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inside:

MISSION

"The Center for AIDS Information & Advocacy empowers people living with HIV to make informed decisions about their healthcare by providing the latest research and treatment information and by advocating for accessible, affordable, and effective treatment options until there's a cure."

About *HIV Treatment ALERTS!*

HIV Treatment ALERTS! is a publication of The Center for AIDS Information & Advocacy (The CFA). This newsletter is intended for those affected by HIV and their caregivers. The statements and opinions expressed in this newsletter do not imply recommendations or endorsement. Always consult your doctor before altering a prescribed drug regimen or taking any drug or supplement.

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The CFA also publishes Research Initiative/*Treatment Action!* (RI*TA!*). RI*TA!* is a literature-review journal that covers issues in HIV research and policy. This and other publications are available on The CFA website or can be requested by mail (see contact information below). CFA publications are supported in part with unrestricted funding from AIDS Walk Houston, AIM Investments, CFP Foundation, Gilead Sciences, and GlaxoSmithKline.

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13th **Retrovirus** Conference **Highlights**

Cancer and HIV

Several studies reported on the types of cancer affecting the HIV+ community. One study focused on how the **incidence** of AIDS-defining cancers has changed during the years 1980 through 2002 (abstract 810). This time period includes the years before and after the introduction of potent combination HIV therapy (also called HAART). AIDS-defining cancers are Kaposi's sarcoma (KS), non-Hodgkin's lymphoma (NHL), and cervical cancer. By studying large databases of AIDS and cancer patient registries, the researchers identified people with both cancer and AIDS. They found that the incidence of cervical cancer has not changed significantly since 1990, and continues to affect HIV+ women to a large extent. However, when the researchers grouped cases by the following years: 1980-1989, 1990-1995, and 1996-2002, they found that the risk of developing KS and NHL began to decline in the mid-1980s and continued to do so into the early 1990s, with another significant drop in 1996. While the most recent decline is most likely because of the availability of HAART, researchers are unclear as to why incidence began to decrease in the 1980s. Possible reasons include the initial availability of nucleoside reverse transcriptase inhibitors ("nukes"), changes in the AIDS population, changes in the definition of AIDS, or decreases in HHV8 **prevalence** (the virus associated with KS). It is important to point out that while incidence of KS and NHL has dropped significantly over the years, HIV+ people are still very much at risk for developing these types of cancers.

Lung cancer is also a very real threat to HIV+ people, in part because smoking is so widespread in this population. According to a study presented at the conference (abstract 811), an HIV+ person is 3 times more likely to die from lung cancer compared to an uninfected person. For this study, researchers studied deaths from lung cancer as a way to measure incidence of lung cancer because survival is so poor after being diagnosed. Smoking cigarettes, being older, and having had pneumonia in the past, especially multiple times, also increased the risk of dying from lung cancer. Though cancers like KS and NHL seem to be decreasing, this is not the case for lung cancer. In fact, risk of developing lung cancer (and therefore dying from it) appears to be on the rise in people with HIV.

As part of the HIV Outpatient Study (HOPS) and the Adult/Adolescent Spectrum of Disease (ASD) projects, another study examined the incidence of both AIDS-defining and non-AIDS-defining cancers (abstract 813) in 59,101 HIV+ patients during the years 1992 through 2002. Compared to the general population, HIV+ people are much more likely to develop some types of cancer. Not surprisingly, incidence of KS, NHL, and cervical cancer were higher in the HIV+ population. However, cancers like anal cancer, Hodgkin's disease, liver cancer, testicular cancer, melanoma (a very serious form of skin cancer), and oropharyngeal cancer (cancer of the middle part of the throat) were also dramatically higher in the HIV+ population. Lung cancer was also significantly higher in the HIV+ population. Risk of breast cancer and prostate cancer was actually lower in the HIV+ population, while no differences were seen for colorectal or kidney cancer.

Get a healthy start

The best time for an HIV+ person to start taking HIV meds is not known for sure. However, according to a large study (abstract 769), HIV+ patients who start potent combination HIV therapy (also called HAART) with higher T-cell counts do better in the long run. As part of HOPS (HIV Outpatient Study), more than 8000 HIV+ patients were studied for 8 years. The researchers discovered that patients who started HAART with higher T-cell counts were less likely to die or develop an **opportunistic infection**. The higher the T cells, the better the patients were. These risks were even lower in patients who had good **adherence** to their HIV meds and took their HIV meds at least 95% of the time. The risk of developing kidney problems or **neuropathy** was also lower in both patients who started HAART with higher T-cell counts and patients with good adherence. In addition, patients with good adherence were better able to suppress HIV viral load and maintain good T-cell counts. These findings stress the importance of taking your HIV meds consistently and starting HAART while still healthy.

Hepatitis B infection

Infection with the hepatitis B virus (HBV) is a serious public health issue, especially for people who also have HIV. "Occult" HBV is also a problem because this form of HBV is almost hidden—the infection is not detected with the usual tests and requires specific DNA tests to detect it. Serious liver disease, including liver cancer, is a risk for patients with occult HBV infection. Many people with occult infection may not know they are infected and may spread the infection to others.

Two studies presented at the conference reported on rates of occult HBV infection in HIV+ patient populations. One group (abstract 836) determined that 10% of the HIV+ individuals in their study had occult HBV. In particular, patients with high HIV viral loads and lower T-cell counts were at an increased risk of having occult HBV. In contrast, patients taking HIV meds that were also effective against HBV (like 3TC or FTC, brand names Epivir and Emtriva) were less likely to have HBV. Another study (abstract 835) examined stored blood samples from 967 HIV+ patients. These researchers reported an overall HBV rate of 10.4% in this population, though the rate of occult HBV was only 1.24%. Surprisingly, they detected HBV in many samples that were previously thought to be negative for HBV. These findings emphasize the importance of regularly

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screening HIV+ patients for HBV, especially those patients who did not receive an HBV **vaccine** or for whom the HBV vaccine does not work.

While testing new HIV+ patients for HBV is standard, regular testing of chronically infected HIV+ patients is not typically done. In contrast to previous reports, the current study did not see any evidence of liver damage in patients with occult HBV. However, the researchers point out the importance of knowing HBV status because it could affect a person's HIV disease and choice of HIV meds. Both studies stress the importance of getting vaccinated for hepatitis B. (HIV+ patients should also receive a hepatitis A vaccine. There is no vaccine for hepatitis C.)

To illustrate the importance of hepatitis vaccinations, another study (abstract 840) reported that HIV+ people who were vaccinated for HBV were 4 times less likely to become infected with HBV. Unfortunately, some vaccines are not effective in many HIV+ people. According to this study, the HBV vaccine was much more likely to work in patients taking potent combination HIV therapy (also called HAART) at the time of vaccination.

HIV-related neuropathy: The heat is on

Neuropathy is a painful nerve condition that affects about 1 in every 3 HIV+ patients. Some HIV meds in the family of nucleoside reverse transcriptase inhibitors ("nukes") can cause neuropathy or make it worse. These include ddI (Videx), d4T (Zerit), and AZT (Retrovir, also in Combivir and Trizivir). At this year's conference, Dr. David Simpson presented results on the use of capsaicin (pronounced "cap-SAY-sen") to reduce the pain associated with neuropathy (abstract 79). Capsaicin is the substance in chili peppers that makes them spicy or hot. (We previously wrote about a capsaicin **pilot study** by this same group in the June 2004 *HIV Treatment ALERTS!*) While topical (on the skin) capsaicin creams are available, they are not very potent and need to be applied many times a day, in contrast to the patch, which only needs to be applied about once every 12 weeks. The current study included 307 patients who were randomly chosen (by chance, like flipping a coin) to receive the capsaicin patch or a **control** patch (which contained a very low concentration of capsaicin to mimic the burning sensation caused by capsaicin). In addition, the study was "double-blind," meaning that patients and healthcare workers did not know which treatment each patient was receiving. Patients were first treated with a topical anesthetic followed by a 30-, 60-, or 90-minute application of the capsaicin skin patch or control patch to the painful area. The area was then cleaned to remove any lingering capsaicin. Patients were only treated once and then studied for 12 weeks. A variety of tests showed that patients who were treated with the capsaicin patch experienced significant pain relief during the study period. Skin reactions at the treatment site were the most common side effect, but most patients tolerated the treatment well.

Test of the future?

Ziagen is an HIV med that works well for controlling HIV in many HIV+ people. Unfortunately, about 5% of patients experience a **hypersensitivity** reaction to the drug that can be very serious. Symptoms of a hypersensitivity reaction usually appear within the first 6 weeks of treatment and include a skin rash and 2 or more of the following symptoms: fever, nausea, vomiting, diarrhea, abdominal pain, severe tiredness, achiness, or a general sense of ill-health. Respiratory symptoms including cough, shortness of breath, and sore throat occur in about 20% of patients having a hypersensitivity reaction. Patients who believe they are experiencing Ziagen hypersensitivity should stop taking the drug and call their healthcare provider immediately. In fact, those who experience hypersensitivity to Ziagen must never take the drug again since restarting the drug can be life threatening. Because of the seriousness of this problem, some healthcare providers are reluctant to treat HIV+ patients with Ziagen.

A few years ago, a strong link between a unique immune protein (known as HLA-B*5701) and the risk of having Ziagen hypersensitivity was identified. People have all kinds of HLA proteins, and people with HLA-B*5701 are more likely to have this reaction when treated with Ziagen. One study (abstract 667a) examined the usefulness of screening patients for HLA-B*5701 as a way to help select HIV meds. A total of 271 HIV+ patients from the United Kingdom were tested, and HLA-B*5701 was detected in 11% of White patients and 7% of Black patients. Both rates were higher than expected when compared to previous studies. As part of this study, the researchers compared the number of hypersensitivity reactions that occurred in their clinic before and after they started using this test. In the time before the testing, 20 cases of hypersensitivity occurred in 322 patients (a 6% rate). In contrast, of the 81 patients who started Ziagen after testing negative for HLA-B*5701, none had a hypersensitivity reaction.

These findings emphasize the usefulness of this test in *some* populations. White and Hispanic patients who test negative for this particular immune protein can still have Ziagen hypersensitivity. In addition, this test is not recommended for HIV+ patients of African descent/ethnicity because previous studies showed that having HLA-B*5701 was not linked to Ziagen hypersensitivity in that population. The above study was performed in the United Kingdom where the Black patients were mostly from southern and southeastern Africa and may have a slightly different **genetic** makeup than many African Americans. Also, this test is still not widely available and is not currently recommended in HIV treatment guidelines. Perhaps in the future, as additional research is done in this area, this test will become more widely available as a way to identify individuals who are more likely to have a hypersensitivity reaction and who therefore should not take Ziagen.

Reyataz: Do you need Norvir?

A study performed by Bristol-Myers Squibb, maker of the protease inhibitor Reyataz, and others (study BMS 089) looked at the effect of **boosting** Reyataz with Norvir (abstract 107LB). Two hundred patients who had never taken HIV meds before were randomly chosen (by chance, like flipping a coin) to receive Reyataz alone (400 mg once a day) or boosted (Reyataz, 300 mg once a day + Norvir, 100 mg once

a day). Both groups of patients also received the nucleoside reverse transcriptase inhibitors ("nukes") Epivir (3TC) and an extended-release version of Zerit (d4T) that is not commercially available. After 48 weeks of treatment, the results show that the effects of boosted Reyataz are very similar to unboosted Reyataz, at least in terms of HIV viral load and T-cell counts. For example, 86% of the patients in the boosted group had an HIV viral load less than 400 copies compared to 85% of the patients in the unboosted group. In addition, 75% of the boosted group had a viral load less than 50 copies compared to 70% of the patients in the unboosted group. Both groups also experienced an increase in T-cell count. However, more patients in the unboosted group experienced a virologic failure, defined as a viral load more than 400. Both treatments were generally safe and well tolerated, though more patients in the boosted arm had side effects compared to the unboosted arm. The most common side effect was hyperbilirubinemia, which means that high levels of bilirubin were found in the patient's blood. While this usually indicates some sort of liver problem, in the case of Reyataz it is more cosmetic and generally means a yellowing of the skin and whites of the eyes. In addition, more patients in the boosted group stopped treatment because of these side effects. Currently, boosted Reyataz is recommended for anyone who has taken protease inhibitors in the past, especially if they have **drug-resistant HIV**. Longer-term studies are still needed to see if the effectiveness of unboosted Reyataz remains similar to boosted Reyataz for longer than 1 year.

Hepatitis C: Early response means success

Currently available treatments for the hepatitis C virus (HCV) don't work for all patients. These treatments can also cause serious side effects in some patients, especially in those co-infected with HIV and HCV. Finding a way to predict whether a patient will respond to HCV treatment is an important research goal. It makes sense that if a patient isn't responding to treatment, why should they suffer the side effects? Previous studies have shown that HCV+ patients (who are HIV-negative) who have an early virologic response (EVR) after 12 weeks of treatment have a good chance of achieving a long-term or "sustained virologic response" (SVR). However, little research has been done in patients infected with both HIV and HCV.

One study (abstract 855) found that patients with an EVR were more likely to have an SVR, even if they were co-infected with both viruses. (For this study, EVR was defined as having a reduction of at least 2 logs in HCV viral load after 12 weeks of treatment. A reduction by 1 log is like taking a zero off a number, for example from 10,000 to 1,000. So a 2-log drop might be going from 1,000,000 to 10,000 or 100,000 to 1,000.) Ninety-five HIV/HCV co-infected patients were treated with peginterferon or interferon in combination with ribavirin. Overall, 64% of the patients (35 out of 55) who achieved an EVR at 12 weeks went on to have an SVR. In fact, if a patient did not have an EVR, they never had an SVR, at least in this study.

Similarly, another study (abstract 856) focused on rapid virologic response (RVR), which was measured after only 4 weeks of HCV treatment (defined as undetectable HCV viral load, less than 50 copies). As part of APRICOT (AIDS PEGASYS Ribavirin International Co-infection Trial), 176 co-infected patients with HCV genotype 1 were treated with peginterferon plus ribavirin. Of the 172 patients whose results were available at the end of the study, 22 (13%) had an RVR. Of these 22 patients, most (82%) went on to have an SVR. Only one patient with an RVR relapsed during the study period. In contrast to the above study, patients who did not have an RVR could still achieve an SVR, but it didn't happen as often. For example, only 22% of these patients achieved an SVR.

Both studies emphasize the importance of early response to HCV treatment and may motivate patients to stay **adherent** to their HCV treatment. Obviously, an early response to HCV treatment can only happen if patients take their HCV meds.

Another study (abstract 863) may help explain why some patients do not achieve an SVR. Researchers found that patients with **insulin resistance**, a condition associated with the development of **diabetes**, were less likely to respond to HCV treatment. For example, only 20% of co-infected patients with insulin resistance had an SVR, while 52% of patients without insulin resistance had an SVR. Results were similar in HIV-negative patients infected with HCV.

Viread and the Kidneys

Viread (generic name: tenofovir) is a potent, once-daily HIV med that is commonly taken as a part of an HIV treatment **regimen**. Viread is also part of the combination pill "Truvada." This HIV med is generally well tolerated, but some people may experience side effects such as nausea, vomiting, headache, diarrhea, and abdominal pain. A less common, but perhaps more serious, side effect is kidney problems.

One study presented at the conference looked at the differences in kidney function using a special measurement known as "glomerular filtration rate" (GFR) in people being treated with Sustiva or Viread (abstract 777). By measuring GFR, doctors can assess how well a patient's kidneys are functioning. This study of 144 HIV+ people found a small but significant decrease in GFR rates in patients treated with Viread who have previously taken non-nucleoside reverse transcriptase inhibitors ("non-nukes"), when examined at weeks 24 and 48. A lower GFR means that the kidneys are doing less filtering, which is a sign of damage or impairment. Researchers report that the long-term health effects of

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this GFR change in patients is unknown. A decrease in GFR was not seen in patients who had never taken non-nukes and who were then treated with the non-nuke Sustiva. In this study, outside factors that could affect kidney function, like taking meds to treat other conditions or having **diabetes** or hepatitis C, were not considered. Also, all patients were taking a **boosted** protease inhibitor regimen, so researchers were unable to find out what role Norvir might play in Viread-associated kidney damage. Researchers recommend that GFR be routinely monitored by healthcare providers, especially for patients at risk for kidney disease.

In another study (abstract 778), 222 HIV+ patients at the Atlanta Veterans Administration Medical Center were studied to identify potential risk factors for Viread-associated kidney damage in the first year of therapy. In this study, 17% developed kidney damage and 4% developed decreased kidney function. The researchers note that the 17% incidence rate is higher than other studies have reported. Study results also indicate that people who have never been on meds were almost 12 times more likely to develop decreased kidney function and 3.5 times more likely to develop kidney damage. Intravenous drug users were at an increased risk (4 times) of decreased kidney function.

In one other study (abstract 779), Centers for Disease Control and Prevention researchers analyzed results from more than 9,500 people (both new and experienced with HIV meds) from 10 different states and more than 100 clinics. After taking into account age, sex, race, viral load, and history of diabetes or high blood pressure, researchers report that Viread was associated with all levels (mild, moderate, or severe) of kidney damage. Broken down, 31.7% of the people had mild impairment, 6.1% had moderate impairment, and 2.4% had severe impairment. Older age was associated with increased risk for all levels of damage. Factors associated with more severe impairment included a T-cell count below 200 cells, and having **anemia**, diabetes, or high blood pressure.

Metabolic syndrome: still a concern

Metabolic syndrome (MetS) is a group of symptoms that can increase your risk for heart disease, stroke, and **diabetes**. Going by National Cholesterol Education Program guidelines, a patient has metabolic syndrome if he or she has 3 or more of the following:

- Abdominal obesity: a waistline of 102 cm (about 40 inches) or more for men, and 88 cm (about 34.5 inches) or more for women (measured across the belly).
- Elevated triglycerides: fasting level 150 mg/dL or above.
- Low high-density lipoprotein level (HDL) cholesterol less than 40 mg/dL for men, or less than 50 mg/dL for women.
- Hypertension: blood pressure above 130/85 or currently on hypertension medication.
- Elevated glucose (sugar): fasting level 100 to 125 mg/dL.

MetS affects 22% to 24% of the US population in general. Recent studies suggest that HIV meds cause elevated cholesterol/triglyceride levels, increases in abdominal fat, and **insulin resistance** (a condition associated with the development of diabetes) – the same symptoms of MetS. To see how these issues relate to HIV in a real-world setting, researchers surveyed patients at their Adult Outpatient HIV clinic (abstract 748). In studying the information, the researchers conclude that there is a high **prevalence** of MetS (25%) among their HIV+ patients, but the percentage is similar to the general US population. Of more than 600 people surveyed, 25% had MetS and 81% had at least one risk factor. Hypertension (high blood pressure) was a strong predictor of MetS, followed by low HDL (higher numbers of HDL are desirable), and then increased waistline. In this study, HIV therapy (specifically protease inhibitor use) was a predictor of high triglycerides only, and not MetS. Researchers also report that higher T-cell counts (between 535 and 560) predicted MetS, even when all other risk factors were excluded.

Another study compared MetS in 645 HIV+ and 398 HIV-negative men (abstract 747). This study showed a 20% to 33% higher MetS prevalence among HIV+ men than HIV-negative men. Also, HIV+ men were more likely to have elevated triglycerides, low HDLs, and higher blood sugar. However, HIV+ men had smaller waistlines. The 2 groups had similar rates of high blood pressure. In contrast to the first study, people with T-cell counts below 200 were at greater risk for having MetS. Being older and being on HIV meds, especially a protease inhibitor, also increased MetS risk. Finally, alcohol use (one or more drinks per day) decreased the likelihood of MetS. Obviously more research, preferably in larger number of patients over longer periods of time, is needed to find answers to the questions that still remain about HIV and metabolic syndrome.

Biological clock for HIV?

In the human body, many different kinds of cells regularly divide to form new cells. These cells replace old or dying cells and keep the body healthy. This is true for T cells as well. Every time a cell divides, a copy of its **genetic** material or its "chromosomes" goes into each new cell. The ends of chromosomes have extra material that is protective, almost like insulation. The extra materials at the ends of chromosomes are called "telomeres." But each time a cell divides, the telomeres become a little bit shorter. In fact, as a person ages, telomeres continue to slowly shorten. This makes cells more vulnerable to damage, which may be why aging is associated with changes to how the body looks or works. In this way, telomere length can be considered a kind of "biological clock" in our cells.

In people with HIV, the immune system is constantly activated, which means that T cells are dividing more often than normal. Because of this, researchers in Canada looked at whether HIV infection affects the rate of telomere shortening in T cells and whether taking potent combination HIV therapy (also called HAART) makes any difference in terms of telomere shortening (abstract 311). Their theory is that HIV might accelerate the "aging" of T cells, which could affect their function. The researchers studied 16 HIV+ patients over 10 years (including years before HAART

was available). In a group of uninfected adults who were age-matched with the 16 HIV+ patients, the researchers found that the usual rate of telomere shortening (measured in loss of base pairs or "bp") was 52 bp per year. However, in the HIV+ people, that loss was greater than 180 bp per year when they were not taking HAART. When the patients were taking HAART, the telomere shortening slowed down to 65 bp per year, which is much closer to the regular rate but still faster than normal. This study supports the idea that HIV therapy may help decrease immune activation, which may help preserve better immune function over time.

An update on SMART

Earlier this year, the international "SMART" trial stopped enrollment because one of the 2 treatment strategies being studied was clearly more effective than the other. SMART stands for **S**trategies for the **M**anagement of **A**nti-**R**etroviral **T**herapy. The study began enrolling in January 2002 with a goal of 6,000 patients; it was planned to continue for at least 8 years. As of January 11, 2006, 318 enrollment sites in 33 countries had enrolled almost 5500 patients in the trial. The goal of the study was to learn whether delayed, broken-up treatment for HIV ("drug conservation") is as effective as immediate, uninterrupted treatment ("viral suppression"). Information was also gathered on the long-term side effects of HIV treatment and the effects on quality of life. Patients in the drug conservation group would start treatment when their T cells reached 250 or lower; they would stop treatment when their T cells reached 350 or higher. Enrollment in the trial was stopped because patients in the drug conservation group (who were receiving interrupted therapy) had more than twice the risk of developing AIDS or dying than those who stayed on continuous HIV therapy. Total AIDS-related events or deaths were 117 (or 3.7%) for the drug conservation group and 47 (or 1.5%) for the viral suppression group. After researchers discovered these differences, patients in the drug conservation group were placed on uninterrupted HIV therapy and became part of the viral suppression group.

At the conference, a special session was arranged to give an update on what information was being learned from the trial. A preliminary look at the patient information showed that there were no obvious patient characteristics that predicted AIDS events or death except for being in the drug conservation group. The researchers looked at such characteristics as sex, race, lowest-ever T-cell count, geographic location (US or outside US), T-cell count and viral load when entering the trial, and others. According to the researchers, only about 5% of the deaths were AIDS-related. However, **cardiovascular** events (like heart attacks) accounted for more than 23% of the deaths. The researchers will continue to look at the data collected so far in an attempt to answer why one group did worse than the other, and if there were any predictors for why this occurred. Also, for the time being, the study will continue to follow all patients in the viral suppression arm. Several community groups, including The CFA, have called for the study to continue because of the valuable information it will likely provide (as this early analysis has shown already). Some would like to see the study continue but with higher T-cell trigger-points for stopping and starting therapy, while others see value in continuing the trial as a large, observational study of many patients on therapy. To keep up with the latest SMART developments, visit the "News" section of the SMART Study website: ***www.smart-trial.org***.

Integrase inhibitors: Packing some punch!

Integrase is a protein HIV uses to insert its **genetic** material into the DNA of a T cell. Once that happens, the infected T cell can become a "virus factory" when the immune system is activated, producing many new copies of HIV that go on to infect other T cells. Even though scientists have known about integrase as a potential target for new HIV therapies, finding safe and effective drugs to stop integrase has been a major challenge. One company that has been working in this area for several years is Merck, which presented information about its integrase inhibitor "MK-0518" at the conference. So far, the drug seems to have few side effects. Better yet, when given to patients with **drug-resistant HIV**, the drug (in combination with other "background" HIV meds) caused a 2-log drop in viral load at 2 weeks, which continued through 16 weeks at all doses studied (200, 400, and 600 mg twice a day). (A 1-log reduction in viral load is like taking a zero off a number, for example from 10,000 to 1,000. So a 2-log drop might be going from 1,000,000 to 10,000 or 100,000 to 1,000). Patients who took just the other "background meds" did not experience such good results. A reduction of 2 logs in viral load is important because the best HIV meds to date have shown viral load decreases of 1 to 1.5 logs, so MK-0518 may be setting new standards in potency. Also, T-cell counts increased by about 100 on average. At 16 weeks, 80% of patients had viral loads less than 400, while 56% to 72% of patients had viral loads less than 50. This promising, potential HIV med is now being studied in greater numbers of patients over longer periods of time as part of Merck's application for getting this drug approved. More information about current studies can be found at ***www.benchmrk.com***.

Gilead Sciences also presented information on its new integrase inhibitor, "GS-9137." This drug will need **boosting** with Norvir, but will only need to be taken once a day. Although further behind in development than the Merck drug, patients taking boosted GS-9137 also experienced an average viral load drop of 2 logs. This suggests that the HIV-fighting strength of this new class of medications is very strong. More studies are needed in greater numbers of people over longer periods of time. If integrase inhibitors are proven safe and effective in clinical studies, they may be approved in the next few years and become an important new weapon for fighting HIV. Stay tuned for future updates in *HIV Treatment ALERTS!*

treatment news

Quality of care

Many HIV+ patients see a nurse practitioner (NP) or physician assistant (PA), rather than a doctor, to manage their HIV disease. These healthcare professionals are trained to treat patients and can perform physical exams, order tests, prescribe drugs, and make treatment decisions. By law, PAs must have a doctor's supervision, while NPs do not have this requirement. In a recent study published in *Annals of Internal Medicine* (143:10, p. 729, 2005), researchers reviewed medical charts from 6651 HIV+ patients at 68 clinics to determine how well patients were being cared for by NPs, PAs, and doctors. They studied information like how well the patient's HIV viral load was controlled and whether the patient was receiving potent combination HIV therapy (also called HAART). They also checked whether the patients had been screened for tuberculosis, hepatitis C, and cervical cancer, and if they had received a flu shot. They found that NPs and PAs with HIV expertise provided a similar or higher level of care compared to doctors. In fact, PAs and NPs were better at screening for tuberculosis and cervical cancer when compared to all doctors. In addition, when compared to doctors who were not HIV experts, NPs and PAs were better at helping patients control viral load, prescribing proper HIV meds, and giving flu shots. These findings suggest that for routine care, seeing a PA or NP with HIV expertise is a good alternative for some patients, and is better than seeing a doctor without expertise in HIV. However, HIV+ patients with more complex needs may be better served seeing a doctor who is an HIV specialist.

Mind-body CONNECTION

The idea that feeling bad emotionally can make a person feel bad physically is being recognized more and more in Western medicine. In fact, science is beginning to show that when people are depressed, their immune systems actually become weaker. A study published in *The American Journal of Psychiatry* (162, p. 2125, 2005) investigated the connection between depression and a person's immune system in 57 HIV+ women during a 2-year period. Specifically, researchers examined the activity of a type of immune cell called a natural killer cell (see this issue's "HIV 101" on page 13). This type of immune cell is very important in keeping us healthy because they attack and kill abnormal or damaged cells, including cancer cells, HIV-infected cells, and cells infected with other kinds of viruses or bacteria. In particular, the researchers focused on 11 women whose depression improved during the 2 years of the study. In these women, natural killer cell activity increased dramatically. These findings strongly indicate that depression has a negative impact on HIV disease progression. Staying emotionally positive (in combination with taking HIV meds, getting enough rest, and eating healthy foods) may be one additional way to fight HIV.

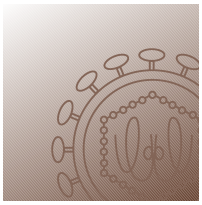
Shingles remains a problem

Shingles (also called herpes zoster) is an **opportunistic infection** caused by the same virus that causes chicken pox. After a person has chicken pox, the virus becomes inactive, but can become active again in a person with a weakened immune system. The immune system can be weakened because of illness (for example, HIV or cancer), certain meds, older age, or excessive emotional or physical stress. When the chicken pox virus becomes active again, it causes shingles rather than chicken pox. Shingles specifically infects the nerve roots along the spine and early symptoms include headache, sensitivity to light, and flu-like symptoms without a fever. A characteristic band-like rash that can be itchy and painful will appear on a person's back or neck and sometimes around the eye. The rash progresses into clusters of blisters that eventually crust over. It takes 2 to 4 weeks for the blisters to heal, although some scars may remain.

Before the introduction of potent combination HIV therapy (also called HAART), HIV+ individuals were more likely to get shingles compared to the general population. However, little research has been done to determine if HAART has lowered the frequency of shingles. In the April 2005 issue of *HIV Treatment ALERTS!*, we reported on a study (*Journal of Acquired Immune Deficiency Syndromes*, 37:5, p. 1604, 2004) showing that even in the era of HAART, HIV+ women are much more likely to have shingles compared with uninfected women, especially if they have low T-cell counts.

A more recent study published in the *Journal of Acquired Immune Deficiency Syndromes* (40:2, p. 169, 2005) examined the frequency of shingles in both HIV+ men and HIV+ women in the years following the introduction of HAART (1997 through 2001). By examining medical records from 2543 HIV+ patients, researchers identified 239 patients from their urban clinic who had shingles. According to this study, the frequency of shingles has not changed since the introduction of HAART and was almost 10 times the rate of shingles in the general population. In addition, HIV+ patients were more likely to have recurrent episodes of shingles compared to the general population and were more likely to experience complications of the shingles, including **neurological** and eye problems. The researchers also found out that patients with T-cell counts between 50 and 200 were at the highest risk for shingles. Also, those on HAART were more at risk, which may be explained by the effects of HAART in people with low T cells—sometimes their immune systems bounce back too quickly and start seeing and attacking all kinds of "foreign invaders" (like viruses or bacteria) in the body. This is known as "immune reconstitution syndrome."

Is HIV getting weaker?

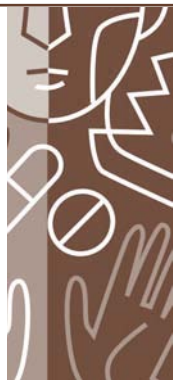


According to a recent study published in the journal *AIDS* (19, p. 1555, 2005), HIV could be getting weaker over time. Researchers examined 12 "historical" blood samples collected at the beginning of the AIDS epidemic in 1986 through 1989. These stored samples were compared to 12 recent blood samples collected in 2002 and 2003. All samples were taken from HIV+ patients who had never taken HIV meds before so that the development of **drug-resistant HIV** in the patients was not a factor in their findings. Of the 24 total patients, 8 had advanced HIV disease and 16 patients had early disease. Each historical sample was matched with a recent sample, meaning that disease characteristics like the patient's T-cell count, HIV viral load, **co-receptor tropism** (see Definitions, page 15!), and **genetic** makeup of the HIV were similar. Researchers isolated actual virus from these samples and performed tests in healthy cells as a way to compare the HIV collected in the 1980s to today's HIV. They concluded that HIV from the historical samples reproduced better than the HIV from recent samples. These findings indicate that today's HIV may be losing strength. The researchers also found that today's HIV is more sensitive to the HIV med Epivir (3TC) and an experimental **CCR5 antagonist**, though these results were not that dramatic. It is important to point out that this was a small study. While this may be good news for those recently infected with HIV, it is important to remember that all HIV infections are serious and can be life threatening.

Triple-nuke therapy: STILL NOT A GOOD IDEA

Five or 6 years ago, the idea of using 3 nucleoside reverse transcriptase inhibitors ("nukes") together as an HIV treatment **regimen** seemed like a good idea. Patients generally tolerated certain drugs in this class well, experiencing fewer side effects while suppressing HIV. In addition, some nukes have been combined into 1 pill for convenience. While problems associated with triple-nuke therapy have been reported in the last few years, the results of a large clinical trial now provide solid evidence that HIV+ patients taking a triple-nuke regimen are less likely to control HIV, as well as providing some answers why. In this study, published in *The Journal of Infectious Diseases* (192, p. 1921, 2005), 340 HIV+ patients who had never taken HIV meds before were randomly chosen (by chance, like flipping a coin) to receive Epzicom (1 pill that contains 2 nukes: Epivir and Ziagen) and either the nuke Viread (thus making it a triple-nuke regimen) or the non-nucleoside reverse transcriptase inhibitor ("non-nuke") Sustiva. However, early into the study, the researchers began getting reports of patients not responding to the triple-nuke regimen. They immediately analyzed the results from patients who had been in the study for at least 8 weeks and found that 49% of the patients receiving the triple-nuke regimen were not responding to the HIV treatment, compared to only 5% of the patients not responding in the Sustiva group. Moreover, within 12 weeks of treatment, the majority of patients (98%) not responding to the triple-nuke regimen had developed **drug-resistant HIV**. The researchers believe that the combination of these 3 drugs did not provide a good enough "barrier" against HIV becoming resistant to the meds. As a result, drug resistance **mutations** developed, and the HIV was no longer sensitive to these drugs, leading to uncontrolled viral loads. The researchers strongly recommend that the combination of Ziagen, Epivir, and Viread (in addition to other triple-nuke regimens) not be used to treat HIV+ patients. These findings emphasize the importance of performing and analyzing the findings from large, randomized, clinical trials as a way to design effective treatments. While all 3 of these nukes work well individually, the combination failed miserably.

CAUTION: Norvir + corticosteroids



Patients taking prednisone while also taking the HIV protease inhibitor, Norvir, may be at increased risk for side effects. Prednisone is a type of synthetic (man-made) corticosteroid, which is used to treat a variety of conditions such as arthritis, colitis (inflammation of the large intestine), asthma, inflammation of the lungs, certain skin rashes, allergic or inflammatory conditions of the nose and eyes, or following a liver or kidney transplant. Corticosteroids are **hormones** and, in addition to man-made versions, are naturally produced by our bodies in the adrenal glands, which are located on top of both kidneys. In a recent study published in the *Journal of Acquired Immune Deficiency Syndromes* (40:5, p. 573, 2005), researchers examined the effect of taking both prednisone and Norvir in 10 HIV-negative volunteers for 14.5 days. They found that Norvir dramatically increased the amount of prednisone in the subjects' bodies. As a result, patients taking this combination could experience dangerous side effects, including bone loss and Cushing' syndrome, a serious disorder caused by high levels of the naturally-occurring corticosteroid, cortisol.

Importantly, Norvir may also interact dangerously with other types of corticosteroids. For example, symptoms of Cushing's syndrome have already been reported in HIV+ patients taking Norvir in combination with fluticasone (sold as Flonase or Flovent), a corticosteroid used to treat asthma and seasonal allergies. In addition, new precautions were added to the labeling for the HIV protease inhibitor Reyataz stating that patients should not take Reyataz in combination with fluticasone (see FDA Bits in this issue, page 10). These issues are important for HIV+ patients, many of whom take different corticosteroids to treat health problems, who also take Norvir. Furthermore, because of evidence showing interactions between corticosteroids and both Norvir and Reyataz, patients taking corticosteroids in combination with *any* HIV protease inhibitor should discuss these concerns with their healthcare provider.

Update to HIV Treatment Guidelines

The US guidelines for treating HIV were updated on October 6, 2005. Among the changes are the following points:

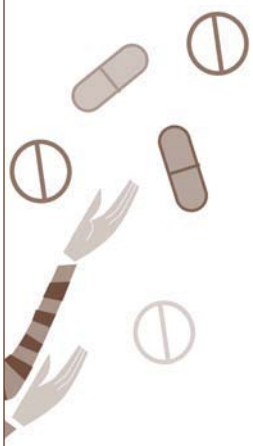
Medications you should NOT start with:

- HIV+ patients who have never taken HIV meds before should NOT use a regimen containing a non-nucleoside reverse transcriptase ("non-nuke") in combination with Videx and Viread. This combination is not good at suppressing HIV and patients taking this combination are more likely to develop **drug-resistant HIV**.
- While the protease inhibitor Aptivus is a new HIV med, it is not intended for everyone. HIV+ patients who have never taken HIV meds before should NOT take Aptivus. This drug should only be used by patients who are highly treatment experienced (with multi-drug resistant virus) and must be **boosted** with Norvir.

Management of Treatment-experienced Patients

- The goal in treating treatment-experienced patients (patients who have taken several HIV meds in the past AND who have developed **drug-resistant HIV**) is to suppress HIV viral load as much as possible.
- If a patient is not responding to current treatment, tests to determine if drug resistance has developed should be performed while the patient is still taking the failing regimen or within 4 weeks of stopping this regimen.
- If a patient is not responding to current treatment, it is best to design a new regimen that includes at least 2 fully active drugs. Meds that are new are not necessarily active against a person's HIV. A patient's history and presence of drug-resistant HIV will determine which meds and classes of meds will be effective.
- If a new and effective regimen is not possible at the time, then staying on a stable regimen is a good idea (to preserve T cells and suppress virus even partially). New and active meds can be started later on when they become available through clinical trials, expanded access, or after approval. (Always work with a doctor to make these healthcare decisions).

These guidelines can be found online at
www.aidsinfo.nih.gov



Videx + ribavirin dangers

Healthcare providers already advise patients who are infected with both HIV and the hepatitis C virus (HCV) not to take the HIV med Videx (ddI) in combination with ribavirin, a drug to treat HCV. However, a recent report in the *Journal of Acquired Immune Deficiency Syndromes* (40:1, p. 47, 2005) recommends this combination be avoided all together because of the large number of patients experiencing serious side effects. As part of a larger study examining patients co-infected with HCV and HIV, researchers identified 11 patients who showed signs of damage inside their cells (in the mitochondria, which help provide energy to our cells). This type of damage can cause nausea, vomiting, abdominal pain, tiredness, weight loss, and inflammation of the pancreas (a digestive organ that also helps control blood sugar levels). All 11 patients were receiving meds to treat their HIV and HCV. Patients taking Videx in combination with HCV treatment (ribavirin with either peg-interferon or interferon) were 46 times more likely to show signs of this damage. Patients taking some other HIV meds did not experience this side effect. Based on previous studies, the researchers believe the combination of Videx and ribavirin is responsible for this damage and should be avoided. If a patient must take this combination, he or she should be monitored very closely.

FDA BITS

Psoriasis warning

HIV+ patients should not take the drug Amevive because it lowers a person's T-cell count. Amevive is used to treat moderate to severe psoriasis, a common and chronic skin condition that usually causes patches of itchy, scaly, and sometimes inflamed skin.

Warning: fluticasone + Reyataz

New precautions have been added to the labeling for the HIV protease inhibitor Reyataz. Patients taking Reyataz should not take fluticasone, a corticosteroid used to treat asthma and seasonal allergies (sold as Flonase or Flovent). Serious side effects can occur in patients taking this combination. A similar problem has been shown with the combination of Norvir and fluticasone. It is likely that these problems will also occur when taking the other HIV protease inhibitors in combination with fluticasone (see page 9 in this issue). Therefore, patients taking HIV protease inhibitors in combination with fluticasone (or another type of corticosteroid) should discuss these concerns with their healthcare provider.

fact SHEET
Prevention for Positives

What is prevention for positives?

HIV+ individuals deserve to have "…as full and satisfying sexual and emotional lives as anyone else" (*The Denver Principles*, 1983). Prevention for positives aims to inform people living with HIV about: 1) how to avoid infecting others with HIV and 2) how to avoid getting sexually transmitted diseases (such as herpes, gonorrhea, chlamydia, etc.) and other blood-borne illness (for example, hepatitis C and hepatitis B).

Why is prevention for positives important? What does it matter if the other person already has HIV?

Prevention for positives helps people living with HIV to avoid becoming infected with other illnesses (co-infections), especially sexually transmitted diseases (STDs). These other illnesses may put a strain on the immune system, especially if it is weaker because of HIV. In addition, HIV+ people can get infected with another strain of HIV that may be different from the strain they already have. Certain **mutations** (**genetic** changes) in HIV can make it **resistant** to some HIV medications. These drug-resistance mutations can be transmitted from one HIV+ person to another. Why does this matter? Because some HIV treatments might not work even *before* a person has taken them. Prevention for positives is also very important to slow the spread of new HIV infections overall.

Is prevention for positives only about sexual behavior?

No. Prevention for positives focuses on two main areas: 1) sexual behavior and 2) injection drug use. However, HIV+ individuals should practice general prevention for all illnesses including chronic (long-lasting) diseases, such as **diabetes** and hypertension (high blood pressure), and acute (lasting for a short time) illnesses such as the flu or chicken pox—just like HIV-negative people. It is important for people with HIV to be aware that any health/prevention messages for the general public may be extra important for themselves because of their weaker immune system.

What should an HIV+ person NOT do?

1. HIV+ people should not have unprotected, penetrative sex (oral, anal, or vaginal) with another person. This includes fisting, handballing, or fingering. In addition, several scientific studies have shown that men who are uncircumcised can get HIV easier than men who are circumcised. This is because the foreskin provides additional access for HIV to enter the body. Therefore, HIV+ men who are uncircumcised should be extra careful during sex and use protection to prevent re-infection with HIV.
2. HIV+ people who use recreational drugs should not share drug-works (such as needles, crack pipes, cocaine straws, etc.) with other people. Shared drug-works can contain even small amounts of blood from other individuals that may contain hepatitis B, hepatitis C, or other strains of HIV. (IMPORTANT: Positive people should get tattoos only from individuals or businesses using a clean needle AND a clean ink pot AND fresh ink.)

How can an HIV+ person make sex "safer"?

Research studies have shown that viral load plays a part in how likely a person will transmit HIV to someone else through sex. Therefore, an HIV+ person can reduce transmission risk by keeping her or his viral load as low as possible through the use of HIV medications. But, other research studies have shown that the viral load found in the blood can often be different from the viral load that is in the genital tract and fluids. Often, the viral load in the genital tract can actually be higher than that found in the blood, which is where HIV viral load is usually measured. Therefore, it is still important that a person with HIV always practice safe sex with his or her partner(s). Low or "undetectable" viral load is just another layer of protection for sexual partners by reducing risk of transmission.

Sexual contact with another person can be made safer in the following ways:

- *Anal Sex* – Correctly using a latex condom with a water-based lubricant (for example, K-Y Jelly) and using a new condom with each new partner *and* with each new act of intercourse (penetrative sex)
- *Vaginal Sex* – Correctly using a latex condom with a water-based lubricant (for example, K-Y Jelly) and using a new condom with each new partner *and* with each new act of intercourse (penetrative sex)
- *Oral Sex* – Using a dental dam (small piece of plastic that can be bought at sex shops or dental supply stores) OR *non-microwavable* plastic wrap (which can be bought at the grocery store) OR a latex condom cut lengthwise (from the opening to the tip) for oral sex on a woman or anal rimming. Use an intact male condom for oral sex on a man.
- *Other penetrative sex (fisting, handballing, or fingering)* – Using a latex glove and, if necessary, a water-based lubricant (for example, K-Y Jelly)
- *Sex Toys/Other* – Cleaning sex toys with soap and water after each person uses them, and not performing sexual activities that will result in either person bleeding

How can an HIV+ person make using drugs "safer"?

An HIV+ person can make using drugs safer by doing the following:

1. Using only clean needles OR needles that have been and will be used only by the same person
2. Using clean cotton swabs and other drug works
3. Hiding drug equipment so others cannot use it when no one is looking
4. Getting into a rehab program to stop using drugs completely

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What are barriers to prevention for HIV+ people?
The following are major barriers to prevention for HIV+ people:

1. Fear of disclosure (telling others about HIV status) – Open communication is an important tool for preventing the further spread of HIV. People with HIV can prepare themselves for disclosure to others by practicing (by themselves or with a friend) ways to tell others they have HIV. People can also get ideas on ways to disclose from counselors, support groups, and their healthcare givers.

2. Access to condoms/dental dams/lubricants – Condoms may be difficult for individuals to find in the "heat of the moment" so **ALWAYS BE PREPARED** by buying condoms the day before you expect to have sex. You can also prepare by buying condoms and keeping them in your home just in case you want to have sex. Free condoms can usually be gotten from local health department STD clinics or community-based organ izations that work with people who have STDs or HIV. To find these places, check the phone book, ask a friend, or ask a healthcare provider.

3. Access to clean needles for injection drug use – Some places provide "harm-reduction" services for injection drug users. While these services may be controversial, they do provide injection drug users with clean needles and, in some cases, testing for STDs. Contact local community-based organizations or drug treatment centers to find out more information about local harm reduction programs.

What if my HIV-negative partner is accidentally exposed to my HIV?
In 2005, the Centers for Disease Control and Prevention (CDC) recommended that "post-exposure prophylaxis" or PEP be offered to individuals who have been accidentally exposed to HIV in non-work-related situations. (PEP for work-related exposures, such as a needle-stick injury in a healthcare worker, has been recommended for several years).

PEP is simply HIV therapy taken by an HIV-negative person who has been exposed to HIV. If taken soon enough, PEP may prevent that person from getting HIV. PEP requires that a person start taking HIV medications ***within 72 hours*** (3 days) after the possible exposure to HIV. A person on PEP must take 2 or 3 HIV medications for at least 1 month. These HIV medications often have side effects that might make it difficult to continue therapy. However, a person should always check with his or her healthcare provider before stopping PEP therapy.

To get PEP, it is probably easiest for a person to visit a local emergency center; however, some clinics or healthcare providers are now also offering PEP.

ClinicalTrialInformation

Heart Positive Study
Legacy Community Health Services (formerly the Montrose Clinic) and Baylor College of Medicine in Houston are participating in a study called "Heart Positive." The study aims to answer important questions about how to reduce heart disease and **diabetes** risk in people with HIV, especially those who show signs of **lipodystrophy**. The study is open to men and women with HIV, age 18 to 65, who have been taking combination HIV meds for at least 6 months. The study will look at lifestyle changes (diet and exercise) and the use of other meds to control levels of fats in the blood. The study is **placebo**-controlled (study participants may take pills, but only some people get real meds) and randomized (patients cannot choose a group, but are assigned randomly, like flipping a coin). These study rules help the doctors find out what will work or will not work in reducing the risk of heart disease and diabetes in people with HIV. To find out more information or to discuss enrolling in the study, visit ***www.heartpositive.org*** or call 713-830-3034.

Treatments Designed for Drug-resistant HIV
The Clinical Research Center at The University of Texas – Houston, School of Medicine is enrolling patients with **drug-resistant HIV** for a **phase 3 clinical trial**. This study will look at the effectiveness, tolerability, and safety of TMC125 (an experimental non-nuke) as part of an HIV treatment **regimen** that includes TMC114 (an experimental PI that is **boosted** with Norvir). The regimen also will include other HIV medications chosen by a doctor based on each patient's individual HIV resistance (so that drugs that are still effective or partially effective can be included in the regimen). People interested in this study must meet inclusion and exclusion criteria including: 1) must have a viral load above 5000, 2) must be on a stable HIV treatment regimen for at least 8 weeks before starting the study, 3) must not have chronic hepatitis C or chronic hepatitis B, and 4) must not have any active **opportunistic infections**, with the exception of stable Kaposi's Sarcoma and/or wasting syndrome. To find out more information about this study, contact Hilda Cuervo (713-500-6751 or ***hilda.cuervo@uth.tmc.edu***).

Check it out: *The Houston Area HIV/AIDS Clinical Trials Directory* is produced by The CFA. This comprehensive publication is updated quarterly and is available on The CFA website at ***www.centerforaids.org*** under "Publications."

HIV 101

"Natural Born Killers" and Other Important Players – Innate and Acquired Immunity (The Immune System, Part 2)

by **Marjorie Williams, MPH**

The immune system is a complex system whose main job is to protect the body from foreign invaders like bacteria or viruses. The immune system works by distinguishing between the body's own materials (including a fetus, in the case of pregnancy) and things that are foreign or damaging to the body. To accomplish its mission, the immune system has a large army with which to work. In *The Immune System (Part 1 of 2): T cells, B cells, and Cytokines* (April 2005 *HIV Treatment ALERTS!*), we introduced part of this army. This article is meant to give a very basic understanding of what is a very complicated system that scientists are just beginning to really understand.

Foreign invaders that enter a person's body have **antigens**, which cause the immune system to react and protect the body. Invaders and antigens can enter the body in many ways. For example, they can be inhaled into the body through the mouth or nose, absorbed through the skin, or ingested through the mouth. When antigens come into contact with the immune system, they may be destroyed or inactivated in a *general* way or they may trigger *specific* immune responses in the body (see diagram on page 14).

An example of general (or non-specific) immunity is when bacteria are blocked by the skin or destroyed by special substances in saliva or tears. In this case, the specific antigen or invader doesn't matter because the defense is always around or always the same. Some general defenses involve cells and inflammation (see "innate immunity" below). Specific immune responses are coordinated by "acquired" immunity that involves specialized T cells and B cells (see "acquired immunity" below). Although general and specific immune responses are separate, they do interact with each other. In many instances, cytokines (chemicals found in the body that help cells communicate with each other) are used to help these 2 types of responses communicate and coordinate with each other. Acquired immunity often works in combination with innate immunity. All of these components working together allow the immune system to recognize, destroy, and remember foreign invaders.

Innate Immunity

As described above, the innate immune response or "innate immunity" is a more general defense against foreign invaders. Innate immune responses involve some specific parts of our immune system including 1) macrophages, 2) neutrophils, 3) natural killer cells, and 4) the complement system.

Macrophages and neutrophils are immune cells that belong to a group of cells generally known as "phagocytes." These types of cells surround and engulf foreign invaders (like a "blob") that enter the body, therefore destroying the invader. Macrophages are large white blood cells found in places where body organs (like the liver, brain, or kidneys) come into contact with the bloodstream. Macrophages do not continuously circulate in the blood. Instead, they act as guards and screen substances that attempt to enter the organs they are protecting. Good substances, for example nutrients or oxygen, are allowed to enter the organs. In contrast, substances seen as foreign are engulfed and destroyed.

When a macrophage engulfs a foreign invader, it alerts other cells to be on the lookout for similar invaders. The macrophage does this by displaying some of the proteins or "epitopes" of the foreign invader (wearing it like a tag or flag on its outside). As a result, other cells know what the invader looks like, and the immune system is capable of quickly organizing its "troops" to destroy outsiders of the same sort. Neutrophils, another component of the innate immunity response, are also large white blood cells, but they circulate in the bloodstream. Neutrophils engulf foreign invaders that they find floating in the blood. Also, if needed, neutrophils are enlisted to work in other parts of the body where organs or cells may be under attack from foreign invaders.

Natural killer cells help the innate immune response because they are created with the ability to kill defective, changed, or injured cells. (Often this is caused by a foreign invader.) Natural killer cells are one of 3 types of **lymphocytes**, which also include B cells and T cells (see below). Natural killer cells are the largest of the lymphocytes and are capable of secreting cytokines as a way to activate or "turn on" T and B cells, as well as macrophages.

The complement system is also part of the innate immune response system. The complement system functions like a "system within a system" and is actually a group of proteins found in the blood that activate each other in a cascade of reactions, much like dominoes falling down. This cascade of activation enables the proteins to destroy foreign invaders in a number of ways (covering foreign invaders to tag or label them for destruction, working with **antibodies** (which are produced by B cells) to destroy the invaders, or even helping to fill invaders like bacteria with water so that they burst and are destroyed).

Acquired Immunity

The acquired or adaptive immune response begins "training" after birth and is very specific for different kinds of antigens. After birth, as the body comes into contact with the environment (including many viruses, bacteria, toxins, and other potential invaders), this branch of the immune system responds and gradually gets stronger so that it can better fight off new invaders. Acquired immunity consists of different components made up of a variety of T and B cells (such as helper T cells, "cytotoxic" or killer T cells, memory T cells, plasma cells, and memory B cells). Immunity involving T cells is called "cellular" immunity, and immunity involving B cells is called "humoral" immunity.

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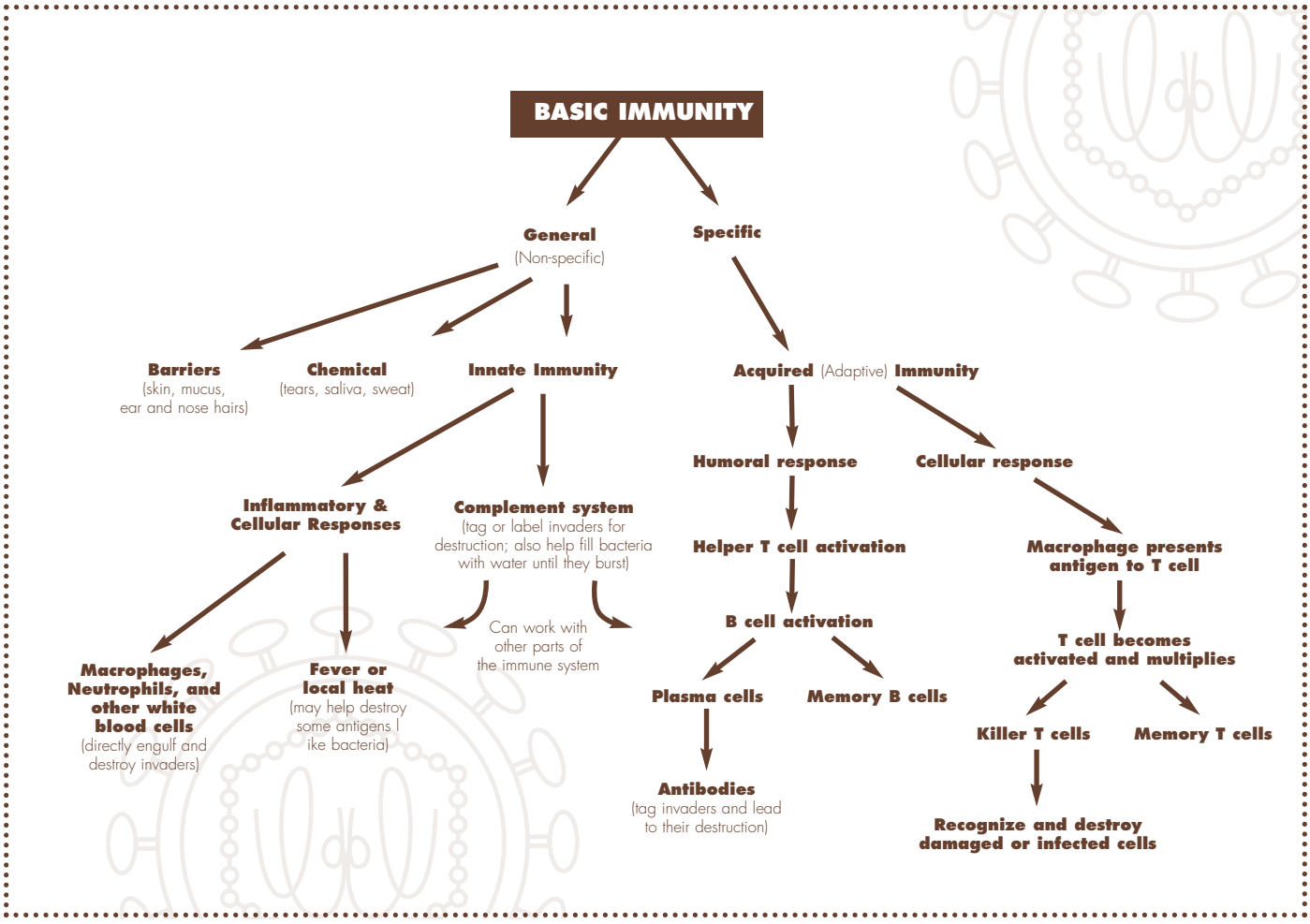
Cellular immunity. The process by which the lymphocytes in acquired immunity perform their duties is both delicate and complicated. Once it engulfs and destroys an antigen, a macrophage displays epitopes (parts) of the invader on its surface. When specific helper T cells and killer T cells from the thymus (a small organ in the chest) meet up with the macrophages, these T cells recognize the epitopes and the type of antigen the macrophage is displaying. The T cells then become activated and multiply.

The killer T cells destroy any cells in the body that may be infected with that kind of foreign invader. Killer T cells and helper T cells also create memory T cells that will remember the invader's antigens and will go to rest. If those antigens appear again, the memory T cells will activate and allow the immune system to clear the foreign invader much more quickly than the first time.

Humoral immunity. Helper T cells also activate B cells, including memory B cells from the bone marrow and spleen. B cells divide into plasma cells and memory B cells. Plasma cells recognize the antigen and begin to produce antibodies that bind only to this specific type of antigen (see explanation of antibodies in the April 2005 issues of *HIV Treatment ALERTS!*). Memory B cells then remember the type of antigen that is present to prepare for future attack by that specific type of antigen.

Regulatory T cells are yet another type of cell that helps slow down or turn off acquired immunity (both cellular and humoral) when the job is complete.

The immune system's process of antigen recognition, memory, and destruction has evolved in animals over millions of years. While the system may appear to be too complicated or even slow in some ways, it is actually quite deliberate and consistent in many of its functions. Because the immune system is so complex, more and more research (including HIV research) is focusing on the body's response to foreign invaders. These immune responses could hold the key to understanding many health complications (for example, T-cell loss) that are associated with certain illnesses, like HIV disease.



Definitions

Adherent (adherence): how well someone takes medication as directed, with respect to number and timing of doses.

Anemia: low levels of red blood cells or hemoglobin in the blood, resulting in poor oxygen transport and usually feelings of tiredness or fatigue.

Antibodies: types of protein that specifically bind to a cell or virus; usually antibodies are produced by the body's immune system against viruses or bacteria.

Antigen: a protein or other substance not made by the body (and usually part of an invading bacteria or virus) that triggers an immune response.

Boosted (boosting): elevated levels of a medication in the body.

Cardiovascular: relating to the heart and blood vessels.

CCR5 antagonist: a potential new drug to treat HIV; it works by binding to a "CCR5" receptor needed by HIV to enter T-cells.

Control: a special situation in research where no drug is given or no test is done. For example, a control group that gets a sugar pill (or "placebo," see below) might be compared to an experimental group that gets a real medication to see what the effects of the medication are.

Co-receptor tropism: the type of "co-receptor" (CCR5 or CXCR4) on T-cells that is used by HIV to enter the T-cell; CCR5-tropic (CCR5-using) virus is usually seen in earlier or mid-stage HIV disease, while CXCR4-tropic virus is usually seen in advanced disease when T-cell loss and viral load increases are more rapid.

Diabetes: a disorder involving insulin (a substance in the body that helps regulate blood sugar) that results in too much sugar in the blood and urine. Symptoms include hunger, thirst, weight loss, and frequent urination.

Drug-resistant HIV: when HIV can reproduce itself in the presence of an HIV medication because of a genetic change (mutation) in the virus.

Genetic: having to do with genes (which carry special biology blueprints made from DNA) and genetic information.

Hormone(s): a substance secreted by one part of the body that stimulates cells in another part of the body (for example, testosterone).

Hypersensitivity (hypersensitivity reaction): extreme sensitivity or allergic reaction to a specific food or drug.

Incidence: the number of people who get a disease or condition in a period of time (for example, in a year); this is like a rate.

Insulin resistance: decreased sensitivity to insulin that is associated with diabetes (see above).

Lipodystrophy: changes in body fat such as loss of fat in the arms and legs and accumulation of fat in the gut or at the back of the neck.

Lymphocytes: a type of white blood cell found in the body and that include B cells and T cells.

Metabolism (metabolize or metabolic): chemical reactions in the body that are part of life; for example, turning food into energy or breathing in oxygen and breathing out carbon dioxide.

Mutation: a genetic change, such as when HIV becomes resistant to a medication.

Neurological: having to do with the brain and nerves.

Neuropathy: damage to nerves (usually peripheral nerves, such as those in the arms and legs) resulting in muscle weakness, pain, and numbness.

Opportunistic infection(s): a disease or infection caused by an organism that is usually harmless, but becomes activated when a person's immune system is impaired or damaged.

Phase 3 clinical trial: a trial done in the later stage of drug development. After earlier trials to find out safety and proper dosing in small numbers of patients, the phase 3 trial for a drug will begin in larger numbers (hundreds) of patients over longer periods of time (a year or longer). Once the study information is complete, the company developing the drug can apply for approval of the drug as a medication.

Pilot study: an initial study done in a few people to test possible treatments or ways to care for patients, to see if it is worth further study.

Placebo: sometimes just the act of taking a pill can make someone feel better; so, to watch for this, a placebo (a pill or substance with no effect, such as a sugar pill) is often used to compare with a real medication to see what the medication's true effects might be.

Prevalence: the proportion of people in a population who have a disease or condition at a specific point in time.

Regimen: a combination or schedule of medications.

Resistance (resistant): a genetic (see definition above) change that allows HIV to reproduce itself in the presence of an HIV medication.

Vaccine: something that stimulates an immune response that can prevent an infection or create resistance to an infection.

Community**spotlight**

Founded in 1982, **AIDS Foundation Houston (AFH)** is the oldest and largest AIDS service provider in Houston:

- Food Assistance Program
- AFH Housing Programs
- Rent, Utilities, and Mortgage Assistance
- Employment Resources
- HIV/AIDS 101 Education
- Prevention Education
- Outreach Programs
- Benefits and Resources Counseling (BARC)
- Gay Men's Health Initiative
- Prison Initiative
- Pediatric and Youth programs
  - Camp Hope
  - Camp H.U.G.
  - Red Ribbon Toy Drive

AIDS FOUNDATION HOUSTON

"Over 20 years of changing lifetimes"

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