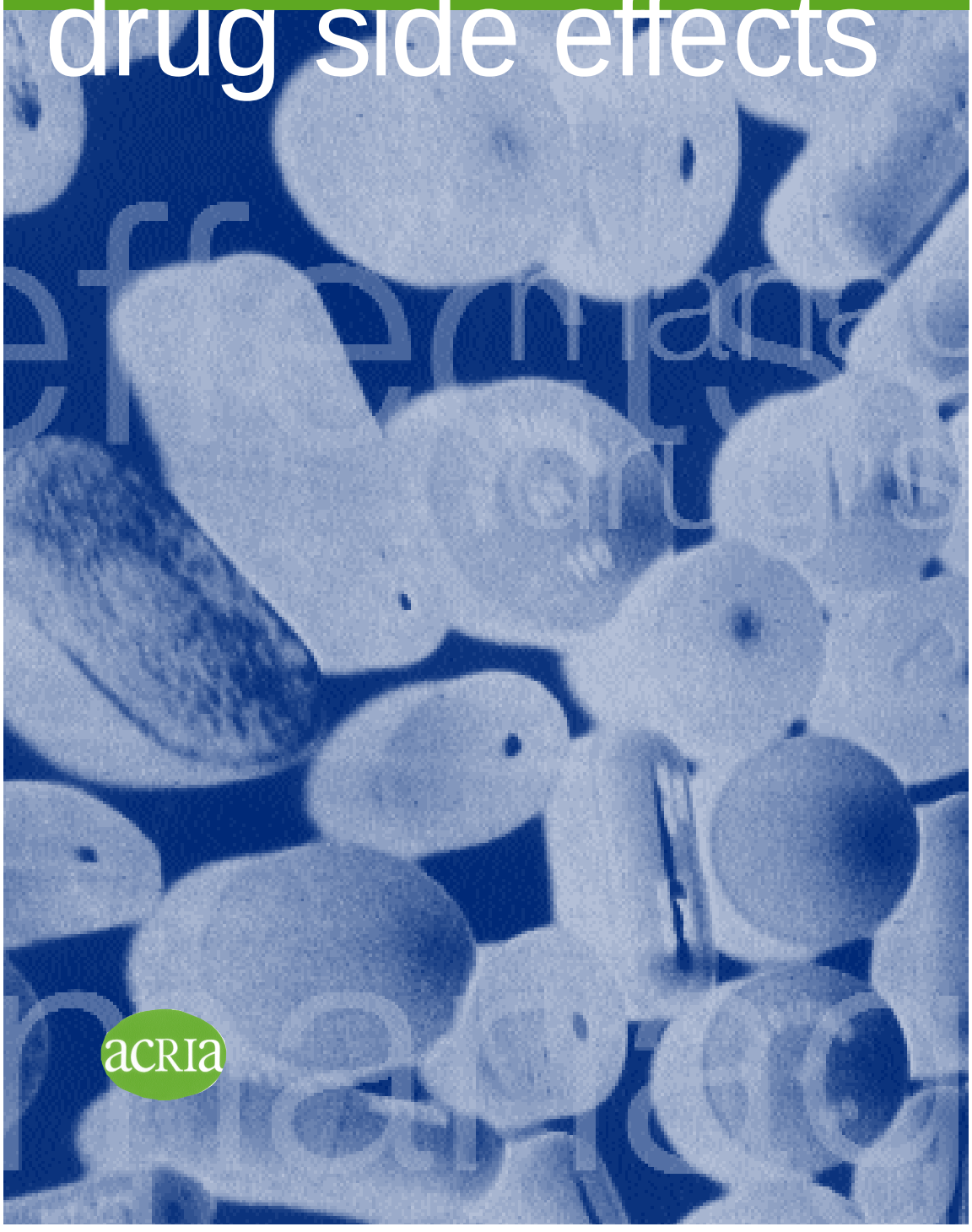
# managing drug side effects



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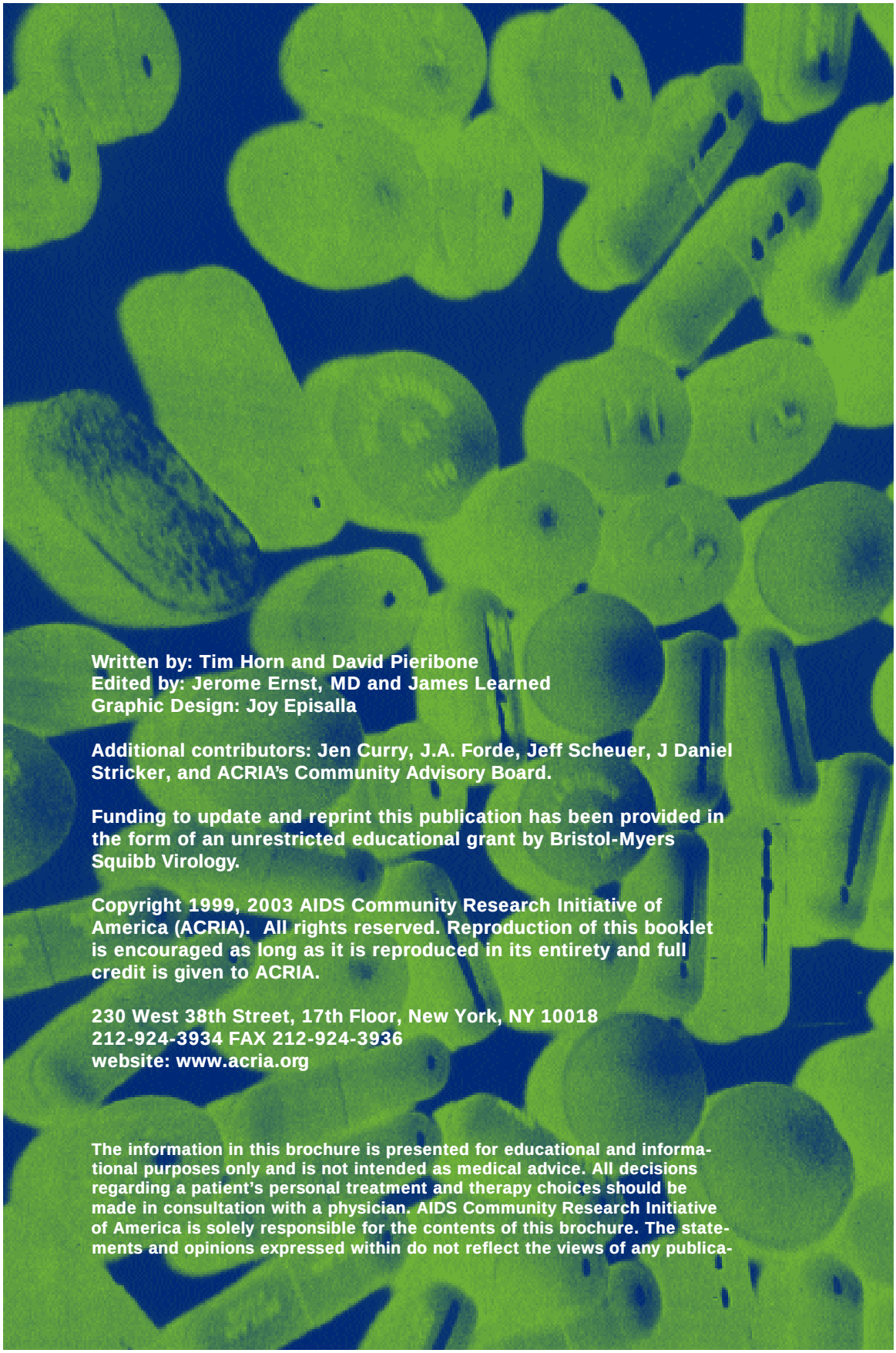

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# Managing Drug Side Effects

Drugs used to treat HIV and AIDS can be a double-edged sword. While they may do a good job of controlling HIV and treating AIDS-related diseases, they also come with problems of their own: side effects.

Let's face it. Side effects are hard to avoid and can make life difficult. In fact, side effects are one of the main reasons why people living with HIV start missing doses of their medications or stop taking their drugs completely. This may lead to resistance and, ultimately, drug failure. Yet many side effects can often be controlled.

This handbook has been produced by the AIDS Community Research Initiative of America (ACRIA) to help you better understand the different side effects that are associated with the drugs prescribed for HIV-positive people and the ways that you can deal with them. With this information, we hope that you will talk with your doctor about the side effects you're experiencing and, if possible, look into ways to prevent or treat them.

This handbook has been divided into four sections. The first section explains how to use the information in this booklet. The second section provides basic information about side effects and how to make sense of standard treatments and complementary therapies to manage them. The third section is a reference of the most common side effects experienced by people taking drugs to treat HIV and AIDS and discusses some of the most popular ways to deal with them. It is intended to serve as a reference guide and does not necessarily need to be read in its entirety. The fourth section of this handbook is a glossary containing some of the medical terms used in this handbook and other publications. This section will be useful if you want to learn about a medical term or while talking to your doctor about side effects.

# I. How To Use This Booklet

This booklet does not cover all of the possible side effects caused by drugs used to treat HIV and AIDS. Nor does it include all of the ways to control side effects. To make this booklet easier to use, we have only included information on some of the most common side effects associated with the most frequently used drugs. The index at the end of this booklet can help you locate information on a particular side effect.

This booklet also discusses some of the most popular ways to manage and prevent side effects. Some of the treatments discussed have been studied extensively in clinical trials, whereas others – particularly the complementary therapies and alternative medicines – have not been thoroughly studied. But there have been many informal studies and word-of-mouth reports. To help make some sense of this information, we have included some of the most popular complementary therapies used by people living with HIV to manage side effects.

## A Word About Complementary Therapies and Nutrition

What do we mean by "complementary therapies?" In this handbook, complementary therapy is a general term used to mean alternative, holistic, natural, herbal, supplemental, or traditional (such as ancient Chinese) therapies. These include agents – such as thioctic acid, DHEA, and NAC – that are commonly sold in health food and sports nutrition stores and haven't been evaluated for their effectiveness by the Food and Drug Administration (FDA).

Some complementary therapies – such as herbs, vitamins, and other supplements – may help manage side effects that damage particular parts of the body, such as the liver and gut. Other complementary therapies – such as relaxation, yoga, acupuncture, Reiki, and exercise – may not control a particular side effect but may instead help support the body as a whole. Doing so may enable your body to better tolerate medications and manage side effects. Good nutrition is another way to support your body, especially while taking drugs known to cause side effects. Eating whole, unprocessed foods from a variety of food groups will help supply your organs – especially those that help the body control the toxic effects of medications – with vital nutrients.

It is important to remember that simply because many complementary therapies can be purchased without a prescription does not mean that they are always safe to take. Some complementary therapies have their own side effects. It's also clear that many complementary therapies can interact with certain anti-HIV medications. This can further increase the risk of side effects or, quite possibly, reduce the effectiveness of the anti-HIV medications being used. Be sure to check with your healthcare provider before starting any complementary therapy.

# II. Side Effects: The Basics

Almost all drugs used to treat any type of disease can cause side effects. But this does not mean that everyone who takes a drug or combination of drugs will experience side effects. We do know that people with lower CD4 cell counts or a long history of anti-HIV drug use may be more likely to experience side effects than patients with healthier immune systems. Things like age, body weight and size, sex, and overall health may also influence how bad side effects will be and how long they will last.

Understanding which side effects might occur while taking drugs to treat HIV and AIDS can help you prepare and deal with them if they occur. Because some side effects might not necessarily make you feel ill – such as the beginning stages of liver damage – it is important for you and your doctor to monitor your health carefully and to have regular laboratory tests to detect any problems you might be experiencing.

Starting a new medication? Here are a few questions to ask your doctor:

- What are the possible side effects of this drug?
- Which side effects am I most likely to experience?
- When will the side effects start?
- How long will they last?
- Will the side effects go away by themselves?
- Are there any long-term side effects?
- What should I do if I have a side effect?
- Can I do anything to prevent certain side effects from happening?
- Are there any dangerous side effects I should know about? If so, what should I do if I start having them?

There are also some questions you might want to ask yourself. Figuring out answers to these questions can help you and your doctor determine which medication is right for you.

- Which side effects do I have the hardest time dealing with? For example, some people have an easier time dealing with nausea than diarrhea.
- Am I willing to take other drugs or complementary therapies to help control the side effects?
- Do I have family or friends I can call on if my side effects are bad?
- How long am I willing to put up with a particular side effect?

Much of what we learn about a drug's side effects comes from studies conducted before its approval by the FDA. However, some long-term side effects may not be spotted in the early months or years of a clinical trial. We are still learning about the side effects of some drugs, especially drugs that were approved only a few years ago.

Pharmaceutical companies are required by law to report the side effects that their drugs may cause. Information about a drug's side effects can always be found in the package insert – also referred to as the prescribing information – which is reviewed by the FDA before the drug is approved for marketing and is routinely updated by the manufacturer. While the pharmacists often remove the package insert – that folded piece of paper that contains information about the drug's chemical structure, efficacy, and side effects – it must be made available to you upon request when the drug is dispensed.

If you think you are experiencing a side effect, be sure to mention it to your doctor. It is sometimes difficult to tell the difference between side effects and symptoms of other complications, such as an opportunistic infection. By reviewing your medical history, the medications you are taking, and conducting a thorough physical exam, your healthcare provider can determine the source of the symptoms and help you figure out how best to treat them. You should not, however, stop or change the doses of any of your drugs without first consulting with your doctor.

# III. Common Side Effects and Possible Treatments

While virtually any side effect can leave someone feeling crummy or ill, most can be broken down into one of several types. In fact, most package inserts list the side effects by type, often using the organ system affected. Here are a few of the most common side effects experienced by people taking drugs to treat HIV and AIDS:

## Body As A Whole

Fat redistribution (lipodystrophy) is one of the most frequently reported body-as-a-whole side effects. Many people who have lipodystrophy experience fat loss (atrophy) in the legs, arms, butt, and face and/or a buildup of fat (adiposity) around the gut and at the base of the neck. Women may also experience an increase in breast size.

While a number of researchers have spent a lot of time over the past five years studying lipodystrophy, they still aren't in agreement about what causes it. However, most experts agree that it is a side effect of antiretroviral drug therapy.

Lipodystrophy was first reported in 1996 when a number of people taking protease inhibitors (PIs) began noticing abnormal changes in body shape and size. Soon after, some people who had never taken a PI – but had taken either a non-nucleoside reverse transcriptase inhibitor (NNRTI) and/or nucleoside reverse transcriptase inhibitors (NRTIs) – began reporting similar body-shape changes. There have also been some patients who have never taken any antiretroviral drugs, but have experienced many of the symptoms that have come to be known as lipodystrophy. Research is ongoing to figure out why lipodystrophy occurs and to determine what can be done about it.

*Possible Treatments:* Currently, there are no treatments that have been proven effective for body-shape changes. It is also not clear if switching regimens – from a protease inhibitor-based combination to an NNRTI-based combination, for example – can help reverse the body-shape changes associated with lipodystrophy. While some studies have reported that switching has some positive effects on body fat, other studies have not been able to confirm these findings. However, substituting an NNRTI for a PI has been shown to have a positive effect on fat levels in the blood (see "Metabolic Side Effects," beginning on page 16).

One of the drugs that shows promise in reversing these abnormalities is recombinant human growth hormone (Serostim), which appears to decrease excess fat buildup in some people taking the drug. Serostim and anabolic steroids might also help boost muscle size, which can help compensate for the loss of fat seen in the arms and legs. Unfortunately, they have not been shown to improve facial wasting. Serostim and anabolic steroids also have side effects, and the positive effects disappear when the drugs are stopped. Even though a few clinical trials have concluded that Serostim can help reduce fat buildup, the drug has not yet been approved by the FDA for the treatment of lipodystrophy.

Another possible option is plastic surgery. Surgeons can remove fat from the back of the neck and around the breasts in a procedure known as liposuction (it is not possible to remove fat from near the abdomen, as the fat is very deep in the body). They can also inject fat (or fat substitutes) into the face to help fill out sunken cheeks. These procedures are expensive and do not always provide results people are happy with.

Researchers are also investigating whether certain drugs (e.g., metformin and rosiglitazone) used to treat diabetes may reverse some of the manifestations of lipodystrophy. The effects of exercise and diet are also being studied.

Lactic acidosis is a rare but serious side effect that can affect the body as a whole. It can occur when the mitochondria – the "powerhouses" inside cells that convert nutrients into energy – become damaged. The condition is more common in women than in men. It is also tied to the use of certain nucleoside analogues – most notably Zerit (d4T), Videx (ddI), and Hivid (ddC) – that are known to damage mitochondria. Symptoms are non-specific and may include shortness of breath, abdominal pain, nausea, vomiting, fatigue and weight loss. Various blood tests, including those that check lactic acid and bicarbonate levels can help confirm the presence of the condition. Untreated lactic acidosis can lead to organ failure and sometimes death.

*Possible Treatments:* People with lactic acidosis may have to discontinue their drugs or switch to other nucleoside analogues. Complementary therapies such as coenzyme Q10, riboflavin, thiamine, and L-carnitine are sometimes used to try to prevent lactic acidosis.

Fatigue, a general term meaning tiredness, weakness, and/or a lack of energy, is another side effect that can affect the whole body. Fatigue has many potential causes, including drug-induced anemia (discussed in Bone Marrow Side Effects on page 15). Other whole-body side effects include fever and flu-like illness (malaise).

*Possible Treatments:* If you are experiencing fatigue, malaise, and low energy, it is always important to discuss these problems with your doctor, as they can be symptoms of a more serious underlying problem or infection. A comprehensive medical examination alone may not uncover some of the most common reasons for fatigue that include: changes in diet, rest and sleep, alcohol, tobacco, recreational drug use, depression and psychological stress.

Some of the complementary therapies that have been found to help boost energy levels and combat fatigue are: multivitamins, DHEA, ginseng root extract, vitamin B12, coenzyme Q10, ginger root, and L-carnitine.

## Digestive System

The digestive system covers a lot of territory and includes several different organs, each of which can be negatively affected by a drug. Beginning with the mouth, some drugs may cause oral ulcers (stomatitis), altered taste, or tingling/numbness around the mouth (circumoral paresthesias). In the throat and chest, some drugs may cause heartburn (acid reflux). The stomach tends to be a chief source of complaint with side effects such as nausea, vomiting, and pains. A number of drugs also cause intestinal problems such as diarrhea, gas (flatulence) and appetite loss (anorexia).

## Nausea and Vomiting

Nausea, a general feeling of sickness or "queasiness" in the stomach, along with vomiting and stomach pains are side effects of many medications. Nausea and vomiting can also cause some people to lose their appetite (anorexia). These side effects can sometimes be controlled by switching the drug causing the side effect to another drug that is less likely to cause nausea and vomiting. Frequently, however, nausea and vomiting go away by themselves after a few weeks.

*Possible Treatments:* Drugs called antiemetics are often effective in helping to control episodes of nausea and vomiting. Examples of antiemetics include Compazine and Zofran. Another option is Marinol, a drug that contains a synthetic version of the active ingredient in marijuana. The drugs that relieve nausea may work better if you take them 30 to 45 minutes before taking the drugs that cause nausea.

A few words of caution when taking medications to control nausea, vomiting, or any other side effect: make sure they do not interact with the anti-HIV drugs you might be taking. For example, Reglan, an antiemetic, can be dangerous if it is taken at the same time as some of the protease inhibitors, especially Norvir.

Also try some of the following:

- Eat small meals frequently instead of two or three large ones. Large amounts of food in the stomach may make feelings of nausea worse.
- Cut a lemon and smell the slices to lessen nausea.
- Bland foods are easier to digest. Stick to foods low in fat but high in starches and carbohydrates to fuel the body's energy needs.
- Relax before meals and chew slowly.

Loss of appetite (anorexia) due to nausea can be treated with anti-nausea (antiemetic) drugs. Anorexia can sometimes be treated using Megace (megestrol acetate) and Marinol, two drugs that have been proven to increase appetite. Megace contains the hormone progesterone and can lower testosterone levels, so people using Megace may want to check their hormone levels after they start taking the drug.

Marijuana itself has also been said to be effective for nausea and appetite loss (anorexia). Aside from being an illegal substance, it is important to note that smoking any substance is dangerous to the lungs and may aggravate existing lung problems, particularly asthma or bronchitis. Ingesting marijuana – by baking it in food – is considered by some to be a safer way to experience the same effects.

## Diarrhea and Gas (Flatulence)

Diarrhea, or watery stools, is one of the more common side effects associated with drugs used to treat HIV and AIDS. Sometimes, diarrhea can be extremely debilitating and can result in a life-threatening loss of body water (dehydration). This is a side effect that should be monitored carefully. Diarrhea that occurs five times or more a day, for five or more consecutive days, or results in five pounds or more of weight loss, should always be brought to the attention of a doctor.

*Possible Treatments:* To help control diarrhea, there are several over-the-counter (OTC) remedies available, including Imodium AD (a prescription version, loperamide, is available for those who need larger amounts of the drug), Kaopectate, and Metamucil; though Metamucil is commonly used as a laxative, its fiber content can also absorb water in the colon and help control diarrhea. Additionally SB-Normal Stool Formula has shown to be effective in controlling diarrhea. Some of the anti-diarrheal drugs available by prescription include Lomotil, Ultrase (a pancreatic enzyme), and tincture of opium. As with drugs used to control nausea and vomiting, anti-diarrhea drugs seem to work best if taken 30 to 45 minutes before taking the medication causing the diarrhea.

Making dietary adjustments may also help control diarrhea. Some foods can actually cause diarrhea – or make it worse – while others can help to relieve it. No matter what the underlying cause of the diarrhea, the BRATT diet – consisting of Bananas, Rice (white), Apple juice or sauce, and Toast and Tea (herbal) – may help to control it. Foods that are high in starch – such as white rice and white bread – are a good bet, along with oatmeal and tofu. Apple, pear, and peach juice – all of which contain much needed sugar to fuel the body – are less harsh on the gut than other types of juices that are high in acid content.

Foods that can make diarrhea worse include: coffee and other caffeinated beverages (cola, some other soft drinks, tea, etc.), alcohol, chocolate, fried and fatty foods, spicy foods, food high in insoluble fiber such as raw vegetables, potato peels, beans, brown rice, fat substitutes (Olean or Olestra) and highly processed foods with little nutritional value such as Twinkies, cookies, cakes, donuts, etc. Dairy products like milk and cheese can also make diarrhea worse.

One of the most important things to remember during bouts of diarrhea – no matter how long they last – is to *drink lots of fluids.* Having diarrhea can seriously deplete the amount of water in the body, as well as vital nutrients called electrolytes. If water is not replaced, symptoms of dehydration may follow. Symptoms include an increase in thirst, anxiety, weakness, confusion, lightheadedness and even fainting. Dehydration may also cause a decrease in urine output, dry and pale skin that doesn't have its normal elasticity, an increase in heart rate, and a decrease in blood pressure. If dehydration becomes severe, it can be a serious problem leading to collapse and even death.

To help the body prevent or recover from dehydration as a result of diarrhea, it is best to drink lots of water or sport drinks like Gatorade that can replenish electrolytes. To make a Gatorade-like drink at home, add five tablespoons of sugar and one tablespoon of salt to one gallon of water. You can also flavor it with some fresh lime or lemon.

Gas (flatulence) and bloating can usually be managed by dietary changes. Eliminating foods such as beans, broccoli and vegetable skins is the first step. Medications such as Phazyme, Charcocaps and Gas-X can be used temporarily to relieve gas, but should not be used for an extended period of time. Some people report gas relief with a fat-digesting enzyme called lipase, which is available both over-the-counter and by prescription.

Heartburn (acid reflux) actually has nothing to do with the heart – it occurs when stomach acid irritates the stomach lining or backs up into the esophagus, causing a burning sensation. Some anti-HIV medications can cause heartburn or make it worse. Prolonged heartburn could be a sign of a more serious problem, such as an ulcer or hernia – if symptoms get worse or continue for more than a few days, talk to your healthcare provider.

*Possible treatments:* There's a long list of foods to avoid if you're experiencing heartburn – spicy or fatty foods, vinegar, peppermint, pickles, alcohol, caffeine (soda, tea, coffee, chocolate), and citrus fruits and juices (orange, grapefruit, lemon, tomato). Aspirin and ibuprofen can also further irritate the stomach. Other contributors to heartburn include smoking, being overweight, and wearing tight belts and pants, which puts additional pressure on your stomach. Many of the strategies that can help manage nausea may help manage heartburn as well – trying not to overeat and eating frequent small meals instead of two or three large ones. Don't sit in a slouched position after a meal, and wait a couple of hours after eating before lying down or going to bed. An after-dinner walk may aid digestion.

Over-the-counter antacids (Mylanta or Maalox) or histamine-2 (H2) blockers (Tagamet, Zantac, Pepcid or Axid) may provide some relief. Always inform your healthcare provider if you start taking one of these medications – they may interact with your HIV medications.

## Liver Damage

Also included in the digestive system is the liver, which helps the digestive process in many ways. The liver can be adversely affected by a number of drugs for HIV, particularly the protease inhibitors and non-nucleoside reverse transcriptase inhibitors. The non-nucleoside Viramune can cause liver problems in some people, particularly during the first three months on the drug. The protease

inhibitors Norvir and Crixivan can also damage the liver, usually after several months or years of taking them.

To make sure that anti-HIV drugs are not harming the liver, it is important to keep an eye on the levels of key enzymes and chemicals that circulate in the bloodstream. Three enzymes that are regularly monitored by doctors are ALT, AST, and alkaline phosphatase. Another chemical in the bloodstream to watch for is bilirubin, the waste product that results from the breakdown of hemoglobin molecules from worn out red blood cells. Reyataz (atazanavir), a new protease inhibitor, can block the liver's removal of bilirubin from the bloodstream, which can cause bilirubin levels to become elevated and lead to jaundice (yellowing of the skin, eyes, and under the nails). Increased bilirubin can be another sign of liver damage. However, this does not appear to be the case if the increased bilirubin levels are being caused by atazanavir. While a small number of people participating in clinical trials of atazanavir needed to stop therapy because of increased bilirubin levels, the levels returned to normal after stopping the drug, and there were no signs of damage to the liver. More information from studies is still needed to determine the significance of increased bilirubin levels caused by atazanavir.

Liver damage is a potential concern in people who are infected with both HIV and a hepatitis virus, particularly the hepatitis C virus (HCV). Two antiretroviral drugs, Norvir and Viramune, have been shown to increase liver enzymes – a possible sign of liver damage – in HIV-positive people with HCV. Even in HIV-positive people who don't have HCV, these and other drugs have the potential to cause liver damage. This is why it is important to have regular blood tests to monitor your liver enzymes.

*Possible Treatments:* Cutting down on alcohol is a key component to maintaining liver health. It is also important to cut down on the amount of processed and fatty foods, as these can be stressful to the liver. There are also some drugs, nutrients, and other alternative therapies that may prevent or control liver damage. Alfa-interferon, in combination with ribavirin, is a drug used to treat HCV. Alfa-interferon is also sometimes used to treat chronic hepatitis B virus (HBV), as are Epivir and Hepsera. Although Epivir for HBV is prescribed at a lower dose than that used to treat HIV, people who are HIV-positive should use the standard HIV dose.

Some complementary therapies that have been suggested to help prevent or control liver damage include thioctic acid, SSKT, glycerrhizin, milk thistle, NAC, astragalus, chickory, dandelion, centaury, American mandrake, and celandine. While most of these products are available in health food/nutritional stores, it is important to discuss these compounds with a doctor before starting them.

### Pancreas Damage

The pancreas is a part of the digestive system and can be adversely affected by some drugs, particularly Videx (ddI), especially if it's used with Zerit (d4T), the

anti-HCV treatment Rebetol (ribavirin), and pentamidine, a drug used to treat PCP. These drugs have been known to cause inflammation of the pancreas, a condition known as pancreatitis. Pancreas toxicity is often suspected if someone has increased blood levels of the enzyme amylase. Some of the physical symptoms of pancreatitis include abdominal pain, nausea, vomiting, and jaundice. Severe pancreatitis can be life-threatening.

*Possible Treatments:* Pancreatitis is a serious problem that often warrants medical care, sometimes in a hospital. Discontinuation of the offending medication may be necessary. A few studies and several anecdotal reports suggest that complementary therapies like alpha-lipoic acid, vitamins E and C, selenium, NAC, calcium, magnesium, glutamine, methionine, taurine, copper, vitamin B12, and folate may be effective in reducing drug-induced damage to the pancreas.

## Urinary Function and Genital Side Effects

The kidneys play a large role in filtering toxic waste in the body. They are also adversely affected by many drugs used to treat HIV and AIDS. One particular side effect is kidney stones (nephrolithiasis), which are caused by an accumulation of minerals or drug crystals that can build up in the kidneys. People taking Crixivan have been known to experience kidney stones. In clinical trials, the rate of people who developed kidney stones was less than 5%. However, studies conducted since the drug was approved suggest that the risk of developing kidney stones increases the longer people remain on the drug. Bactrim, a sulfa drug used to prevent pneumocystis pneumonia (PCP), can also cause kidney stones.

Like the old saying goes: an ounce of prevention is worth a pound of cure. Drinking water, and lots of it, is the best way to prevent kidney stones and to help dilute the toxic effects of drugs on the kidneys. Blood tests, such as those that measure blood urea nitrogen (BUN) and creatinine, are good indicators of kidney function. Drugs such as Foscavir (foscarnet) and Vistide (cidofovir) – both of which are used to treat CMV (cytomegalovirus) – can cause kidney damage and require that BUN and creatinine levels be watched carefully.

Fungal infections (candidiasis) can develop in the mouth and throat (thrush), the urinary or genital tract (i.e. the vagina), or the anal area as a result of prolonged antibiotic use. Antibiotics are often prescribed to treat bacterial infections. While they are usually effective in killing harmful bacteria, they can also kill healthy bacteria that help control fungal overgrowth.

*Possible Treatments:* The best way to treat a fungal infection is by using anti-fungal drugs. For vaginal fungal infections, over-the-counter (OTC) creams like Monistat are often effective. A doctor can also prescribe oral medications like Diflucan (fluconazole) to treat the infection. Some people have had success with acidophilus supplements, a mild bacteria often found in yogurt that can control certain types of fungus from growing in the body.

## Skin-Related Side Effects

The skin, and to a lesser extent nails and hair, can be adversely affected by certain drugs used to treat HIV and various AIDS-related complications. The most common skin-related side effect is rash. The development of a rash – especially when a drug is first started – may indicate an underlying allergy or hypersensitivity reaction. A number of people have an allergy to Bactrim, the drug used to prevent and treat pneumocystis pneumonia (PCP) and toxoplasmosis. Luckily, many people can be desensitized to the drug, a process in which people begin by taking tiny amounts of the drug and eventually work their way up to the full dose. Bactrim can also cause the skin to become highly sensitive to the sun, which may lead to severe sunburn.

The protease inhibitor Agenerase and the non-nucleoside reverse transcriptase inhibitors, particularly Viramune, can also cause rash. In rare instances, the rash can be extremely severe and if accompanied by flu-like symptoms – which include fever, abdominal pain, nausea, vomiting, and muscle/joint pain – is identified as Stevens-Johnson syndrome. The presence of blisters or sloughing of the skin are also signs of a severe rash, requiring immediate medical attention. While only a handful of people taking Agenerase or Viramune have developed Stevens-Johnson syndrome, it can be life-threatening.

Ziagen, a nucleoside analogue that is available separately or as part of Trizivir, has also been known to cause rash. A small percentage of people who take Ziagen also experience severe flu-like symptoms and are considered hypersensitive to the drug. Anyone who experiences flu-like symptoms or a rash while taking this drug should call their doctor immediately. If the doctor decides that the drug should be stopped, it should never be restarted; some pa tients who have done so have ended up in the hospital with serious complications.

Other types of skin-related side effects include dry skin, itchiness (pruritis), dark spots/blotchiness (hyperpigmentation), hair loss (alopecia), and nail deformities (paronychia), including discolored nails and ingrown toenails.

*Possible Treatments:* Skin rashes can often be helped with the use of antihistamines such as Benadryl. Before self-treating, however, it is best to bring the rash to the attention of a doctor, as it may indicate a more serious allergic reaction. A doctor may also write a prescription for an antihistamine or a corticosteroid (such as prednisone) in the event of a serious rash or chronic itching. Drinking

plenty of water is also important for good skin health, as is avoiding harsh soaps that contain antibacterial chemicals and perfumes. Using a good skin moisturizer daily can keep skin from getting too dry. It's also a good idea to avoid prolonged exposure to direct sunlight and use sunscreen, especially when taking certain sulfa drugs such as Bactrim.

Fuzeon (enfuvirtide, T-20), the only approved antiretroviral that is injected, can cause specific side effects. Almost everyone who uses Fuzeon gets "injection site reactions" (ISRs) at the place where they inject the drug. These reactions can include itching, swelling, redness, pain or tenderness, and hardened skin or bumps. They can range from moderate to severe, and usually go away in a week or less (some people have persistent nodules or hardening of the skin that lasts longer). In clinical trials of Fuzeon, only 3% of people had to stop the drug because of ISRs. *Be sure to ask your doctor to carefully explain the correct ways to mix Fuzeon and to inject the drug under the skin!* Following these important instructions will help reduce the risk of ISRs.

## Neurological and Mental Side Effects

Many drugs can adversely affect nerves, the spinal cord, and the brain. Damage such as this can lead to complications like peripheral neuropathy, paresthesias (discussed under digestive system side effects), and mental problems.

### Peripheral Neuropathy

Peripheral neuropathy – which may cause pain, numbing, burning, or tingling in the hands and feet – is one of the most common side effects associated with nucleoside analogue drugs, particularly Hivid (ddC), Zerit (d4T), and Videx (ddI). While no one knows exactly why peripheral neuropathy occurs, it is considered to be a result of adverse drug activity on peripheral nerves in the arms and legs.

*Possible Treatments:* The most effective way of dealing with peripheral neuropathy, especially if it is severe, is to reduce the dose or stop the drug that may be causing it. This should only be done upon the recommendation of your doctor. Peripheral neuropathy can sometimes be treated using non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen. Applying topical creams or lotions that contain aspirin or other pain relievers (such as Ben Gay) has also been effective in some cases. Moderate to severe cases may respond to drugs known as tricyclic antidepressants, including amitriptyline and nortriptyline, or a newer drug called Neurontin. If the pain is severe, narcotic pain relievers such as methadone or Fentanyl patches are sometimes prescribed.

Complementary therapies that have been said to help control neuropathic pain/numbness include vitamins B6 and B12, thioctic acid, choline, inositol, and carnitine. Some people have found relief through acupuncture, acupressure, chiropractics, and massage.

Sustiva, a non-nucleoside reverse transcriptase inhibitor, presents its own unique set of nervous system side effects in approximately 50% of people taking the drug. Included are sensations of sleepiness (somnolence), inability to sleep (insomnia), vivid dreams, depression, anxiety, muddled thinking and difficulty concentrating, and feeling "high." These problems may be especially severe for people who also use recreational drugs or are in recovery from alcohol and drug use.

*Possible Treatments:* No one is really sure why these side effects occur. In most cases, however, the neurological effects of Sustiva lessen or resolve within two to four weeks after starting the drug. Taking Sustiva within a few hours before bedtime is recommended. People taking the drug should avoid driving during the first few days if these side effects are occurring.

There are a number of possible ways to deal with the neurological side effects of Sustiva. It is important to keep in mind, however, that none of these methods have been studied in clinical trials, so much of the information reported here is based on word-of-mouth reports.

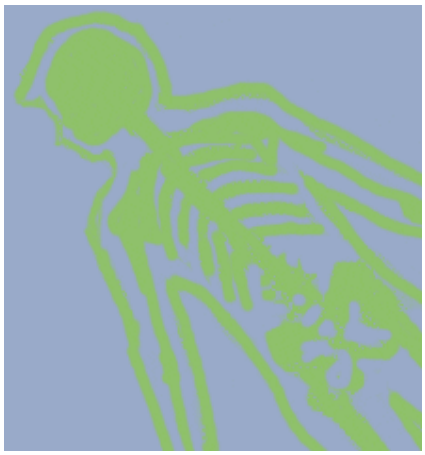
Some of the safest tips in helping manage these side effects include:
- Try to avoid recreational drugs, including marijuana, while using Sustiva.
- Do not drink or eat anything with caffeine or sugar five to seven hours before bedtime.
- Try relaxing before bedtime using techniques like yoga, breathing exercises, a soothing bath, or drink a non-caffeinated tea, such as chamomile.

Some doctors and people taking Sustiva have suggested that drugs like Ativan, Valium, Ambien and Restoril can help decrease insomnia and, possibly, anxiety. While there is no research concluding that these remedies will necessarily help, it might be worth asking your doctor about them if the side effects are severe. However, these drugs must be used with caution since they can be addictive. Benadryl, an over-the-counter antihistamine used to treat allergies, is relatively safe and can be used to treat occasional insomnia. While there is no research concluding that these will necessarily help, it might be worth asking your doctor about them if the side effects are severe.

For insomnia or anxiety believed to be caused by Sustiva, complementary therapies like melatonin, valerian root, L-carnitine, and ginseng root extract have been said to be helpful. As for memory and concentration problems, therapies such as gingko biloba, ginseng root, DMAE, lecithin, and peptide-T may have positive effects.

## Muscoloskeletal System (Bones and Muscles)

Three of the most common musculoskeletal side effects are muscle decrease or weakness (myopathy), muscle pain (myalgia), and joint pain (arthralgia). Many of the drugs used to treat HIV and AIDS are associated with these side effects. Prolonged AZT use, for example, has been shown to cause muscle mass breakdown in some people.



*Possible Treatments:* Joint and muscle pain can often be managed using non-steroidal anti-inflammatory drugs (NSAIDs) and other mild pain-relievers such as Tylenol. While very little is known about how to effectively reverse myopathy, some doctors prescribe hormonal drugs such as anabolic steroids and human growth hormone to help prevent additional muscle destruction. L-carnitine and coenzyme Q10 have both been said to have some positive effects.

### Bone Marrow Side Effects

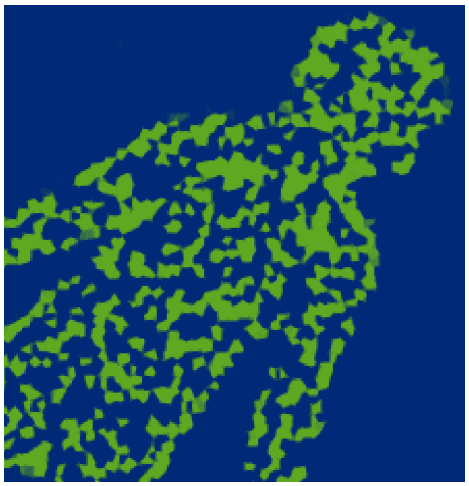
A number of drugs used to treat HIV, particularly the nucleoside analogues, can affect the ways in which the bone marrow produces new blood cells. Important cells such as white blood cells (leukocytes), red blood cells (erythrocytes), and platelets are produced in the bone marrow. A decreased number of white blood cells (leukopenia) may slow the immune system's response to bacterial and other infections. Anemia, a decreased number of red blood cells, can interfere with the ways oxygen is distributed throughout the body and often results in fatigue. A decreased number of platelets (thrombocytopenia) is also problematic, as these cells are responsible for stopping bleeding.

*Possible Treatments:* In most cases, stopping or switching the drug causing the bone marrow side effects is the best solution. However, this may not be realistic, especially for people who have no other treatment options or are receiving necessary – but highly toxic – drugs such as chemotherapeutics for cancer. Drugs such as granulocyte-colony stimulating factor (Neupogen) can be used to treat leukopenia. For the treatment of anemia, Procrit and Epogen have been shown to be highly effective and may reduce the need for blood transfusions.

As for complementary therapies, some reports suggest that compounds like astragalus, Siberian ginseng, Marrow Plus, dong quai, bai shao, and chuan xiong may have positive effects on bone marrow production of vital cells.

## Metabolic Side Effects

Metabolic side effects are defined as alterations in the ways the body makes use of vital nutrients, such as sugars, fats, and proteins. In recent years, many people with HIV – particularly those taking protease inhibitors – have reported increased levels of sugar (glucose), insulin, and fat (lipids and cholesterol) in their blood. In turn, these people may be at a higher risk for developing diabetes, heart disease, pancreatic problems, and possibly experiencing a stroke. These side effects are often reported in conjunction with lipodystrophy – loosely defined as a redistribution of body fat (see "Body As A Whole" on page 4).



*Possible Treatments:* To watch for these side effects, people living with HIV – along with their healthcare providers – are encouraged to monitor the results of their blood tests very carefully. At the present time, there is no definitive treatment for these metabolic side effects, but lipid-lowering drugs (the "statins") are often used to help reduce cholesterol levels. Only one of the statins – Pravachol (pravastatin) – can be safely combined with the protease inhibitors. Another drug, Lipitor (atorvastatin), may be taken, provided that its dose is reduced. A third statin, Zocor (simvastatin), should not be combined with a protease inhibitor or an NNRTI. Other cholesterol-lowering statins that are approved include Mevacor (lovastatin) and Lescol (fluvastatin). It is not yet known if these drugs can be combined safely with either protease inhibitors or NNRTIs.

Some people use garlic supplements at high doses in an attempt to reduce cholesterol. Recent studies have shown that taking garlic supplements regularly can reduce blood levels of Fortovase and, possibly, other protease inhibitors and NNRTIs. Lower levels of these anti-HIV drugs could lead to drug resistance, so caution is in order.

Increased insulin and glucose levels are warning signs of diabetes. To treat these problems, doctors rely on antidiabetic drugs. Two of the most common antidiabetic drugs are Avandia (rosiglitazone) and Glucophage (metformin). Avandia "primes" cells to make better use of excess insulin and glucose in the blood, whereas Glucophage helps reduce the amount of glucose produced by the liver. There is also some evidence that these drugs can help reduce lipid levels in the blood and may also decrease excess body fat caused by lipodystrophy.

Another option may be to switch anti-HIV drugs. While it is not clear if protease inhibitors are truly to blame for these metabolic side effects, a handful of studies have demonstrated that NNRTIs are less likely to cause increased lipid levels and glucose and insulin levels than PIs. Thus, switching from a PI to an NNRTI (or the nucleoside analogue Ziagen in some cases) can sometimes help bring these levels under control.

# Special Concerns for Pregnant Women

For many HIV-positive pregnant women, making treatment decisions can be very difficult. While pregnant women with HIV have the same access to triple-drug therapy as anyone else, we still don't know which drugs – or which combination of drugs – are the best for a woman to take during pregnancy.

Only a few anti-HIV drugs have been studied in HIV-positive pregnant women. Retrovir (AZT) has been studied most extensively, followed by Viramune (nevirapine). We know that AZT is safe for the woman taking the drug and does not usually cause long-term side effects to her baby.

Women may want to consider delaying or temporarily stopping therapy for the first 14 weeks (1st trimester) of pregnancy since the fetus' development is most sensitive at this time.

Viramune, Epivir (3TC), and Videx (ddI) have all been shown to be safe for pregnant women and their developing babies. While Videx is safe, it might not be the best drug to use during pregnancy, as only small amounts of the drug actually reach the baby while it is developing. If Videx is used, it should not be combined with Zerit (d4T). Pregnant women who take these two drugs together are at increased risk for lactic acidosis, a complication that can cause serious illness and, in some cases, death (see page 6).

The NNRTI Sustiva has caused severe birth defects in animals. Although there have been reports of HIV-positive pregnant women taking Sustiva and giving birth to healthy babies, it is probably best to avoid it if you are pregnant or trying to conceive. High doses of both Ziagen and Rescriptor have caused toxicity to the developing fetuses of smaller animals (rats and rabbits), and similar toxicities were seen in fetuses of laboratory animals given small doses of the protease inhibitor Agenerase. All of these anti-HIV drugs are best avoided during pregnancy.

As for the other protease inhibitors, it is not clear which side effects they might cause in pregnant women or their babies. One study conducted in Switzerland showed that women who took protease inhibitors in combination with two nucleoside analogues had a higher chance of delivering a pre-term baby (a baby born early). However, researchers are still questioning if protease inhibitors were really to blame – an analysis of pregnant women treated in the U.S. did not find a connection between pre-term births and this class of drugs.

Since protease inhibitors may put people at risk for diabetes, they might also be a problem with regard to gestational diabetes, a pregnancy-related condition that can develop in some women, regardless of whether or not they are infected with HIV (see "Metabolic Side Effects," on page 16). While this does not mean that HIV-positive pregnant women should avoid protease inhibitors, it does mean that they – along with their doctors – should monitor their glucose and insulin levels very carefully.

# IV. Glossary

**Adiposity:** A buildup of fat, usually around the gut, in the breasts, and/or the base of the neck. This is a possible symptom of lipodystrophy (See Lipodystrophy).

**Alopecia:** Hair loss.

**Anaphylaxis:** A severe generalized allergic reaction, characterized by low blood pressure, difficulty breathing and, sometimes, hives.

**Anemia:** An abnormally low number of red blood cells, as measured by hematocrit or hemoglobin (the cells and proteins responsible for transporting oxygen to the body's tissues and organs). Anemia can result in feelings of fatigue.

**Anorexia:** An involuntary lack or loss of appetite that can lead to significant weight loss.

**Aphasia:** An inability to speak or understand speech.

**Aphthous Ulcer:** A painful sore in the mouth or throat; also called canker sore.

**Arthralgia:** Joint pain.

**Asthenia:** A general feeling of weakness; similar to fatigue.

**Ataxia:** A lack of muscular coordination, frequently leading to the inability to walk.

**Atrophy:** A loss of tissue. Fat loss in the arms, legs, face, or butt is a possible symptom of lipodystrophy (See Lipodystrophy).

**Bone Marrow Suppression:** A general side effect associated with many chemotherapeutic drugs used to treat cancer and some anti-HIV drugs. Bone marrow suppression may lead to a decrease in red blood cells (See Anemia), white blood cells (See Leukopenia), platelets (See Thrombocytopenia) or all three. Bone marrow suppression is also referred to as myelosuppression.

**Buffalo Hump:** A build-up of fat at the back of the neck associated with lipodystrophy.

**Cardiomyopathy:** Damage to the heart muscle.

**Diabetes:** An inability of the body to regulate the amount of glucose (sugars) in the blood. Type 1 diabetes typically occurs in childhood and is characterized by an inability of the pancreas to produce insulin, a hormone; this type of diabetes often requires injections of insulin. Type 2 diabetes, or adult onset diabetes, occurs when the body "resists" insulin, and glucose levels remain increased. Therapy with protease inhibitors has been associated with Type 2 diabetes. Symptoms of diabetes include excessive thirst, frequent urination, unexplained weight loss, increased hunger, vision changes and fatigue. If left unchecked, diabetes can be life-threatening.

**Dyspepsia:** Indigestion or "upset stomach."

**Dysphagia:** Difficulty in swallowing.

**Dyspnea:** Difficulty breathing or shortness of breath.

**Edema:** Swelling caused by an abnormal accumulation of fluid in body tissues.

**Gastritis:** Inflammation of the stomach.

**Granulocytopenia:** An abnormally low number of granulocytes, a type of white blood cell responsible for controlling bacterial infections.

**Hematuria:** The presence of blood in the urine.

**Hemiparesis:** Paralysis on one side of the body.

**Hepatitis:** Inflammation of the liver caused by either a microorganism (such as Hepatitis C Virus) or chemicals (such as medication or alcohol). Hepatitis can cause yellow or darker skin (See Jaundice), enlarged liver, fever, fatigue, nausea and increased liver enzymes.

**Hepatomegaly:** An enlarged liver.

**Hepatotoxic:** A substance that damages the liver.

**Hypercholesterolemia:** Increased levels of cholesterol in the blood. If left unchecked or untreated, hypercholesterolemia may increase the risk of a heart attack or stroke.

**Hyperglycemia:** An increased level of glucose, or sugars, in the blood. May be a sign of diabetes (See Diabetes).

**Hyperhydrosis:** Excessive sweating.

**Hypertension:** Increased blood pressure.

**Hypertriglyceridemia:** An increased level of triglycerides, or fat, in the blood.

**Insomnia:** Lacking the ability to fall asleep or stay asleep throughout the night.

**Insulin Resistance:** The inability of cells in the body to make proper use of insulin, a hormone needed to process sugar (glucose) correctly. Insulin resistance is often a precursor to diabetes. It can cause insulin levels and glucose levels to increase in the blood and may play a role in the development of lipodystrophy (See Lipodystrophy).

**Jaundice:** Yellow pigmentation or darkening of the skin and whites of the eyes caused by elevated blood levels of bilirubin. The condition may be caused by liver or gallbladder damage.

**Lactic Acidosis:** a buildup of lactic acid in the body. It can be caused by nucleoside analogues, which may damage the mitochondria (the powerhouses of cells). Severe lactic acidosis can be life-threatening.

**Leukopenia:** An abnormally low number of leukocytes – more commonly referred to as white blood cells – circulating in the blood; frequently the result of drug-induced bone marrow suppression.

**Lipodystrophy:** A syndrome believed to be associated with antiretroviral therapy and generally referred to as a redistribution of body fat. Lipodystrophy may be defined as an increased amount of fat around the gut and at the base of the neck, as well as decreased fat in the legs, arms, face, and butt. Lipodystrophy is often associated with high levels of cholesterol, triglycerides, insulin, and glucose in the blood (See Hypercholesterolemia; Hypertriglyceridemia; Insulin Resistance; Hyperglycemia).

**Lymphadenopathy:** Swollen lymph nodes.

**Malaise:** A general feeling of discomfort or illness.

**Mitochondrial Damage:** damage to the mitochondria of cells caused by factors such as heredity, aging, infections or certain anti-HIV medications, particularly nucleoside analogues. Mitochondrial damage may be responsible for such side effects as muscle weakness and muscle loss, peripheral neuropathy, pancreati-

tis, low platelets, loss of other blood cells, and lactic acidosis.

**Mutagenicity:** The ability of a drug or medical procedure to cause damage to the genetic material (DNA) contained in sperm or eggs.

**Myalgia:** Muscle pain.

**Myelitis:** Inflammation of either the spinal cord or the bone marrow.

**Myelosuppression:** (See Bone Marrow Suppression)

**Myelotoxic:** Causing damage to bone marrow (See Bone Marrow Suppression).

**Myopathy:** Muscle weakness.

**Nephritis:** Inflammation of the kidneys.

**Nephrolithiasis:** More commonly referred to as kidney stones.

**Nephrotoxicity:** Damage to the kidney cells.

**Neuropathy:** Nerve injury. Peripheral (in the extremities) neuropathy is often described as numbness, tingling, burning or pain in the hands and feet.

**Neutropenia:** A decreased number of neutrophils in the blood. Neutrophils are a specific type of white blood cell responsible for combating bacterial infections (See Granulocytopenia).

**Pancreatitis:** Inflammation of the pancreas. If left unchecked, it can result in severe abdominal pain and death. Pancreatitis is often associated with an increase in blood levels of amylase, an enzyme produced by the pancreas.

**Paresthesia:** Numbness, burning or tingling sensations, which may also be a sign of neuropathy. Oral (circumoral) paresthesia, a side effect of some of the protease inhibitors used to treat HIV, is described as numbness, burning, or tingling around the mouth.

**Paronychia:** Deformities of fingernails or toenails; ingrown toenails.

**Photosensitivity:** Increased sensitivity of the skin to sunlight.

**Pruritis:** Itchy skin.

**Pyrogenic:** Drugs that can cause fever.

**Retinal Detachment:** A condition in which a portion of the retina separates from the inner wall of the eye. If left untreated, it can lead to vision loss. Some treatments for CMV retinitis, such as intraocular implants or injections, can cause retinal detachment.

**Side Effect:** An unintended reaction to a drug or medical procedure.

**Somnolence:** Feelings of sleepiness.

**Stevens-Johnson Syndrome:** A serious and sometimes fatal disease characterized by fever, severe rash, blisters and sometimes nausea and vomiting. The syndrome may be triggered by a severe allergic reaction to certain drugs.

**Stomatitis:** Swelling or inflammation of the mucous membranes in the mouth.

**Teratogenicity:** The ability of a drug to cause damage to a developing fetus.

**Thrombocytopenia:** Abnormally low number of platelets in the blood. Platelets are produced by the body to stop bleeding.

**Toxicity:** The harmful side effects of a drug.

**Uveitis:** Swelling or inflammation of the uvea, a section of the eye.

# Index

ACRIA is an independent, non-profit community-based AIDS research and education organization committed to improving the length and quality of life for people living with HIV/AIDS through medical research and treatment education.

ACRIA conducts a free Treatment Education Program to offer people living with HIV/AIDS the tools and information to make informed treatment decisions. Education program services include: workshops conducted on site at community-based groups throughout the New York City area in English and Spanish; technical assistance trainings for staff of AIDS service organizations; individual treatment counseling and publications, including our quarterly treatment newsletter, ACRIA Update, and topic-specific brochures in English and Spanish. ACRIA's National Treatment Education Technical Assistance Program offers ongoing support to help non-medical service providers and community members in various parts of the country acquire the skills and information needed to provide HIV treatment education in their communities.

To learn more about ACRIA's research studies or the Treatment Education Program, please call 212-924-3934. Information about ACRIA's programs and copies of ACRIA Update are also available on our web site: www.acria.org.

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