HIV and AIDS By Joanne Jansen PharmD and Anjanette Dymerski PharmD

Understanding the Virus

The human immunodeficiency virus (HIV) is the virus that causes AIDS. Acquired immune deficiency syndrome (AIDS) is the disease caused when a person's immune system becomes too weak to fight off the virus. A person can have HIV without having AIDS but cannot have AIDS without having HIV.

HIV is spread through sexual contact, intravenous drug use and contact with infected blood. It is not spread through toilet seats, hugging or touching, kissing, or using towels or dishes that have previously been used by someone with HIV. Even if someone has HIV, in order for you to get it you must come into contact with his or her blood, and you must have a way for the virus to get inside your body. The virus can enter through places such as your eyes, mouth, vagina, rectum and cuts.

It is true that HIV can be spread through blood transfusions. However, since we now know what causes HIV and what to look for, blood is screened when donated. Any blood that has HIV in it is *not* used and is safely discarded.

When HIV enters the blood it looks for and enters certain cells called T-helper cells (or CD4 cells). These cells are the part of the immune system that tells the immune system it is time to work. The virus prevents T-helper cells from doing their job. When too many of the T-helper cells become infected, the body is no longer able to mount a proper immune response to any bacteria, viruses, parasites or other organisms with which a person may come into contact. It is at this time when we begin to see diseases not normally seen in healthy people. These are called opportunistic infections. As a person's T-helper cell count drops below these levels, we use medications to prevent the person from getting this disease.

Opportunistic Infections

A normal T-helper cell count is 700-1100 cells per milliliter of blood. As the Thelper cell count drops, we see certain opportunistic infections at different levels. *Pneumocystis jirovecii pneumonia (PCP)* – This type of pneumonia used to be called *Pneumocystis carinii* pneumonia but it was later determined that the bacteria that caused these two pneumonias were not the same. Although it was renamed, it is still called PCP instead of PJP.

This pneumonia usually occurs when a person's T-helper cell count drops below 200 cells per milliliter. If the T-helper cell count drops below that, we use Bactrim® (sulfamethoxazole and trimethoprim) to prevent PCP. If a person gets PCP we use the same medication at a higher dose.

Toxoplasmosis – This disease is caused by a parasite called *Toxoplasma gondii*. You may be familiar with this parasite because it is why pregnant women are told to avoid kitty litter. An HIV+ person is at greater risk of getting this disease when the Thelper cell count drops below 100 cells per milliliter. Bactrim® is used to prevent this disease, as well. If you get this disease, though, it is treated with a combination of other medications not Bactrim®.

Mycobacterium avian-intracellulare complex (MAC) - Below 50 cells per milliliter of T-helper cells, this disease becomes more common. Azithromycin once a week is usually used to prevent this disease when the person's immune system becomes this weakened. It is treated with a combination of medications for up to 18 months.

Histoplasmosis - The fungus *Histoplasma capsulatum* is common in the soil in some areas, such as most of Kentucky. Bird droppings that have been not been cleaned up for a long time give this fungus the nutrients it needs to grow well, so you are more likely to get this infection if you are working in, say, a barn where pigeons or starlings have roosted. Construction workers and farmers sometimes get histoplasmosis because they stir up the soil and breathe the tiny fungus that is released into the air. People with strong immune systems are almost always able to fight off this disease, but those whose immune systems are not that strong can get this infection. We usually do not give a medicine to prevent it unless the person has a job that would make him more likely to be exposed to it and has a T-helper cell count less than 150 cells per milliliter. The treatment can last up to 12 months. Because this fungus can hide in the body this disease can sometimes return; your doctor may recommend that you take a medication all the time once you have had histoplasmosis to prevent you from getting this again.

Natural Medicines

Many people turn to natural medicines for many illnesses thinking that these products are safer than prescription medications since they are natural. However, natural products are not necessarily safe. Datura (also called devil's trumpet or angel's trumpet) is natural but all parts of the plant are poisonous and can be deadly when eaten or even handled. Certainly, there are natural products that are safe and can be used for medicinal purposes; it is wise to check out any product before you use it so you know whether it really works and what the side effects are.

Herbal supplements, homeopathic products and vitamins are not regulated by the Food and Drug Administration (FDA). This means that the safety studies done on prescription and over-the-counter (OTC) medications (such as Tylenol) do not have to be done on them. It also means that the manufacturers do not have to prove that the ingredients they say are in there actually are, or that the products do not contain anything not listed on the label. They have side effects just like prescription medications and can make your other medications not work as well or increase side effects from them. Natural medicines also do not have to do what they say they do, so you should carefully consider what you take and how it may affect your other medications.

There are some natural medicines that can actually be bad for a person with HIV. Echinacea, an herb commonly used in cold medicines to boost the immune system, can actually lower the number of T-helper cells in someone who is HIV positive. Marijuana is also particularly unsafe because it is not treated before it is smoked. Histoplasmosis, one of the opportunistic infection we worry about, can easily be transmitted this way.

If you do decide to take an herbal supplement or even a vitamin, you should choose one brand and stay with it. While the manufacturers do not have to prove that they pills are the same strength from batch to batch each time they make it, you are more likely to get the same amount by staying with one brand rather than switching.

There are many natural medicines that people will tell you are good if you have HIV/AIDS. It is true that certain natural medicines that can safely be taken when you have HIV, but there are others that absolutely should not be taken. Always check before you believe.

HIV Medications

HIV medications are not a cure for HIV. They help the body fight the disease and boost the immune system. Right now, there is no cure for HIV, but if you take the medications properly you can live a long and healthy life.

You must take several medications to help fight the virus, and these must be taken exactly as they are prescribed. "Every dose, every day" is very important for you to remember. When these medications are not taken as they are supposed to be, the virus can develop ways to keep from being hurt by the medicine. Your medications will not work if that happens, and you will have to switch medications.

All medications have side effects; HIV medications are no different. Each type of medication tends to have the same type of side effects. However, if you can keep taking the medicine for two weeks the side effects usually disappear.

Here are the common side effects and the things to watch for when taking these medications.

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

NRTIs keep HIV from making more copies of itself by binding to an enzyme called reverse transcriptase. This is an important step in the virus's life cycle.

NRTIs can cause nausea, vomiting and diarrhea. An important side effect of this class is liver damage. Your doctor will do blood tests to make sure your liver is not being hurt.

Another common side effect, especially with Zerit® (stavudine), Videx EC® (didanosine) and Retrovir® (zidovudine), is lactic acidosis (LA), meaning that lactic acid is building up in your blood faster than your body can remove it. You may notice nausea and weakness. You have probably experienced very slight cases of LA before: when you exercise hard and get a muscle cramp, it is because you have too much lactic acid in that area, and your body is telling you to take it easy. If you get LA, your doctor may switch you to a different NRTI.

NRTIs can also cause lipodystrophy, meaning that your body stores fat differently from normal. For instance, you may lose fat in your arms and legs but gain it around your belly.

In addition to what the drugs do as a class, some of the NRTIs have other side effects which others may not have. Here are some important things to know about each drug.

- Retrovir® (zidovudine or AZT): May cause anemia. Your doctor will do blood work. Headache and extreme fatigue are not uncommon.
- Ziagen® (abacavir): Hypersensitivity reactions are sometimes seen with this drug but usually not with the first dose. Around Day 9, you may have flu-like symptoms including fever that does not go down with Tylenol® or Advil®, rash, sore throat, nausea, vomiting and diarrhea. If this happens, make sure you tell your doctor. He may tell you to keep taking it for a few more days. If you continue to feel worse with each dose, this is a true allergy and you should never take this medication again. Sometimes the doctor will do a test first, and if it is positive you should not take this drug.
- Videx EC® (didanosine): Peripheral neuropathy (pain or tingling in your fingers and toes), diarrhea, abdominal pain and rash are common side effects.
 Pancreatitis is sometimes seen with this medication. Taking this with a meal high in fat can keep you from absorbing as much of the medicine and it may not work as well.
- Zerit® (stavudine): This medication can also cause peripheral neuropathy and pancreatitis. Headache, rash, nausea, vomiting and diarrhea are common.
- Epivir® (lamivudine or 3TC): This drug is not as likely to cause side effects, but when they occur they include headache, fatigue, nausea, vomiting, diarrhea, abdominal pain, cough and sore throat.
- Emtriva® (emtricitabine): This is a longer-acting version of Epivir® so it has the same side effects.

Nucleotide Reverse Transcriptase Inhibitors (NRTIs)

Notice that this class is nucleo<u>T</u>ide not nucleo<u>S</u>ide. This works very similar to the previous class, but the place it works is just a little different. Right now there is only one drug available. Viread® (tenofovir) can cause kidney damage and osteopenia (softening of the bones). Make sure you drink plenty of water with this to reduce the chance of

damaging your kidneys. Viread[®] can also cause gas, and Gas-X[®] or other anti-gas products work well to treat it.

Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

NNRTIS keep reverse transcriptase from working too, but in a slightly different way. As a class, they can cause liver damage, rash and high cholesterol. These are even more sensitive to missed doses than other types of HIV medications, and when one stops working the entire class (except Intellence®) stops working. NNRTIS also have many drug interactions.

- Sustiva® (efavirenz): This medication should be taken at bedtime but it can cause vivid dreams. Taking it on an empty stomach decreases this effect somewhat. Common effects are dizziness, depression, headache, insomnia, anxiety, nausea, vomiting, diarrhea and fever.
- Viramune® (nevirapine): You must take low doses of Viramune® to start with, and then increase the dose gradually. If high doses are started at once, you may get a rash which may increase the risk of liver damage. Notify your doctor right away if you get a rash, fever, blisters on your body or in your mouth, swelling of the face or muscle or joint aches.
- Intellence® (etravirine): This one may still be useful if the other two have developed resistance. Common effects are a mild to moderate rash in the second week. This does not necessarily mean you are allergic to this drug, and your doctor may decide to leave you on it. You may also get high blood sugar or high cholesterol. Your doctor should do blood work to watch for these.

Protease Inhibitors (PIs)

Protease inhibitors keep the virus from making useful proteins, keeping them from making more copies of the virus. There are several side effects associated with PIs as a class including increased risk of heart attack and stroke, liver damage, lipodystrophy, high cholesterol and drug interactions. Drink plenty of fluids with these drugs.

• Norvir® (ritonavir): This drug is often used to "boost" the effects of other PIs, allowing you to take a lower dose than you would without it.

It can cause quite a bit of nausea, vomiting and diarrhea, so it should always be taken with meals. It can cause your sense of taste to be not quite right; to help cover that taste, you may want to suck on dark chocolate or butterscotch candies. Freezing bite-sized dark chocolate and then holding it in your mouth is very effective.

Norvir® may also cause a numbress or tingling around the mouth, called oral paresthesia.

There are many drug interactions with this medication, so talk with your doctor or pharmacist before you take *any* new medication, including supplements. Norvir® can be a capsule or a solution. The solution contains 43% alcohol, so it will burn your mouth if you have thrush. To help prevent this, you can ice your tongue and mouth first, or squirt it into the back of your mouth. It will cause severe nausea if you take Flagyl® within three days of Norvir®.

Reyataz® (atazanavir): This must have stomach acid in order to be absorbed so you should take it with meals. You should not take any proton pump inhibitors (PPIs) such as Prilosec® (omeprazole), Nexium® (esomeprazole), Protonix® (pantoprazole), Prevacid® (lansoprazole) or Aciphex® (rabeprazole). If you need to take something for heartburn, you can take H2 blockers such as Tagamet® (cimetidine), Zantac® (ranitidine) or Pepcid® (famotidine), but you must take these 12 hours apart from Reyataz®.

This medication may cause yellowing of the skin and eyes. This is a harmless coloring, but if it bothers you, discuss with your doctor switching medications. Reyataz® can sometimes cause kidney stones, so it is especially important to make sure you drink lots of water.

- Lexiva® (fosamprenavir): If you have an allergy to sulfa drugs, you may have a rash with this one, too. Use it with caution or change medications.
 Diarrhea and headache are the most common side effects, but may also have tingling or numbness around the mouth.
- Crixivan® (indinavir): Nausea, vomiting and diarrhea are common side effects. It is also more likely than other PIs to cause kidney stones, so you should drink at least eight 8-ounce glasses of water a day.

If you take this without Norvir[®], you should take it on an empty stomach, at least one hour before meals or two hours after. If you take it with Norvir[®] you should take it with food to lessen the diarrhea Norvir[®] may cause.

- Viracept® (nelfinavir): Diarrhea is a common side effect of this medication. You can take Imodium® (loperamide) to help. Viracept® should be taken with meals.
- Prezista® (darunavir): This medication sometimes causes a low-grade fever, but it should go away with Tylenol® (acetaminophen) or Advil® (ibuprofen).
 Headache is often seen with this drug.

If you have an allergy to sulfa drugs, you should use this medication with caution or consider a different PI.

• Aptivus® (tipranavir): This medication must be taken with a high-fat meal in order to allow it to be absorbed into the body. Headache is a common side effect. Intracranial bleeding has been seen with this medication, but since other PIs are usually tried before this one, it could be that the person is sicker to begin with. If you are allergic to sulfa drugs, use caution with this drug or consider a different PI.

Fusion Inhibitors

In order for the virus to infect your cells, it must first bind or "fuse" to them. If the virus cannot enter the cells, it cannot make more copies of itself.

• Fuzeon® (enfuvirtide): This medication is only for people who have tried other HIV medications and have failed them. It is an injection given just under the skin twice a day. It is common to have redness, soreness and swelling where it is injected. Fuzeon® also causes nausea, diarrhea and insomnia. In people who have smoked, have lung disease or have used illegal IV drugs, it can cause pneumonia.

Co-Receptor Blockers

• Selzentry® (maraviroc): There are two main types of receptors the virus can bind to - CCR5 and CXCR4. This medication blocks only CCR5. Your doctor may do

a blood test before giving you this medication because if you do not have mostly CCR5 receptors, this drug will not work for you. Selzentry® can cause liver damage which is usually preceded by an itchy skin rash. If you get this rash, you should notify your doctor at once. Common reactions to this medicine are fever, cough, dizziness and upper respiratory infections. You may also get light-headed when you sit up or stand quickly; rise slowly to keep this from happening.

Integrase Inhibitor

• Isentress® (raltegravir): This medication has very few side effects; some people might get a headache. It has very few interactions with other drugs.