POSITIVELY AWARE
HIV Treatment and Health

REPORT FROM THE 15TH ANNUAL RETROVIRUS CONFERENCE

WHAT IS SACRED?

THE PAPILLOMA CHRONICLES

CLINICAL TRIAL UPDATE: THE SETPOINT STUDY

PLUS

May / June 2008
The Journal of Test Positive Aware Network

Important Information

INDICATION: ATRIPLA® (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate [DF] 300 mg) is a prescription medication used alone as a complete regimen or with other medicines to treat HIV infection in adults.

ATRIPLA does not cure HIV and has not been shown to prevent passing HIV to others. See your healthcare provider regularly.

IMPORTANT SAFETY INFORMATION:

Contact your healthcare provider right away if you experience any of the following side effects or conditions associated with ATRIPLA:

- **Nausea, vomiting, unusual muscle pain, and/or weakness. These may be signs of a buildup of acid in the blood (lactic acidosis), which is a serious medical condition.**
- **Light colored stools, dark colored urine, and/or if your skin or the whites of your eyes turn yellow. These may be signs of serious liver problems.**
- **If you have HIV and hepatitis B virus (HBV), your liver disease may suddenly get worse if you stop taking ATRIPLA. Do not stop taking ATRIPLA unless directed by your healthcare provider.**

Do not take ATRIPLA if you are taking the following medicines because serious and life-threatening side effects may occur when taken together: Hismanal® (astemizole), Vascor® (bepridil), Propulsid® (cisapride), Versed® (midazolam), Orap® (pimozide), Halcion® (triazolam), or ergot derivatives (for example, Wigraine® and Cafergot®).

In addition, ATRIPLA should not be taken with: Combivir® (lamivudine/zidovudine), EMTRIVA® (emtricitabine), Epivir® or Epivir-HBV® (lamivudine), Epzicom™ (abacavir sulfate/lamivudine), SUSTIVA® (efavirenz), Trizivir® (abacavir sulfate/lamivudine/zidovudine), TRUVADA® (emtricitabine/tenofovir DF), or VIREAD® (tenofovir DF), because they contain the same or similar active ingredients as ATRIPLA.

Vfend® (voriconazole) should not be taken with ATRIPLA since it may lose its effect or may increase the chance of having side effects from ATRIPLA. Fortovase®, Invirase® (saquinavir) should not be used as the only protease inhibitor in combination with ATRIPLA.

Taking ATRIPLA with St. John's wort *(Hypericum perforatum)* is not recommended as it may cause decreased levels of ATRIPLA, increased viral load, and possible resistance to ATRIPLA or cross-resistance to other anti-HIV drugs.

This list of medicines is not complete. Discuss with your healthcare provider all prescription and nonprescription medicines, vitamins, and herbal supplements you are taking or plan to take.

Contact your healthcare provider right away if you experience any of the following side effects or conditions:

- **Severe depression, strange thoughts, or angry behavior** have been reported by a small number of patients. Some patients have had thoughts of suicide and a few have actually committed suicide. These problems may occur more often in patients who have had mental illness.
- **Dizziness, trouble sleeping or concentrating, drowsiness, unusual dreams, and/or hallucinations** are common, and tend to go away after taking ATRIPLA (efavirenz 600 mg/emtricitabine 200 mg/tenofovir DF 300 mg) for a few weeks. Symptoms were severe in a few patients and some patients discontinued therapy. These symptoms may become more severe with the use of alcohol and/or mood-altering (street) drugs. If you are dizzy, have trouble concentrating, and/or are drowsy, avoid activities that may be dangerous, such as driving or operating machinery.
- **Kidney or liver problems.** If you have had kidney or liver problems, including hepatitis infection or take other medicines that may cause kidney or liver problems, your healthcare provider should do regular blood tests.
- **Pregnancy: Women should not become pregnant while taking ATRIPLA.** Serious birth defects have been seen in children of women treated during pregnancy with one of the medicines in ATRIPLA. Women must use a reliable form of barrier contraception, such as a condom or diaphragm, even if they also use other methods of birth control.
- **Breast-Feeding: Women with HIV should not breast-feed** because they can pass HIV through their milk to the baby. Also, ATRIPLA may pass through breast milk and cause serious harm to the baby.
- **Rash** is a common side effect that usually goes away without treatment, but may be serious in a small number of patients.
- **Seizures** have occurred in patients taking a component of ATRIPLA, usually in those with a history of seizures. If you have ever had seizures, or take medicine for seizures, your healthcare provider may want to switch you to another medicine or monitor you.
- **Bone changes.** If you have had bone problems in the past, your healthcare provider may want to check your bones.
- **If you have ever had mental illness or use illegal drugs or alcohol.**

Changes in body fat have been seen in some people taking anti-HIV medicines. The cause and long-term health effects are not known.

Common side effects of ATRIPLA include tiredness, headache, upset stomach, vomiting, gas, and diarrhea. Skin discoloration (small spots or freckles) may also happen with ATRIPLA.

You should take ATRIPLA once daily on an empty stomach. Taking ATRIPLA at bedtime may make some side effects less bothersome.

ATRIPLA is one of several treatment options your doctor may consider.

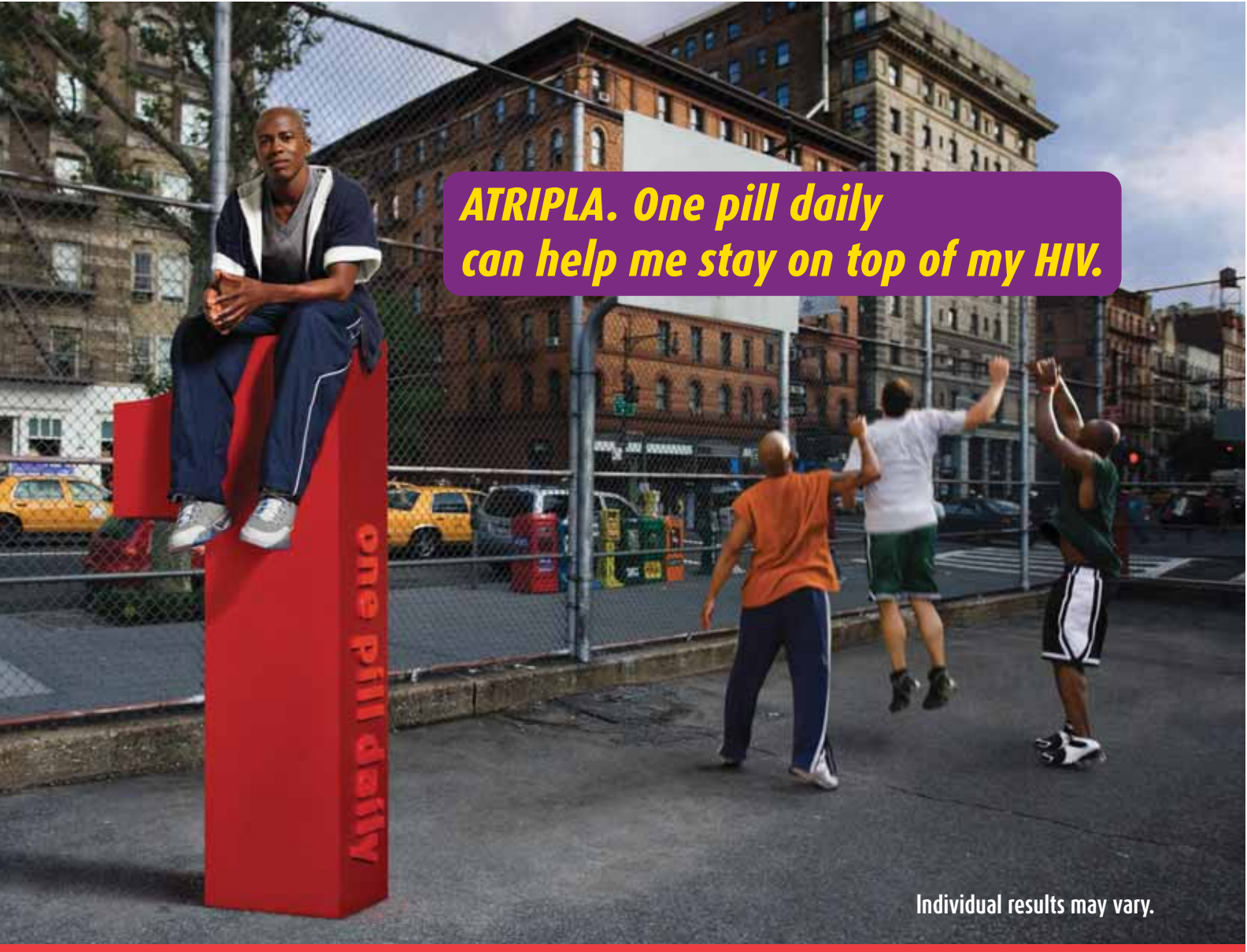
Please see Patient Information on the following page.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

If you or someone you know needs help paying for medicine, call 1-888-4PPA-NOW (1-888-477-2669). Or go to www.pparx.org

Partnership for Prescription Assistance

Bristol-Myers Squibb GILEAD



The first and only complete HIV regimen in one pill daily. ATRIPLA may be taken alone or with other HIV medicines.

- **Effective:** Proven to lower viral load to undetectable† and help raise T-cell (CD4+) count through 48 weeks of a clinical study.
- **One Pill, Once a Day:** Take on an empty stomach, preferably at bedtime, and you're done with ATRIPLA for 24 hours. Taking ATRIPLA at bedtime may make some side effects less bothersome.
- **Tolerability:** Well-established patient experience in clinical studies with the three proven medicines in ATRIPLA.

† Undetectable was defined as a viral load of less than 400 copies/mL.

ATRIPLA®
(efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) Tablets

It all adds up to one.™ *

Ask your doctor if ATRIPLA is right for you.

visit www.ATRIPLA.com

* ATRIPLA is a combination of 3 HIV medicines – SUSTIVA® (efavirenz), EMTRIVA® (emtricitabine), and VIREAD® (tenofovir disoproxil fumarate).

Please see Important Safety Information, including information on **lactic acidosis, serious liver problems,** and **flare-ups of hepatitis B (HBV)** on adjacent page.

PATIENT INFORMATION

℞ ONLY

ATRIPLA™ (uh TRIP luh) Tablets

ALERT: Find out about medicines that should NOT be taken with ATRIPLA (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg).

Please also read the section **"MEDICINES YOU SHOULD NOT TAKE WITH ATRIPLA."**

Generic name: efavirenz, emtricitabine and tenofovir disoproxil fumarate (eh FAH vih renz, em tri SIT uh bean and te NOE' fo veer dye soe PROX il FYOU mar ate)

Read the Patient Information that comes with ATRIPLA before you start taking it and each time you get a refill since there may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. You should stay under a healthcare provider's care when taking ATRIPLA. **Do not change or stop your medicine without first talking with your healthcare provider.** Talk to your healthcare provider or pharmacist if you have any questions about ATRIPLA.

What is the most important information I should know about ATRIPLA?

- **Some people who have taken medicine like ATRIPLA (which contains nucleoside analogs) have developed a serious condition called lactic acidosis** (build up of an acid in the blood). Lactic acidosis can be a medical emergency and may need to be treated in the hospital. **Call your healthcare provider right away if you get the following signs or symptoms of lactic acidosis:**
  - You feel very weak or tired.
  - You have unusual (not normal) muscle pain.
  - You have trouble breathing.
  - You have stomach pain with nausea and vomiting.
  - You feel cold, especially in your arms and legs.
  - You feel dizzy or lightheaded.
  - You have a fast or irregular heartbeat.
- **Some people who have taken medicines like ATRIPLA have developed serious liver problems called hepatotoxicity,** with liver enlargement (hepatomegaly) and fat in the liver (steatosis). **Call your healthcare provider right away if you get the following signs or symptoms of liver problems:**
  - Your skin or the white part of your eyes turns yellow (jaundice).
  - Your urine turns dark.
  - Your bowel movements (stools) turn light in color.
  - You don't feel like eating food for several days or longer.
  - You feel sick to your stomach (nausea).
  - You have lower stomach area (abdominal) pain.
- **You may be more likely to get lactic acidosis or liver problems** if you are female, very overweight (obese), or have been taking nucleoside analog-containing medicines, like ATRIPLA, for a long time.
- **If you also have Hepatitis B Virus (HBV) infection and you stop taking ATRIPLA, you may get a "flare-up" of your hepatitis. A "flare-up" is when the disease suddenly returns in a worse way than before.** Patients with HBV who stop taking ATRIPLA need close medical follow-up for several months, including medical exams and blood tests to check for hepatitis that could be getting worse. ATRIPLA is not approved for the treatment of HBV, so you must discuss your HBV therapy with your healthcare provider.

What is ATRIPLA?

ATRIPLA contains 3 medicines, SUSTIVA® (efavirenz), EMTRIVA® (emtricitabine) and VIREAD® (tenofovir disoproxil fumarate also called tenofovir DF) combined in one pill. EMTRIVA and VIREAD are HIV (human immunodeficiency virus) nucleoside analog reverse transcriptase inhibitors (NRTIs) and SUSTIVA is an HIV non-nucleoside analog reverse transcriptase inhibitor (NNRTI). VIREAD and EMTRIVA are the components of TRUVADA®. ATRIPLA can be used alone as a complete regimen, or in combination with other anti-HIV medicines to treat people with HIV infection. ATRIPLA is for adults age 18 and over. ATRIPLA has not been studied in children under age 18 or adults over age 65.

HIV infection destroys CD4 (T) cells, which are important to the immune system. The immune system helps fight infection. After a large number of T cells are destroyed, acquired immune deficiency syndrome (AIDS) develops.

ATRIPLA helps block HIV reverse transcriptase, a viral chemical in your body (enzyme) that is needed for HIV to multiply. ATRIPLA lowers the amount of HIV in the blood (viral load). ATRIPLA may also help to increase the number of T cells (CD4 cells), allowing your immune system to improve. Lowering the amount of HIV in the blood lowers the chance of death or infections that happen when your immune system is weak (opportunistic infections).

Does ATRIPLA cure HIV-1 or AIDS?

ATRIPLA does not cure HIV infection or AIDS. The long-term effects of ATRIPLA are not known at this time. People taking ATRIPLA may still get opportunistic infections or other conditions that happen with HIV infection. Opportunistic infections are infections that develop because the immune system is weak. Some of these conditions are pneumonia, herpes virus infections, and *Mycobacterium avium complex* (MAC) infection. **It is very important that you see your healthcare provider regularly while taking ATRIPLA.**

Does ATRIPLA reduce the risk of passing HIV-1 to others?

ATRIPLA has not been shown to lower your chance of passing HIV to other people through sexual contact, sharing needles, or being exposed to your blood.

- **Do not share needles or other injection equipment.**
- **Do not share personal items that can have blood or body fluids on them, like toothbrushes or razor blades.**
- **Do not have any kind of sex without protection.** Always practice safer sex by using a latex or polyurethane condom or other barrier to reduce the chance of sexual contact with semen, vaginal secretions, or blood.

Who should not take ATRIPLA?

Together with your healthcare provider, you need to decide whether ATRIPLA is right for you.

Do not take ATRIPLA if you are allergic to ATRIPLA or any of its ingredients. The active ingredients of ATRIPLA are efavirenz, emtricitabine, and tenofovir DF. See the end of this leaflet for a complete list of ingredients.

What should I tell my healthcare provider before taking ATRIPLA?

Tell your healthcare provider if you:

- **Are pregnant or planning to become pregnant** (see "**What should I avoid while taking ATRIPLA?**").
- **Are breastfeeding** (see "**What should I avoid while taking ATRIPLA?**").
- **Have kidney problems or are undergoing kidney dialysis treatment.**
- **Have bone problems.**
- **Have liver problems, including Hepatitis B Virus infection.** Your healthcare provider may want to do tests to check your liver while you take ATRIPLA.
- **Have ever had mental illness or are using drugs or alcohol.**
- **Have ever had seizures or are taking medicine for seizures.**

What important information should I know about taking other medicines with ATRIPLA?

ATRIPLA may change the effect of other medicines, including the ones for HIV, and may cause serious side effects. Your healthcare provider may change your other medicines or change their doses. Other medicines, including herbal products, may affect ATRIPLA. For this reason, **it is very important to** let all your healthcare providers and pharmacists know what medications, herbal supplements, or vitamins you are taking.

MEDICINES YOU SHOULD NOT TAKE WITH ATRIPLA

- The following medicines may cause serious and life-threatening side effects when taken with ATRIPLA. You should not take any of these medicines while taking ATRIPLA: Hismanal (astemizole), Vascor (bepridil), Propulsid (cisapride), Versed (midazolam), Orap (pimozide), Halcion (triazolam), ergot medications (for example, Wigraine and Cafergot).
- ATRIPLA also should not be used with Combivir (lamivudine/zidovudine), EMTRIVA, Epivir, Epivir-HBV (lamivudine), Epzicom (abacavir sulfate/lamivudine), Trizivir (abacavir sulfate/lamivudine/zidovudine), SUSTIVA, TRUVADA, or VIREAD.
- Vfend (voriconazole) should not be taken with ATRIPLA since it may lose its effect or may increase the chance of having side effects from ATRIPLA.

It is also important to tell your healthcare provider if you are taking any of the following:

- Fortovase, Invirase (saquinavir), Biaxin (clarithromycin); or Sporanox (itraconazole); **these medicines may need to be replaced with another medicine when taken with ATRIPLA.**
- Calcium channel blockers such as Cardizem or Tiazac (diltiazem), Covera HS or Isoptin (verapamil) and others; Crixivan (indinavir); Methadone; Mycobutin (rifabutin); Rifampin; cholesterol-lowering medicines such as Lipitor (atorvastatin), Pravachol (pravastatin sodium), and Zocor (simvastatin); or Zoloft (sertraline); **these medicines may need to have their dose changed when taken with ATRIPLA.**
- Videx, Videx EC (didanosine); tenofovir DF (a component of ATRIPLA) may increase the amount of didanosine in your blood, which could result in more side effects. **You may need to be monitored more carefully** if you are taking ATRIPLA and didanosine together. Also, the dose of didanosine may need to be changed.
- Reyataz (atazanavir sulfate) or Kaletra (lopinavir/ritonavir); these medicines may increase the amount of tenofovir DF (a component of ATRIPLA) in your blood, which could result in more side effects. **You may need to be monitored more carefully** if you are taking ATRIPLA and either Reyataz or Kaletra together. Also, the dose of Reyataz or Kaletra may need to be changed.
- Medicine for seizures [for example, Dilantin (phenytoin), Tegretol (carbamazepine), or phenobarbital]; your healthcare provider may want to switch you to another medicine or check drug levels in your blood from time to time.
- **Taking St. John's wort (*Hypericum perforatum*), or products containing St. John's wort with ATRIPLA is not recommended.** St. John's wort is a herbal product sold as a dietary supplement. Talk with your healthcare provider if you are taking or are planning to take St. John's wort. Taking St. John's wort may decrease ATRIPLA levels and lead to increased viral load and possible resistance to ATRIPLA or cross-resistance to other anti-HIV drugs.

These are not all the medicines that may cause problems if you take ATRIPLA (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg). Be sure to tell your healthcare provider about all medicines that you take.

Keep a complete list of all the prescription and nonprescription medicines as well as any herbal remedies that you are taking, how much you take, and how often you take them. Make a new list when medicines or herbal remedies are added or stopped, or if the dose changes. Give copies of this list to all of your healthcare providers and pharmacists **every** time you visit your healthcare provider or fill a prescription. This will give your healthcare provider a complete picture of the medicines you use. Then he or she can decide the best approach for your situation.

How should I take ATRIPLA?

- Take the exact amount of ATRIPLA your healthcare provider prescribes. Never change the dose on your own. Do not stop this medicine unless your healthcare provider tells you to stop.
- You should take ATRIPLA on an empty stomach.
- Swallow ATRIPLA with water.
- Taking ATRIPLA at bedtime may make some side effects less bothersome.
- Do not miss a dose of ATRIPLA. If you forget to take ATRIPLA, take the missed dose right away, unless it is almost time for your next dose. Do not double the next dose. Carry on with your regular dosing schedule. If you need help in planning the best times to take your medicine, ask your healthcare provider or pharmacist.
- If you believe you took more than the prescribed amount of ATRIPLA, contact your local poison control center or emergency room right away.
- Tell your healthcare provider if you start any new medicine or change how you take old ones. Your doses may need adjustment.
- When your ATRIPLA supply starts to run low, get more from your healthcare provider or pharmacy. This is very important because the amount of virus in your blood may increase if the medicine is stopped for even a short time. The virus may develop resistance to ATRIPLA and become harder to treat.
- Your healthcare provider may want to do blood tests to check for certain side effects while you take ATRIPLA.

What should I avoid while taking ATRIPLA?

- **Women taking ATRIPLA should not become pregnant.** Serious birth defects have been seen in the babies of animals and women treated with efavirenz (a component of ATRIPLA) during pregnancy. It is not known whether efavirenz caused these defects. **Tell your healthcare provider right away if you are pregnant.** Also talk with your healthcare provider if you want to become pregnant.
- Women should not rely only on hormone-based birth control, such as pills, injections, or implants, because ATRIPLA may make these contraceptives ineffective. Women must use a reliable form of barrier contraception, such as a condom or diaphragm, even if they also use other methods of birth control.
- **Do not breast-feed if you are taking ATRIPLA .** The Centers for Disease Control and Prevention recommend that mothers with HIV not breast-feed because they can pass the HIV through their milk to the baby. Also, ATRIPLA may pass through breast milk and cause serious harm to the baby. Talk with your healthcare provider if you are breast-feeding. You should stop breast-feeding or may need to use a different medicine.
- Taking ATRIPLA with alcohol or other medicines causing similar side effects as ATRIPLA, such as drowsiness, may increase those side effects.
- Do not take any other medicines, including prescription and nonprescription medicines and herbal products, without checking with your healthcare provider.
- **Avoid doing things that can spread HIV infection** since ATRIPLA does not stop you from passing the HIV infection to others.

What are the possible side effects of ATRIPLA?

ATRIPLA may cause the following serious side effects:

- **Lactic acidosis** (buildup of an acid in the blood). Lactic acidosis can be a medical emergency and may need to be treated in the hospital. **Call your healthcare provider right away if you get signs of lactic acidosis.** (See "**What is the most important information I should know about ATRIPLA?**")
- **Serious liver problems (hepatotoxicity),** with liver enlargement (hepatomegaly) and fat in the liver (steatosis). Call your healthcare provider right away if you get any signs of liver problems. (See "**What is the most important information I should know about ATRIPLA?**")
- **"Flare-ups" of Hepatitis B Virus (HBV) infection,** in which the disease suddenly returns in a worse way than before, can occur if you have HBV and you stop taking ATRIPLA. Your healthcare provider will monitor your condition for several months after stopping ATRIPLA if you have both HIV and HBV infection and may recommend treatment for your HBV.
- **Serious psychiatric problems.** A small number of patients may experience severe depression, strange thoughts, or angry behavior while taking ATRIPLA. Some patients have thoughts of suicide and a few have actually committed suicide. These problems may occur more often in patients who have had mental illness. Contact your healthcare provider right away if you think you are having these psychiatric symptoms, so your healthcare provider can decide if you should continue to take ATRIPLA.
- **Kidney problems.** If you have had kidney problems in the past or take other medicines that can cause kidney problems, your healthcare provider should do regular blood tests to check your kidneys.
- **Changes in bone mineral density (thinning bones).** It is not known whether long-term use of ATRIPLA will cause damage to your bones. If you have had bone problems in the past, your healthcare provider may need to do tests to check your bone mineral density or may prescribe medicines to help your bone mineral density.

Common side effects:

Patients may have dizziness, headache, trouble sleeping, drowsiness, trouble concentrating, and/or unusual dreams during treatment with ATRIPLA. These side effects may be reduced if you take ATRIPLA at bedtime on an empty stomach. They also tend to go away after you have taken the medicine for a few weeks. If you have these common side effects, such as dizziness, it does not mean that you will also have serious psychiatric problems, such as severe depression, strange thoughts, or angry behavior. Tell your healthcare provider right away if any of these side effects continue or if they bother you. It is possible that these symptoms may be more severe if ATRIPLA is used with alcohol or mood altering (street) drugs.

If you are dizzy, have trouble concentrating, or are drowsy, avoid activities that may be dangerous, such as driving or operating machinery.

Rash may be common. Rashes usually go away without any change in treatment. In a small number of patients, rash may be serious. If you develop a rash, call your healthcare provider right away.

Other common side effects include tiredness, upset stomach, vomiting, gas, and diarrhea.

Other possible side effects with ATRIPLA include:

- Changes in body fat. Changes in body fat develop in some patients taking anti-HIV medicine. These changes may include an increased amount of fat in the upper back and neck ("buffalo hump"), in the breasts, and around the trunk. Loss of fat from the legs, arms, and face may also happen. The cause and long-term health effects of these fat changes are not known.
- Skin discoloration (small spots or freckles) may also happen with ATRIPLA.

Tell your healthcare provider or pharmacist if you notice any side effects while taking ATRIPLA.

Contact your healthcare provider before stopping ATRIPLA because of side effects or for any other reason.

This is not a complete list of side effects possible with ATRIPLA. Ask your healthcare provider or pharmacist for a more complete list of side effects of ATRIPLA and all the medicines you will take.

How do I store ATRIPLA?

- **Keep ATRIPLA and all other medicines out of reach of children.**
- Store ATRIPLA at room temperature 77 °F (25 °C).
- Keep ATRIPLA in its original container and keep the container tightly closed.
- Do not keep medicine that is out of date or that you no longer need. If you throw any medicines away make sure that children will not find them.

General information about ATRIPLA:

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use ATRIPLA for a condition for which it was not prescribed. Do not give ATRIPLA to other people, even if they have the same symptoms you have. It may harm them.

This leaflet summarizes the most important information about ATRIPLA. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about ATRIPLA that is written for health professionals.

Do not use ATRIPLA if the seal over bottle opening is broken or missing.

What are the ingredients of ATRIPLA?

Active Ingredients: efavirenz, emtricitabine, and tenofovir disoproxil fumarate

Inactive Ingredients: croscarmellose sodium, hydroxypropyl cellulose, microcrystalline cellulose, magnesium stearate, sodium lauryl sulfate. The film coating contains black iron oxide, polyethylene glycol, polyvinyl alcohol, red iron oxide, talc, and titanium dioxide.

℞ ONLY

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Distribution of *Positively Aware* is supported in part through an unrestricted grant from GlaxoSmithKline

A model, photograph, or author's HIV status should not be assumed based on their appearance in *Positively Aware*.

You can view these (and other stories from previous issues) online at www.tpan.com and www.positivelyaware.com

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- Rapid HIV Testing
- Yoga, Reiki and Massage
- Needle Exchange Program
- Buddy Program
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- Positively Aware Party at Hydrate
- POWER—Positive Outcomes for Wellness, Education and Recovery
- TEAM (Treatment Education Advocacy Management)
- SMART Sex—Prevention and Outreach Program
- Monthly Educational Forums and Trainings

For detailed descriptions of programs, including dates, times and locations, visit www.tpan.com and click on Client Services, or call (773) 989-9400.

TPAN EVENTS

- Ride for AIDS
  June 7–8, 2008
  visit www.rideforAIDS.org
- Aware Affair Gala
  Saturday, September, 13th, 2008
  visit www.tpan.com
- Other Special Events

For detailed descriptions of these and other TPAN events visit www.tpan.com and click on Events, or call (773) 989-9400.

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EDITOR'S NOTE

Four Minutes to Save the World

When is the last time you heard anything about RED, or bought anything RED? Have you ever bought anything RED? *Should* you buy anything RED?

Recent reports of infection rates among young African American MSM that are spiraling out of control, and increased rates of STIs among young, African American teenage girls, as well as rising HIV infection rates in general, is definitely cause for alarm. It brings into question whether or not we need to rethink and refocus our prevention efforts, as well as the audiences we are targeting.

But where is the sense of urgency? Where are the protests, the call to arms, the sign-ons, and the leadership—both within the HIV community, and on the local, state, and federal level? Have we saturated the market in HIV? Does anybody out there care? Or are we all just too burnt out to even give a damn?

We have an aging group of advocates who yearn for the days when we had staged sit-ins and "die-ins," who wonder what group of individuals is going to step up to the plate when the time finally comes to pass the torch. But the "activist mentality," which served us all too well in the beginning years of the epidemic, for whatever reason, just doesn't seem to wash with today's youth. They simply cannot relate. It's a segment that they view in a documentary downloaded onto their iPod, or read about in a blog on their laptop, but they can't be bothered, they're too busy changing their MySpace page, or text messaging their vote for the next "American Idol." They don't have time to stage a protest—at least not the way that we remember it, anyway. Recent online contributions to the political campaign of a certain presidential hopeful, however, as well as the demographics of that group of contributors, give us *all* reason to hope. We can, and will, come up with new and innovative approaches to end this plague, approaches that will resonate with an entire new generation of advocates—if we *believe* we can.

Today's HIV advocacy community is fractured, splintered, and in dire need of some fresh, new blood. There are many big egos at play here, both in the HIV community as well as the scientific establishment. And that's not necessarily a bad thing, considering what's at stake here. We all want someone out there fighting for us, someone who actually stands a chance of *winning* the fight. It just seems that more and more of us are battling for an ever-shrinking piece of the pie. Most of the advocates and researchers, in fact the vast majority, are truly dedicated to the cause, and are definitely not in it for the fame and fortune (ah, yes, the glamorous life of the HIV advocate, that's a whole other story).

It's a fine line we all walk, those of us in the AIDS "industry" (oh, how I hate that term, but it *is* an industry, whether we like it or not). Just as in our nation's capitol, in the field of HIV/AIDS there are "special interest group lobbyists" (read: Big Pharma) and their public relations firms who continuously clamor for the attention of HIV advocates, doctors, and researchers. But in all fairness, these "lobbyists" have a job to do, and the companies have a product to sell. They have to turn a profit. And if they weren't in the business they're in, many of us wouldn't be alive today.

And believe it or not, and I will probably be taken to task for this, there are a tremendous number of people who work for the HIV pharmaceutical industry who believe in the same cause, and are in it for many of the same reasons—because they want to make a real difference in the lives of people living with HIV. But let's face it, we live in a capitalist society, and the way the free market system in this country works, someone ultimately has to answer to the higher-ups, those whose main concern is turning a profit for their shareholders. We are all, indeed, victims of our own success.

Luckily, we have a diverse and multi-talented group of individuals in this country, those who are truly dedicated to the cause of bringing some of the most important issues to the forefront of our collective, national consciousness. These individuals advocate for those who have no voice, and seek to create and deliver effective prevention messages, to educate, to improve access to health care, to effect change and set new public policy, and to give input on the research and development of vaccines, microbicides, and HIV therapies that are less toxic and easier to take.

But where will the next generation of HIV advocates come from? Where is their voice? What will their rallying cry become? What will be *their* cause? And will we be listening? Are they out there somewhere and we just aren't hearing them, or including them, or inviting them into the process? Are we unwittingly turning them off by our infighting and posturing, our egos? Or are we just not trying hard enough to reach them, looking in the wrong places, or sending the wrong messages? Has HIV become, dare I say it—passé?

Just like Madonna, we need to reinvent ourselves if we are ever going to win the fight against HIV/AIDS. We need to bring sexy back to AIDS, baby. We have to throw common sense out the window and become the fifty-year old mother of two who wears lacy underwear and rolls around on stage in front of millions, while gesturing provocatively to agile, half-naked dancers young enough to be her own children. We have to be willing to change our tactics as often as she changes her hair color. Willing to do what it takes to get noticed, and not afraid to look foolish. If we don't, what we stand to lose is infinitely more important than any special recognition or individual accomplishments we may achieve along the way. We must learn to adapt, or risk becoming inconsequential and obsolete. And our voice will get lost in the crowd.

Take care of yourself, and each other.

Jeff Berry
Editor
publications@tpan.com

Photo © Russell McGonagle

test positive aware NETWORK

POSITIVELY AWARE

MORE THAN JUST ANOTHER BRICK IN "THE WALL"

Want a piece of TPAN?

TPAN is growing and we need your help! Not only are we expanding our variety of programs to include the new POWER (Positive Outcomes for Wellness, Education and Recovery) Program, as well as thinking ahead towards future growth, but we're also expanding our physical space into 5541 N. Broadway. There, we will have room for new staff members, a meeting room large enough for 75 people, modern equipment and facilities that will serve us well for years to come.

But, as you can imagine, all of that costs money. True to our long history of being peer-led, we are creating a grassroots campaign to support this growth. One of the large walls in the new space is made of bricks – we are inviting everyone to buy a brick in the wall at whatever level is right for them. In order to show our gratitude and acknowledge your ownership of TPAN's future, the bricks will bear the names of every contributor who wants their name, or the name of someone they donate in honor or memory of, to appear there. We believe that even the smallest donation deserves to be recognized for helping to make this exciting growth possible.

If you would like to donate, you can do so in several ways:

By mail: Use the form below and send a check or money order to TPAN at 5537 N. Broadway, Chicago, IL 60640.

Online: By credit card, go to www.tpan.com and click on "The Wall"

In person: forms and donation envelopes are available at reception

There are four levels of giving:

Bronze: $5–$99; **Silver:** $100–$249; **Gold:** $250–$499; **Platinum:** $500 and above. And, yes, your donation is tax deductible!

Additionally, there are other opportunities to become a conference or counseling room sponsor starting at $1,500. Contact Ron Schnorbus, Director of Development, at 773-989-9400, ext. 229, for more information.

If you've ever felt that TPAN has helped you or someone you know to live a healthier, more informed, more empowered life, now is your chance to help us to continue to do that for all who enter here. Thanks for being part of TPAN's continued success!

Yes! I want my piece of TPAN!

Name _____

Address _____

Phone _____ Email _____

Is your donation in honor ❍ or in memory ❍ of someone?

How would you like your donation to appear on the "The Wall"? (please print legibly): _____

❍ I prefer to donate anonymously.

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Payment method: ❍ Cash ❍ Check/MO ❍ Credit Card

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READERS FORUM

Clarifications

In the profile of Martell Randolph ("Rare Virus, Rare Strength") which appeared in the March/April issue of *Positively Aware*, Ms. Randolph's first name was spelled incorrectly. In addition, Martell was not officially diagnosed with HIV until 2000, and the status of the gentleman from West Africa that she mentioned dating while living in Europe is unknown. Lastly, Martell is a member of the AIDS Treatment Activists Coalition (ATAC), not the AIDS Clinical Trials Group (ACTG).

In the profile of Tony Mills, M.D. ("Tony Mills, MD.—International Dr. Leather"), the first sentence at the beginning of column two was cut off. It should read, "Mills is open about his own status with his patients and has been since the mid-nineties."

Positively Aware apologizes for the oversights.

It was your love that got me by

I read with great interest the article from Thom Hudson [see Editor's Note: Why We Care, March/April]. Being an HIV counselor for the past 14 years, I was touched by Thom's personal saga. I have lost several friends (clients) over the years I have been doing this work. It is never easy.

People often ask how I can do this work day after day, and I respond, how can I not do it? It has become my life passion. This is not just a job to me, but a way for me to reach out to the HIV community in a positive way, being there when clients feel they have nowhere else to go. In the 32 years I have worked in the field of medicine, I have never held a job as rewarding as this. I use your magazine with my clients and make sure they always have a copy when they leave.

Thanks on behalf of me and my clients for a great magazine, and keep up the great work.

Diane Attanasco, Flemington, New Jersey

Drug Guide kudos

Bravo for your 12th Annual HIV Drug Guide (January/February)! I have been an HIV social worker for four years and found the issue extremely easy to read for myself and my clients. I even gave a copy of it to the physicians in the clinic! Each medication was explained by your staff, Dr. Gallant and Martin Delaney in a way that most people can understand. The general information on each of the drugs is so helpful—I keep it in my top drawer to pull out when I forget the generic name or the dosage of a medication. I loved the medication class color coding, the Drug Interactions Chart, the Side Effects Chart, and especially the "centerfold" Drug Chart. It is the only one I have gotten with all the new medications. Thank you, and keep up the amazing work!

Amy in Michigan, via the Internet

[The following was received via voicemail]: I'm a case manager out in Joliet, and this is just a call to tell you thank you, thank you, thank you, for the great article, the great HIV Drug Guide, and the picture chart. As I was putting it up in my office, I noticed it's horizontal, instead of vertical this year. It's part of my office, and it's a great teaching method for working with clients so they can see the pills they are taking and we can talk about them. I just want you to know that your hard work is appreciated by one, lowly case manager out in Joliet. Keep up the good work, your agency is just a great agency and serves enormous numbers of people…keep up the good work!

Name withheld, Joliet, Illinois

Fighting the numbers

About a year and a half ago, I was working full time and finally decided to pursue my goal of becoming a nurse practitioner. For years I wanted to specialize in working with individuals testing HIV-positive. I wanted to become a specialist in infectious diseases. As I was only a certified nursing assistant, I knew my journey would be a long one with lots of work and dedication to my education. Shortly after starting school, I found a job at a hospital with better hours and better pay, which was perfect with the hours of studying I would have to do to achieve my goal. Not a month after beginning work at the hospital, I started to feel tired, worn out. A pre-employment physical with blood work, required by the hospital, showed low counts of red blood cells, white blood cells, and platelets. I immediately thought that I was anemic, which would explain why I was so tired. After all, I was severely anemic as a young child. It was either that or I had to slow down on work and school.

In any case, the employee health nurse advised me to follow up with my regular doctor. I did. I was sent to a hematologist at the Mayo Clinic. I had every test known to man run on me. Everything from what must have been a gallon of blood drawn to

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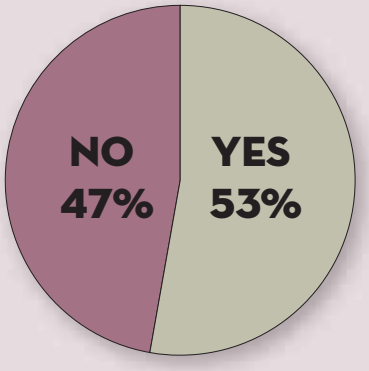
PA ONLINE POLL

JANUARY / FEBRUARY POLL RESULTS

Do you know enough about the current classes of drugs and how they work that you feel comfortable in helping to manage your own care?



MAY / JUNE POLL QUESTION

Where do you find your support and strength?

VOTE AT WWW.TPAN.COM

JANUARY / FEBRUARY POLL COMMENTS

NO 47%:

- There are some holes in my knowledge about the medication choices out there now. I wish my doctor would discuss them with me more.
- I've had good numbers for several years, so I haven't kept up on the new options.

YES 53%:

- It is continually complex balancing treatment options, and I notice that few doctors care to discuss those options with you at length.
- Thanks to TEAM [Treatment Education Advocacy Management] at TPAN, I've learned a lot about the classes of drugs, but it's always good to take a refresher to know more.
- The three new drugs are promising for those they will work for. I am on one of them in a clinical trial and it is working well, though soon I may have to add the other two.
- As the old saying goes, "Knowledge is Power"!

a bone marrow biopsy (ouch!). A couple of weeks later, I followed up with the hematologist for the results. As he read them off, I was feeling relieved yet hopeless as to why I was so tired. The last test was an HIV test. Thinking nothing of it, since I hadn't participated in any high-risk behavior, I said to the doctor that it should be negative. It wasn't. I was stunned, speechless, emotionless. How was I going to tell my partner of three and a half years, who was sitting in the waiting room, that I tested positive? I was in complete shock. The doctor went on about numbers. My T-cell count was 2, my viral load was more than 100,000. What did this mean? Was I about to die? The doctor told me that these numbers classify me as having AIDS. That didn't help. What did help was that he told me that because I hadn't had any of the opportunistic infections, I could change that status to just being HIV-positive. [Editor's note: this is mistaken information. Possibly the doctor said therapy could bring T-cells above the level of an AIDS diagnosis, which is 200.]

That was just what I needed to hear. From that instant, I decided that there is no way in hell I'm giving up without one hell of a fight. So I did. Aggressive therapy with oral meds helped to raise me to 72 T-cells and the viral load came down low. Then I found a good family doctor who was very up-to-date on the treatment of HIV. He immediately recommended Fuzeon. It required giving myself injections, but that didn't bother me. What did bother me was that my insurance denied the $2,500-a-month medication. My doctor, however, had the resources to supply me with the monthly Fuzeon kit. I've been on Fuzeon for just over a year and my T-cells have gone from 74 to over 350 and holding. My doctor wanted to take me off Fuzeon and put me on the oral medication mavaviroc (Selzentry). We couldn't do that, however, because I have an undetectable viral load and you have to have one that's at least 1,000 so that a Trofile test can be done for maraviroc. So for now we're putting that on the back burner.

These days I feel fantastic. I've been doing super in school, holding at least a 3.7 GPA. I expect to be starting the nursing program in just a year (because of a waiting list), and then I'll soon be well on my way to one day finding a cure. I want to tell readers to not let the numbers determine your future; let your heart determine your future. Where there's a glimmer of hope, that is the doorway giving you permission to fight like hell and not give in to this disease. Thanks for being there. If it wasn't for the first issue of *Positively Aware* I picked up in the doctor's office, I might not have gotten the extra boost I needed at times. I hope to someday read about new breakthroughs in HIV in *Positively Aware*.

Name withheld, Arizona

NEWS BRIEFS

by Enid Vázquez

New Prezista pill

Good news—the new Prezista (darunavir) pill has been completed and given approval by the U.S. Food and Drug Administration (FDA). People on Prezista can now take one 600 mg tablet instead of taking two pills at 300 mg each. Either way, 100 mg of Norvir (ritonavir) must be taken with Prezista. The 300 mg tablets will continue to be available. The 600 mg tablets are expected in the pharmacy in mid-May.

New 600 mg tablet of Prezista

New Prezista warning

A warning about liver toxicity has been added to the label of the blockbuster protease inhibitor Prezista. A Dear Healthcare Professional letter was also issued by manufacturer Tibotec Therapeutics with the FDA in March.

The "Warnings" section of the Prezista label now has updated information.

- In studies of Prezista/Norvir, drug-induced hepatitis (acute hepatitis, cytolytic hepatitis) was seen in less than half of one percent of people.
- After becoming commercially available, cases of liver injury, including deaths, have been seen.
- It has not been established that Prezista/Norvir was the cause.
- These cases generally occurred in people who 1) have advanced HIV disease and are taking other medications at the same time; 2) have hepatitis B or C; and/or 3) develop immune reconstitution inflammatory syndrome (IRIS).
- Liver function should be measured before starting Prezista/Norvir and increased monitoring should be considered for people with underlying chronic hepatitis, cirrhosis, or elevated levels of AST/ALT (lab measurements of liver function), especially during the first several months of therapy.
- No dose adjustment is required for people with mild or moderate liver impairment, but in people with severe hepatic impairment, Prezista/Norvir is not recommended.
- The incidence of adverse events or lab abnormalities was not greater in people with hepatitis B or C, except for increased hepatic enzymes (AST/ALT).
- Interruption or stopping therapy must be considered if an individual develops signs of new or worsening liver dysfunction, including medically significant elevations of liver enzymes and symptoms such as fatigue, anorexia (loss of appetite), nausea, jaundice (yellowing of the eyes and skin), dark urine, and tenderness or enlargement of the liver.

Prezista must be taken with a small booster dose of another protease inhibitor, Norvir, which is known to be liver toxic.

U.S. treatment guidelines updated

In January, the U.S. Department of Health and Human Services made changes to its HIV treatment guidelines. Added to the "preferred list" of medications to use in people taking HIV therapy for the first time was Invirase along with a small booster dose of Norvir, under the protease inhibitor drug class. Under the nucleoside analog drug class, Epzicom (a combination of Ziagen and Epivir) was moved up from the "alternative" list to the "preferred" one, if the individual first tests negative on HLA-B*5701, an inexpensive genetic test that only looks for whether or not a person is at risk of experiencing a hypersensitivity reaction to Ziagen. Also in that drug class, Combivir (a combination of zidovudine and Epivir) was moved down from the preferred list to the alternative list. In essence, Combivir was being traded for Epzicom, now that the safety of Epzicom is virtually assured with the proven effectiveness of the HLA test last year. See also below.

Invirase *Norvir* *Combivir*

ACTG 5202: Epzicom vs. Truvada

The HIV meds Epzicom and Truvada are head-to-head competitors. Either one or the other, but not both, may be included in an HIV drug regimen. So the question for these two powerful drugs has been: is one better than the other?

In the sometimes rollercoaster world of HIV treatment, Epzicom was recently up and then rapidly down. First there was the good news that Epzicom had been added to the "preferred list" of U.S. guidelines at the end of January (see above), followed the next week by the negative news that Ziagen, one of the drugs contained in Epzicom, had been associated with heart complications (see page 27). A week later, there was more bad news.

A large, independent study found that in a subgroup of participants, people on Epzicom were not doing as well as those on Truvada. Although both groups did very well overall, the difference was statistically significant.

ACTG 5202, conducted by the U.S. AIDS Clinical Trials Group, compares Sustiva to Reyataz, taken with either Epzicom or Truvada. Although all groups saw very good results, Epzicom did not

Don't lose yourself to your meds HIV.

Lipoatrophy: unwanted fat loss

Learn the facts that may help keep you looking your best

Q. What is lipoatrophy?

A. Lipoatrophy (lipe-oh-AT-troh-fee) is the loss of fat under the skin. You may not lose much weight, but it may change how you look and feel about yourself.

Q. What are the signs of lipoatrophy?

A. Lipoatrophy can affect the face, arms, and legs. Flat buttocks and veiny legs and arms are common. Women may notice they are losing their "shape." Other signs include sunken cheeks and hollow eyes.

Q. What are some of the common risk factors identified with lipoatrophy?

A. Some of the risk factors that have been associated with lipoatrophy include[1,2]:

- HIV itself
- The number of years on HIV therapy
- HIV meds

Q. What can I do about lipoatrophy?

A. If you have signs of lipoatrophy, or have concerns about getting lipoatrophy, discuss them with your healthcare provider.

For more information, visit **www.MyHIVLife.com**

Learn more at

MyHIVLife.com

References: 1. Lichtenstein KA. Redefining lipodystrophy syndrome: risks and impact on clinical decision-making. *J Acquir Immune Defic Syndr.* 2005;39:395-400. **2.** Behrens G, Schmidt RE. Lipodystrophy syndrome. In: *HIV Medicine.* 14th ed; 2006. Available at: http://www.hivmedicine.com/textbook/ls.htm. Accessed June 19, 2007.

GILEAD

Part of an ongoing series from Gilead

do as well as Truvada in those people who started the study with more than 100,000 viral load.

As a result, the study's Data Safety Monitoring Board (DSMB) recommended that these participants be unblinded (let them know they were being given Epzicom and not Truvada). The study was unblinded for the people who started with more than 100,000 viral load, and participants on Epzicom could switch to Truvada or other medications, if needed, or, if doing well on Epzicom, given the option to switch if they desired.

Epzicom

Truvada

In a conference call with community representatives of ACTG, study researcher Eric Daar, M.D., said it's reassuring that "the overall response rate is really good for all people" and that study participants know their lab numbers so they can see how well they're doing.

The DSMB also saw a quicker time to a Grade 3 (on a scale of one to five) adverse event in the Epzicom group, mostly malaise (generally feeling ill) and laboratory test abnormalities, such as increased blood levels of cholesterol and triglycerides. There were no problems with safety, however. The National Institute of Allergy and Infectious Diseases (NIAID), which funds the ACTG, reported that, "In general, these side effects were obvious to participants or the study physicians and would have been readily managed or treated." The statement also noted that, "All regimens effectively reduced the amount of virus in most participants," but that Epzicom's being less effective was important to consider.

These findings are from a preliminary analysis. The study is ongoing and has more scientific data to uncover.

The ACTG findings came a week after Epzicom's manufacturer, GlaxoSmithKline (GSK), presented 48-week data at CROI (see conference reports elsewhere in this issue) comparing Epzicom to Truvada, also with treatment-naïve individuals. The 96-week HEAT study found non-inferiority of Epzicom to Truvada. ("Non-inferiority" is a statistical standard imposed by the U.S. Food and Drug Administration.) The ACTG study, however, is much larger: nearly 2,000 participants compared to 688 for HEAT.

The company also reported that, "Data from six GSK studies with 2,595 patients show higher viral load reduction (94% and above in patients with viral load 100,000 copies at 24 weeks) than was seen in the ACTG study." Although 24 weeks is early data and the studies are being lumped together without regard for other considerations, the participants in 5202 had not all reached that point.

GSK also pointed to the fact that the study did not require testing for hypersensitivity to the Ziagen medication contained in Epzicom. Malaise is one of the symptoms of this potentially dangerous allergic-like reaction. Moreover, a company representative said that under ACTG 5202's strict intent-to-treat analysis, anyone who was started on Epzicom but switched to Truvada and failed to do well would be counted as a failure for Epzicom.

Regardless of how everything shakes out, not all people can take Truvada, or Viread, one of its components. For example, it is not recommended for people with kidney problems because of its potential for renal toxicity. Further results from 5202 (the next analysis is due in June) are now eagerly awaited. As *Positively Aware* went to press, the DHHS panel recommended no changes to the guidelines at this time (see above).

Lactobacillus for a healthy vagina

It looks like once again, *Lactobacillus* does a vagina good.

Researchers found that when HIV-positive women had increased levels of the naturally occurring vaginal bacteria, their genital HIV decreased, and vice versa. The study, presented at CROI in February looked at naturally occurring levels of hydrogen peroxide-producing (H_2O_2+) *Lactobacillus* in 57 women in Seattle and Rochester, New York.

Women who acquired H_2O_2+ *Lactobacillus* had a drop in genital HIV while those who lost it had an increase (-.7 vs. +.5 log). The changes were statistically significant, although HIV was found in only 17% of samples to begin with.

The research group expected these results. They report in their abstract that, "[H_2O_2+] *Lactobacillus* is a key regulator of the vaginal ecosystem and may decrease HIV-1 replication through direct efforts as well as by suppression of pathogenic bacteria."

HIV-positive women have taken offense at health efforts that seem solely important for lowering their risk of transmission to others. *Positively Aware* asked lead researcher Jane Hitti, M.D., of the University of Washington about this and whether less vaginal viral load was a good thing in itself. Hitti responded, "Yes, absolutely it's a good thing." It helps, for example, in fighting bacterial vaginosis, another sexually transmitted disease. It also did no damage to the other good bacteria found in the vagina.

Chewing infant's food can lead to HIV

Also at CROI, the CDC reported on three cases where HIV-positive women who pre-chewed food for infants transmitted the virus this way. According to a CDC press release, "A thorough investigation of three cases of pediatric HIV infection in two U.S. cities between 1993 and 2004 indicates that pre-masticated (pre-chewed) food can be a source of HIV transmission if infected blood is present in the saliva. Researchers attribute the HIV transmission

in these cases to the children's ingestion of HIV-infected blood—not saliva—present in the pre-masticated food."

The researchers were able to rule out other possible causes of transmission such as breastfeeding, sexual abuse, and needle stick injury, and believe that blood from bleeding gums caused the infections. The blood then entered the child's bloodstream through a cut, sore, or inflammation of the mouth or digestive tract. According to the CDC, these conditions are common during teething and some childhood diseases such as inflamed tonsils. The CDC outlined the three infections as follows:

"Case 1 (Memphis): African-American girl diagnosed in 2004 at the age of 9 months. The infant had previously tested negative for HIV three times (at 41, 60, and 118 days). The mother is HIV-positive and reported providing pre-masticated food to the child, beginning when the girl was 4 months old. The child is currently receiving HIV care.

"Case 2 (Miami): African-American male diagnosed in 1995 at the age of 39 months. The child previously tested negative for HIV twice (at 20 and 21 months). The infant's mother had AIDS and reported providing pre-masticated food to the child, though she could not specify the time frame. The child died of AIDS in 1996.

"Case 3 (Miami): African-American boy diagnosed in 1993 at the age of 15 months. The infant's mother is HIV-negative. However, the child's HIV-positive great-aunt served as a caregiver and provided pre-masticated food to the infant when he was between the ages of 9 and 14 months. The child's mother did not know that the aunt was HIV-positive until the aunt's death due to AIDS in 1993. The boy is currently receiving HIV care.

"In the course of the investigation, researchers found that HIV-infected caregivers in Cases 1 and 3 reported bleeding gums and/or mouth sores during the time that they were providing pre-masticating food for the infants; the details of Case 2's oral health at the time of pre-mastication are unknown. Further genetic analysis of the children's specific HIV strains indicated that the caregivers who pre-masticated the food were the sources of transmission in Cases 1 and 2. Although Case 3's caregiver died before a blood sample could be obtained, there was no match between the caregiver's HIV-infected male partner and the child's HIV strains."

Swiss experts say people with undetectable viral load and no STI cannot transmit HIV during sex

(The following is taken from the National AIDS Map, in London. Visit www.aidsmap.org for the full report.) Swiss HIV experts have produced the first-ever consensus statement to say that HIV-positive individuals on effective antiretroviral therapy and without sexually transmitted infections (STIs) are sexually non-infectious. The statement is published in this week's [January 30, 2008] Bulletin of Swiss Medicine (Bulletin des médecins suisses). The statement also discusses the implications for doctors, HIV-positive people, prevention, and the legal system. The statement, on behalf of the Swiss Federal Commission for HIV/AIDS, was authored by four of Switzerland's foremost HIV experts… . The statement's headline statement says that "after review of the medical literature and extensive discussion," the Swiss Federal Commission for HIV/AIDS resolves that, "An HIV-infected person on antiretroviral therapy with completely suppressed viraemia ("effective ART") is not sexually infectious, i.e. cannot transmit HIV through sexual contact." It goes on to say that this statement is valid as long as:

- the person adheres to antiretroviral therapy, the effects of which must be evaluated regularly by the treating physician, and
- the viral load has been suppressed (less than 40 copies/ml) for at least six months, and
- there are no other sexually transmitted infections.

The article begins by stating that the Commission "realizes that medical and biologic data available today do not permit proof that HIV-infection during effective antiretroviral therapy is impossible, because the non-occurrence of an improbable event cannot be proven. If no transmission events were observed among 100 couples followed for two years, for instance, there might still be some such events if 10,000 couples are followed for 10 years. The situation is analogous to 1986, when the statement 'HIV cannot be transmitted by kissing' was publicized. This statement has not been proven, but after 20 years' experience its accuracy appears highly plausible." [Editor's note: There has been at least one documented U.S. case of HIV transmitted via deep kissing when the infected person had oral disease and blood present in his mouth.]

GET SHARP

The Papilloma Chronicles

A personal perspective on HPV and anal cancer

by Matt Sharp

1981—Los Angeles

The first sign that I was infected with human papilloma virus (HPV). I discovered several little bumps on my anus that turned out to be warts or anal chondyloma caused by HPV, a sexually transmitted infection. I had them removed with acid, which wasn't the most pleasant experience I've had. But then those were the days before HIV, when any "venereal disease" was easily treated and dealt with. It was really no biggie, and the implications of what HPV could do were really not on anybody's radar at the time.

DESPITE THE FACT THAT THERE WERE NO SYMPTOMS AND NO APPARENT PROGRESSION, I REMAINED CONFUSED AND PUZZLED ON HOW TO DEAL WITH MY SITUATION, LIKE THE EARLY DAYS OF HIV.

1988—Oklahoma City

My HIV diagnosis. It was obviously a turbulent time when HIV was hitting the Midwest hard. I was tested for HIV in the only anonymous clinic in OKC. I had no apparent symptoms and there were no further issues with anal warts at that time. But alas, I found out I was HIV-positive. I immediately sprang into action to fight this new and terrible disease by moving to the West coast, the center of the epidemic.

1998—San Francisco

Studying HPV. Ten years after learning my HIV diagnosis I entered a clinical trial studying the (HPV) natural history in gay men. At the time many of my buddies entered the study, wanting to further the research. We also were afraid of anal cancer—which is caused by HPV—and this study offered us examinations and diagnosis, and for the first time a better understanding of what might be happening "down there". My buddies and I had been at death's door with HIV, and now we were willing to be a part of anal cancer research. We knew we were at risk for HPV infection and wanted to be as aggressive as we had been with treating HIV. What we didn't realize is that even in 2008 there would be little medical consensus on diagnosis, monitoring or treatment for anal HPV. I continued to be followed in the study until I left the Bay Area for the Windy City.

2000—Chicago

I came to the Midwest with two diagnoses: AIDS and high grade anal dysplasia. But since leaving the HPV study in San Francisco, I had no concrete plan for follow up for monitoring or treatment. In Chicago my doctors never seemed that concerned, even when I showed them the pathology reports from the study. Despite the fact that there were no symptoms and no apparent progression, I remained confused and puzzled on how to deal with my situation, like the early days of HIV.

2001—San Francisco

Cross country HPV follow-up. I visited the Bay Area, and went back to the UCSF anal dysplasia clinic for monitoring. My HPV had not progressed but there was "concern" from the clinic as to who would follow my HPV progression back in Chicago.

2003-2007—Chicago

The first signs of cancer. I eventually was referred to a colo-rectal surgeon in Chicago for follow up. He was concerned but unsure about my case. We decided to continue monitoring my ever-changing HPV. Eventually in 2007, a biopsy taken during a routine colonoscopy presented me with a new daunting diagnosis—*anal carcinoma in situ*—which is sort of like a pre-cancer. Once again, I was left with the decision as to how to handle my situation. Surgery or chemotherapy? Wait and see? Or just follow-up in three months? No one could agree.

2008—New York City

The big "C"—cancer. Frustrated, I found my way to the East coast where I begged for another opinion from an expert East coast butt doc who specialized in HPV. I had conducted considerable research in finding him. After a dozen biopsies that left my anus a battlefield, I received a full-blown "superficial" anal cancer diagnosis, in only *one* of the 12 biopsies. I knew it wasn't something like pancreas or lung cancer, but the fear was still pervasive. HPV had progressed to cancer despite all my efforts to deal with it for the past 10 years. Now I was faced with chemotherapy and radiation, certainly a big blow.

2008—Chicago

A second opinion. I wasn't sure I needed chemotherapy and radiation since I had very early stage cancer, and a lot of other high grade lesions. Horror stories of being

Photo © Russell McGonagle

hospitalized due to chemo were enough to make me delve deeper into other options. So the next few weeks got even more confusing. I made phone calls, more appointments and had conversations with doctors back at UCSF, in NYC and in Chicago. I joined anal cancer list serves and spoke to several friends I knew who had been through treatment. There seemed to be no consensus on what to do with me. After all the back and forth I found my way to another colorectal surgeon at Northwestern. I finally decided to have the lesion removed through an outpatient surgical intervention that would be a better option than the toxic chemotherapy and radiation. But the surgery was no cakewalk despite the fact that it was a 15-minute procedure. I was sore for weeks.

2008 AND BEYOND

What the future brings. As a "patient" I'm not sure being more aware of HPV has been a good thing, especially a disease where the care is sketchy and treatment indefinite. My own HIV advocacy was a totally different story, as I wouldn't be alive today had it not been for all the HIV drugs that I fought for. But with HPV, while I thought I was being proactive, the field of diagnosing and treating is all rather new. In fact, the researchers doing the HPV study at UCSF, Joel Palefsky and his colleagues, are pioneers in the field. It turns out I actually was lucky that I found out about my anal cancer before it was too late.

Over the years that I have dealt with HPV I learned that there is a lot of professional controversy over the best way to diagnose and treat, much to the detriment of people who don't find out until it's too late, or they have to cope through the confusion with less information than I had. I learned that the doctors doing HPV research appear to be more assertive, for good reasons, and some HIV doctors more passive. I knew through anecdotes from clients that some primary care doctors won't even take a look "down there" because "we don't know what to do with HPV." Or they'll prescribe treatments that are painful and not effective. Clearly, much more research needs to be done in this field. And the doctors need to agree to disagree and develop a standard of care for HPV disease for the sake of the patient.

Bottom line is that no matter what your doctor says, *demand* an anal pap smear. And if they look at you like you told them the world is flat, demand to see someone who *will* check your butt out. And remember, since we all have anuses and most of us are sexually active, both men *and* women should be checked.

Ask the HIV Specialist

Tonia Poteat, AAHIVS

Miss Saigon

I am a 39 year-old male. I recently visited a bar in Vietnam, where I was kissed open-mouth by a commercial sex worker (CSW). I generally have mouth ulcers, and her tongue was in my mouth for about five seconds. There was no sexual activity. I never have had any bleeding gums or dental problems before. Now I have the following symptoms: On the third day, generalized itchy feeling all over my body, and constant irritation of facial skin (my main worry). Diarrhea after the ninth day, lasting just one day. A red rash 5 mm in diameter on my forehead after the 10th day, lasting for 3-4 days.

I have no fever or night sweats, no dry or wet cough, no apparent swollen glands, and no weight loss or visible white spots in my mouth (but I do have red ulcers in my mouth).

Am I at risk for HIV? Should I be tested? Is itchiness a symptom of HIV, as I have read on a North Carolina medical school website?

Signed, Itchy and Worried

Dear I&W:

The U.S. Centers for Disease Control and Prevention (CDC) states that open-mouth kissing is considered a very low-risk activity for the transmission of HIV. HIV is transmitted when infectious fluid such as blood, semen, vaginal secretions or breast milk enters another person's bloodstream, usually through unprotected anal or vaginal intercourse, the sharing of contaminated needles, or when an HIV-positive mother nurses an infant. A mouth ulcer could be an HIV transmission point, but even if the CSW was HIV-positive, it is unlikely she had enough virus in her mouth to transmit HIV. In 25 years of the epidemic, the CDC has found only one case of HIV transmission through blood exposure during open-mouth kissing. (For the CDC's HIV transmission fact sheet, visit http://www.cdc.gov/hiv/resources/factsheets/transmission.htm.)

Currently, CDC recommends routine HIV testing for everyone ages 13-64 years old. The test looks for the presence of antibodies to HIV, not HIV itself, so it will not be positive until enough antibodies are present in the blood. Most people develop enough antibodies within 30 days after infection, and 99% of those infected will have antibodies detected by three months, so it is best to get tested at least three months after your most recent exposure to HIV. (Lindback S, et. al. AIDS, 2000).

Some people who contract HIV experience symptoms within a few weeks of infection. Symptoms include fever, fatigue and often, rash. However, itching is rare and tends to be mild (visit http://patients.uptodate.com/topic.asp?file=hiv_aids/4460). Other common symptoms include headache, swollen lymph nodes, and sore throat, but HIV testing is the only way to know if you have been infected. Visit http://www.thebody.com/content/art5998.html for information on early symptoms of HIV.

Tonia Poteat, AAHIVS

Tonia Poteat, MMSC, PA-C, MPH, AAHIVS, has been providing medical care to people with HIV since 1996. She is a physician assistant at the Grady Infectious Disease Program in Atlanta, Georgia.

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Due to space limitations, not all submitted questions can be answered in this column, but every effort is made to ensure you receive the information you have requested. For more information about AAHIVM, call 202-659-0699 or visit www.aahivm.org.

Photo courtesy of Tonia Poteat

Do you qualify for a research study?

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Antiretroviral Therapy Roundup from CROI

Report on newer drugs in development and some already approved drugs

by Jeff Berry

Editor's Note: For access to webcasts, audio presentations, slides, and abstracts from the conference, visit www.retroconference.org.

Encouraging results were presented at this year's 15th Conference on Retroviruses and Opportunistic Infections (CROI) on many of the newer drugs which have recently been approved in the last year or two, including drugs from new classes. Much of it confirms what we already know about these newer drugs, that they are much more potent, easier to take, with fewer side effects, and they offer hope for many individuals who have never been able to achieve undetectable viral load up until now.

Sharon Walmsley, M.D., Professor of Medicine from the University of Toronto, Canada, gave an excellent oral presentation on Wednesday morning entitled "Management of the Treatment Experienced Patient: The Second Wave of HAART." In her opening remarks she pointed out that "we all know that 60 is the new 40; in HIV, what I hope to convince you of today is that the treatment-experienced patient is the new antiretroviral naïve patient."

By looking at results from recent trials over the last few years, and subdividing the trials and comparing the treatment naïve individuals to those who were treatment-experienced, for those with two or three active drugs, the percentage achieving undetectable viral load was roughly the same.

"We treat the experienced patient now exactly the same way that we treat the naïve patient, and it's funny that it took us this long to learn that."

Photo © Jeff Berry

Vicriviroc, newest CCR5 inhibitor in development

Barry Zingman of Montefiori Medical Center in Bronx, New York presented data on the Phase 2 48-week trial of vicriviroc (VCV) in treatment-experienced adults. VCV is a small-molecule oral CCR5 receptor antagonist whose plasma levels are markedly increased by CYP3A4 inhibitors (requiring Norvir boosting), resulting in prolonged half-life, once-daily dosing without regard to food, and potent activity in ART (antiretroviral therapy)-experienced, CCR5-tropic patients. (See "Continued Challenges for CCR5 inhibitors" below.)

VICTORI-1 was a multinational trial with 37 sites in 12 countries. 116 individuals were randomized to receive either 20 or 30 mg of VCV or a placebo, plus optimized background therapy (OBT). Everyone received a ritonavir-boosted protease inhibitor (PI) in this study.

Key eligibility requirements for this study included R5 tropism at screening, triple-class experience with at least one NNRTI and one PI mutation, and viral load greater than 1,000. Individuals were stratified to greater than or less than 100,000 VL and T-20 (Fuzeon) use. This study was largely enrolled outside of the U.S. and Europe, in an advanced population with CD4 counts of around 200 and, a viral load of 4.5 log, with 30% having over 100,000 viral load. A minority of individuals in the study had some T-20 or Prezista use. Among the three groups, 23%, 25% and 14% were new to T-20, and 31%, 23% and 16% were new to Prezista in the 30 mg, 20 mg and placebo groups respectively. The majority (82-85%) had less than

three active drugs in their OBT. Of 116 randomized participants, 114 received their first dose and are included in intent-to-treat (ITT) analyses. Most patients completed the study. Those who did not finish in the placebo group were mostly due to treatment failure.

There was a substantial reduction in viral load in both VCV 30 and 20 mg compared to placebo (1.77, 1.75 and 0.79 log respectively). In a subgroup that enrolled with viral load greater than 100,000 there was a trend towards improvement in the VCV groups, especially the 30 mg group. Substantially more (60-67%) achieved less than 400 viral load at 48 weeks in both VCV groups compared to placebo (26%), and similar results were seen in those achieving viral load less than 50 (53-56% of those on VCV vs. 14% on placebo) regardless of the number of active drugs in the OBT. As expected, greater CD4 increases were seen in those on vicriviroc (102 and 134 in the 30 and 20 mg groups respectively) than those on placebo (65). There was no significant difference seen in serious and other adverse events for those on vircriviroc or placebo, and no deaths in the study. The primary adverse events were gastrointestinal (GI) and respiratory symptoms (not including respiratory infections).

No seizures or malignancies were reported during the study. Patients were allowed to continue on an open-label continuation phase of VCV after 48 wks. Three months into the continuation phase, one patient developed Hodgkin's lymphoma. It was noted that the patient's CD4s never reached above 100 either during the study or afterwards in the continuation phase.

There were no Grade 3 or 4 elevated ALTs in the VCV groups. There were a few Grade 3 and 4 bilirubin events in the study, but all occurred in those also receiving Reyataz. An analysis of the emergence of dual-mixed/X4 virus during the study noted a few more in the 30 mg group and it was suggested that this be followed in larger studies. After the session during Q&A, Dan Kuritzkes, Associate Professor of Medicine and Microbiology at the University of Colorado Health Sciences Center, pointed out that in earlier studies of VCV there was actually more emergence of DM/X4 in those on lower doses of VCV, and cautioned against drawing any conclusions based on the small numbers in these studies. Schering is moving forward with the 30 mg dose in Phase 3 studies.

Another Schering CCR5 inhibitor in Phase 1

Data was presented on a Phase 1 study of a new CCR5 antagonist, SCH532706 (706). Twelve HIV-1-infected individuals received 10 days of 706 (60 mg) twice daily plus Norvir (100 mg) once a day. After 10 days there was a washout period, where they received no antiretroviral therapy for another 14 days, then started on combination therapy.

The mean reduction of viral load at day 10 was -1.3 log. Interestingly the drug had a post-antibiotic effect—a further reduction in viral load from baseline was seen after individuals stopped taking the drug.

The most common adverse event reported was GI upset in about two-thirds of patients, which could have been related to the Norvir in some of those individuals. One serious adverse event—pericarditis (inflammation of tissue surrounding the heart)—was reported and possibly related, occurring around two weeks after the individual had received the study drug and resolving after four days. No emergence of X4 virus was detected during the study.

The drug's half-life when given with ritonavir is 40 hours, and it has a very slow disassociation from the CCR5 receptor, meaning it may be possible to give this drug once daily.

Once-daily boosted Reyataz more than matches up to Kaletra twice daily in treatment-naive

The CASTLE study is the first large-scale head-to-head study comparing boosted Reyataz to boosted lopinavir (Kaletra) in previ-

"I THINK THE TAKE-HOME MESSAGE IS THAT KALETRA, ONCE FELT TO BE THE BEST, IS NOT AS EFFECTIVE IN PATIENTS WITH ADVANCED DISEASE COMPARED NOW WITH THESE NEWER PROTEASE INHIBITORS—REYATAZ OR PREZISTA."

ously untreated patients. This is an open-label, international, multicenter, randomized 96-week study with 883 participants. Study entry criteria included those with a viral load greater than 5,000 with no CD4 restrictions. One group received 300 mg once-daily Reyataz boosted with 100 mg Norvir (ritonavir), and the other received Kaletra twice daily; both in combination with Truvada once daily.

The study's primary endpoint was met, showing once-daily boosted Reyataz to be non-inferior to twice-daily Kaletra. Similar efficacy was seen in both groups, with 78% in the boosted Reyataz group and 76% in the Kaletra group having an undetectable viral load at 48 weeks.

Similar CD4 increases were also seen between both groups—203 in the boosted Reyataz group vs. 219 in the Kaletra group. To address the issue of response rates in those with advanced disease and low CD4 counts, a *post hoc* analysis was performed to assess response rates according to baseline CD4 count. The analysis showed that those receiving boosted Reyataz had similar response rates across four pre-specified baseline CD4 categories, while a trend towards reduced response rates in those with a lower CD4 count at baseline was seen in the Kaletra group. Also, of the patients who had viral loads greater than 100,000, there was a larger disparity between the two agents, with Reyataz performing better and Kaletra's effect not holding as well for patients with high viral loads, (as with lower CD4 count). "This phenomenon was also seen when Kaletra was studied in a similar population in both the ARTEMIS and TITAN trials, where Kaletra's potency again was not matched by Prezista," commented Dan Berger, M.D., of Northstar Healthcare in Chicago. "I think the take-home message is that Kaletra, once felt to be the best, is not as effective in patients with advanced disease compared now with these newer protease inhibitors—Reyataz or Prezista."

Interestingly only 2% of those on boosted Reyataz and 3% on Kaletra discontinued due to adverse events by week 48, the lowest discontinuation rate of any Kaletra study thus far according to presenter Jean-Michel Molina. 26% and 30% experienced some type of Grade 2-4 adverse events in the Reyataz and Kaletra groups respectively, with jaundice the most common AE in the Reyataz group (4%); nausea (8%) and diarrhea (11%) was the most common AE in the Kaletra group. More individuals had elevations in cholesterol and triglyecerides in the Kaletra group as expected, while elevated levels of bilirubin were seen in those on Reyataz. Of note, the capsule formulation of Kaletra (which is associated with a greater number of side effects) was used in the first 48 weeks of this study, and patients were allowed to switch to the newer formulation at 48 weeks.

Kaletra once daily vs. twice daily

Abbott presented 48 week results of study 703 which showed similar efficacy for Kaletra once daily vs. Kaletra twice daily in combination with Truvada in those new to antiretroviral treatment. Similar virologic suppression was seen regardless of an individual's viral load or baseline CD4 count, with 77% of those on Kaletra once daily and 76% of those on twice daily achieving undetectable (less than 50 copies) at 48 weeks. No protease inhibitor (PI) or Viread-associated mutations were observed in either treatment group.

Isentress at 48 weeks

48-week data from BENCHMRK-1 and BENCHMRK-2, two identical Phase 3 studies of Isentress (raltegravir) in treatment-experienced individuals, were consistent with 24-week data upon which accelerated approval was granted last October. The ongoing studies compare Merck's Isentress 400 mg twice daily in combination with optimized background therapy (OBT) vs. placebo twice daily plus OBT.

"The results show that after 48 weeks, Isentress in combination with other anti-HIV medicines continued to provide significantly greater antiretroviral activity and increases in CD4 cells compared to placebo with other antiretroviral medicines," said David Cooper, M.D., D.Sc., professor of medicine and director of the National Centre in HIV Epidemiology and Clinical Research, University of New South Wales, Sydney, Australia.

In the two identical studies BENCHMRK-1 & BENCHMRK-2, 74 and 71% of individuals reached viral load below 400 copies compared to 36 and 38% of those on placebo, and 65 and 60% achieved viral load below 50 copies compared with 31 and 34% of those on placebo, respectively. CD4 cell counts increased by 120 and 98 for those on Isentress compared to increases of 49 and 40 for those on placebo in the two studies.

Common adverse events in these highly-treatment experienced study groups remained relatively low, with diarrhea, nausea and headache the most common side effects reported at 24 weeks.

Intelence at 48 weeks

48-week data was presented on Intelence (etravirine), a new non-nucleoside reverse transcriptase inhibitor (NNRTI or non-nuke) from Tibotec Therapeutics which was approved in January of this year. The new data showed significantly more treatment-expe-

rienced adults with HIV-1 who had documented drug resistance to NNRTIs and protease inhibitors (PIs) reached undetectable viral load (less than 50) with Intelence plus optimized background therapy (OBT) compared to placebo plus OBT.

In the two ongoing Phase 3 studies, DUET-1 and DUET-2, 60 and 61% of those in the Intelence group were undetectable at 48 weeks compared with 39 and 41% in the placebo group, respectively. Mean CD4 increases were 103 and 94 in the Intelence groups, compared with increases of 74 and 72 in the placebo groups.

The most common reported side effects at 48 weeks were rash, diarrhea, and nausea. Rash was generally mild to moderate and usually resolved within 1-2 weeks on therapy; 2% discontinued taking the drug due to rash.

Long-acting TMC-278

Encouraging results were presented on a small Phase 1 study of TMC-278 LA, a long-acting injectable form of TMC-278 (rilpivarine), the second generation non-nuke currently in development from Tibotec. Single doses gave prolonged exposure to TMC-278 for several months, and were well tolerated. TMC-278 LA was injected both intramuscularly and subcutaneously; injection-site reactions were mild to moderate and more frequent in those receiving subcutaneous injections. No serious adverse events or rash were reported.

48-week results given last year from a Phase 2b study of oral TMC-278 showed a greater than 2.5 log reduction in viral load from baseline in treatment-naïve individuals, almost identical to the Sustiva comparator group. The oral TMC-278 program is ongoing, and Phase 3 studies start soon. Should further studies pan out from the nanoparticle formulation, once-monthly injections of TMC-278 LA could possibly achieve the same results as once-daily oral TMC-278.

New data on Pfizer investigational compounds

Data from Phase 1 studies on PF-232,798, a second generation CCR5 antagonist, suggest it is well tolerated in healthy volunteers with a potential for once-daily administration, and Phase 2 studies should start soon.

UK 453, 061 is a second generation NNRTI shown to be effective against virus resistant to first generation NNRTIs and is now moving into Phase 2 study.

Selzentry at CROI

A presentation was given on a sub-analysis from the 48-week results of the MERIT study, which was conducted in treatment-naïve individuals. It suggested that Selzentry (maraviroc), the first-in-class oral CCR5 inhibitor which was approved last year, may have minimal impact on lipids and is at least lipid neutral compared with Sustiva (efavirenz) in this population.

Continued challenges for CCR5 inhibitors

With Selzentry now approved, and vicriviroc and other CCR5 antagonists in development, there continues to be interest around this new class, especially with the immunological benefits seen with these drugs. However, there are still some stumbling blocks that are inherent with the science and not necessarily the drugs, says Dan Berger, MD, of Northstar Healthcare in Chicago.

HIV uses two different co-receptors to attach to a CD4 cell—CCR5 (R5) or CXCR4 (X4). Some people have HIV which uses R5, while some use X4, and others use both (dual/mixed). A tropism assay is required before starting a CCR5 inhibitor to identify which co-receptor(s) your virus uses. Your HIV must be R5-tropic or you will not benefit from taking the drug (around 50% of those with HIV are R5-tropic, and even less for those with more advanced HIV disease).

With the current tropism assay (the Trofile test by Monogram) some studies have shown that dual/mixed tropism later emerges in approximately 5-10% of those who initially test as R5-tropic. "Additionally," says Berger, "clinicians sometimes consider switching their patients off of Fuzeon or other antivirals to a more patient-friendly medication. However, to consider a CCR5 inhibitor in a patient whose viral load is undetectable, physicians are not able to use the required Trofile since the test requires a viral load of greater than 1,000." Add to that the high cost of the Trofile test, and the use of this drug class continues to remain limited.

Clinicians are awaiting the arrival of the Enhanced Sensitivity Trofile Assay (ESTA) by Monogram, which was reported on at the conference and should be commercially available sometime later this year. However the more sensitive test will probably still be expensive, and this fact coupled with the same viral load restrictions as the current Trofile test will most likely continue to limit the wide use of this drug class, at least for the immediate future.

Special thanks to Dan Berger, MD for his thoughtful review of this article.

Update on Preventing Mother-to-child Transmission

Post-partum therapy for moms and infants, plus drug resistance in offspring

by U.S. Centers for Disease Control and Prevention

Editor's note: The following is a press release from the CDC, with slight changes for writing style.

Two separate clinical studies in Kenya and Malawi investigating the use of antiretroviral drugs (ARVs) to prevent mother-to-child transmission (PMTCT) of HIV through breastfeeding have both shown significant reductions in transmission, paving the way for new prevention approaches in areas where breastfeeding by HIV-positive mothers cannot be avoided. Each study examined a different method of drug delivery: one trial assessed the extended use of ARVs by HIV-positive mothers, and the other investigated the efficacy of ARVs administered to their infants.

Breastfeeding by HIV-positive mothers is a significant source of infection among infants in developing nations—with observed MTCT rates of 25 to 48%. While HIV-positive mothers in the United States and other industrialized countries generally do not breastfeed, in resource-limited settings many HIV-positive mothers have no other option. This is due to a number of factors including the lack of affordable and safe alternate food sources (such as formula and access to clean water), strong cultural traditions of breastfeeding, and reluctance to use formula for fear of being identified as infected with HIV. For HIV-positive mothers who must breastfeed, the World Health Organization (WHO) recommends exclusive breastfeeding for six months, with rapid weaning as soon as an "acceptable, feasible, affordable, sustainable, and safe" replacement feeding option is available, in order to minimize the risk of infection for nursing infants.

Kisumu (Kenya) Breastfeeding Study (KiBS)

Led by CDC's Timothy Thomas, KiBS is a Phase 2b clinical trial that investigated the extended use of ARVs by HIV-positive mothers in reducing MTCT during breastfeeding. All women in the study were given ARVs (AZT/3TC plus either nevirapine [NVP] or nelfinavir [NFV]) from the 34th week of pregnancy through 6 months post-partum (or beyond if clinically indicated). [Editor's note: AZT/3TC is Combivir, nevirapine is Viramune, and nelfinavir is Viracept. Nelfinavir is no longer recommended for pregnant women.] During this 6-month post-partum period, the mothers were advised to exclusively breastfeed their newborns according to WHO guidelines. Newborns in the study were also provided standard single-dose nevirapine (SD-NVP) to help prevent HIV transmission which might have occurred during delivery.

Extended maternal use of ARVs was found to dramatically reduce HIV transmission during the breastfeeding period. Of about 500 births (number=497), only 12 newborns (2.4%) were infected by the end of the first week of life (likely *in utero* or during delivery) and only 15 infants (3.0%) became HIV-positive between 8 days and 12 months of life (via breastfeeding). Researchers found no differences in HIV transmission rates based on the mothers' CD4 counts or on their specific ARV regimen (among mothers with CD4 counts greater than 200, about half of whom were on regimens with NFV rather than NVP).

These low rates of MTCT are roughly comparable to those found in the U.S. and other industrialized countries where breastfeeding is not practiced, indicating that extended use of ARVs by HIV-positive mothers can closely counter the risk of transmission through breastfeeding in resource-limited settings.

Post-Exposure Prophylaxis for Infants (PEPI-Malawi)

PEPI is a Phase 3 trial sponsored by CDC and NIH and conducted in Blantyre, Malawi, examining the efficacy of administering ARVs to uninfected infants who were breastfed by their HIV-positive mothers according to WHO guidelines. Research was led by Taha Taha (Johns Hopkins University), along with Michael Thigpen (CDC) and Lynne Mofenson (NIH).

More than 3,000 infants were included in the study (number=3,016), and were randomly assigned in equal proportions to one of three groups immediately after birth: (1) standard regimen of SD-NVP plus AZT for 1 week (control group, number=1,003); (2) standard regimen plus daily NVP for 14 weeks (ExtNVP, number=1,016), or (3) standard regimen plus both NVP and AZT daily for 14 weeks (ExtNVP/AZT, number=997).

All women participating in the study were referred to existing HIV care and treatment programs operated by the Malawi Ministry of Health so that they could be started on ARVs if necessary. However, the vast majority of mothers in the trial (85%) were never started on ARVs because their CD4 counts were higher than the level at which treatment would be clinically indicated (in other words, CD4 greater than 200). Of the 15% of mothers who did require treatment, 12% initiated an ARV regimen during the study and were represented in equal proportions among the three arms of the study (11.7% in control group, 12.2% in ExtNVP group, and 11.4% in ExtNVP/AZT group). (The remaining 3% of women with CD4 counts equal to or less than 200 were

not started on ARVs due to lack of clinic attendance, loss to follow up, or death.)

By the end of 14 weeks, there were significant differences in HIV infections among the infants (10.0% in control, 3.1% in ExtNVP, and 4.0% in ExtNVP/AZT), which continued over time. By the 9-month endpoint of the trial, 13% of the infants in the control group were infected compared to 7.2% of those in the ExtNVP group and 8.7% in the ExtNVP/AZT group. There were no significant differences in HIV transmission between the ExtNVP and ExtNVP/AZT groups. The trial shows that extended use of ARVs by HIV-exposed infants can substantially reduce HIV transmission during breastfeeding.

Drug resistance as possible key

Both trials demonstrate that ARVs can dramatically reduce MTCT of HIV during breastfeeding—regardless of whether the drugs are provided to HIV-positive mothers (KiBS) or HIV-exposed infants (PEPI). To help determine if one approach might be more beneficial than the other, trial data on potential drug resistance are also being analyzed.

A CDC study of KiBS data (in which mothers were given ARVs) conducted by Clement Zeh and colleagues found that the majority of infants who became infected during the first 6 months of life—the breastfeeding period—developed drug-resistant strains of HIV. Specifically, of the 24 infants in KiBS who became infected by 6 months, two-thirds (67%, number=16) showed genotypic resistance to at least one class of drugs used in the study. Six of 14 babies (43%) whose mothers took the NVP-based regimen developed resistance and all 10 infants whose mothers took the NFV-based regimen developed resistant strains. Researchers believe that sub-therapeutic levels of the ARVs were passed to the infants through breast milk, which contributed to their development of resistance to those drugs.

However, it is important to recognize that the detection of *genotypic* resistance does not necessarily mean that these infants will be unable to be treated successfully with a particular drug. Genotypic resistance refers to the presence of specific mutations, identified through a DNA analysis, that are known to be associated with resistance to particular classes of drugs. However, before *actual* resistance could develop, the infants would first need to be started on a specific treatment regimen. It is premature at this point to know the true impact of the genotypic resistance findings from the KiBS trial, though CDC is continuing to closely monitor the HIV-positive children to evaluate their longer-term health outcomes.

Drug resistance data on the HIV-positive infants from the PEPI trial are not yet available. However, CDC and NIH are working closely with researchers from Johns Hopkins University to collect and analyze that information. Results are anticipated in about a year.

Separately, another CDC-sponsored trial in Malawi (Breastfeeding, Antiretroviral, and Nutrition [BAN] trial) is currently conducting a comparison of ARV use by HIV-positive mothers versus HIV-exposed infants during the 6-month breastfeeding period. Those data are expected to be available next year.

Researchers and public health officials are optimistic that the additional data from all three of these trials will help provide important information on how to optimize PMTCT strategies while reducing the risk for developing drug resistance.

In addition, other potential threats to HIV-exposed infants' health must be considered when assessing optimal PMTCT strategies. For example, at CROI 2007, CDC researchers presented data from three studies showing an elevated risk for severe diarrhea or death among HIV-uninfected infants of HIV-positive mothers who were breastfed according to WHO guidelines. The studies suggested that environmental factors such as inadequate sanitation, unsafe food preparation methods, and lack of clean water contributed to the increased incidence of serious diarrhea.

Translating research into practice

CDC is working with the Ministries of Health in Kenya and Malawi to more fully assess the significance of the trial findings on those nations' PMTCT strategies. In Kenya, where CDC is already coordinating with health officials to make ARVs available for HIV treatment, the agency is now consulting with the nation's Ministry of Health, WHO, and PEPFAR to consider making those same drugs available for PMTCT.

In Malawi, the PEPI trial was designed to complement existing national health policies. For example, newborns in Malawi are typically in care for immunizations through the first 14 weeks of life, and are then seen again at 9 months. In addition, the chairman of Malawi's National AIDS Commission was actively involved in reviewing interim findings from the trial since its inception. CDC and NIH continue to work closely with the Malawi government to help PMTCT of HIV in that country.

As new data become available, CDC will continue to work with policymakers in these and other developing nations, as well as with other international organizations such as WHO, to help identify the most effective approaches for preventing mother-to-child transmission of HIV.

Death of a Vaccine

CROI update on the unexpected failure of the STEP Study

by Enid Vázquez

Late breaker reports at CROI discussed the astonishing failure of the most promising HIV prevention vaccine in development. The analysis presented of what went wrong is still early, and much more work is in progress.

The STEP Study of MRKAd5 (or the Merck vaccine, as it is commonly called) continues, but vaccination was stopped in September 2007 when an early interim analysis found failure to either stop infection or to lower the amount of virus if an individual did become infected, the two primary goals of the study.

One of the lead researchers, Susan Buchbinder, M.D., of the San Francisco Department of Health, said the study then moved rapidly into *post hoc* analysis. She stressed that the vaccine did not cause HIV infection.

Although a third of the participants were women, the multivariate analysis—looking at multiple variables—looked solely at men because there was only one female infection, and that was in the group not given the vaccine.

The STEP Study of the Merck vaccine

Vaccines activate the immune system so that it can provide greater protection against diseases.

But at the first early interim analysis of the STEP Study (in September), its Data Safety Monitoring Board (DSMB) found a higher risk of becoming infected with HIV in one group of vaccinated participants (compared to placebo) and vaccination was stopped.

STEP enrolled 3,000 high-risk individuals around the world, primarily men who have sex with men. Participants were divided by their natural levels of adenovirus-5 (Ad5), a version of the common cold virus that rarely causes serious disease. Participants were separated by four Ad5 levels, from no exposure to the virus detected to three levels of Ad5 antibodies. Participants were then randomized to receive either three doses of the experimental vaccine or a placebo ("fake" or inert vaccine).

Ad5 is a vector in vaccine research—one of the harmless substances used to deliver a vaccine being studied into the human body. The virus was replication-defective (it could not reproduce—or grow—in the body). In this case, the vaccine was carrying synthetic (created in the lab) gag, pol, and nef. These are three of HIV's genes, unable to cause an infection but used to stimulate the immune system to recognize and fight the virus if it ever enters the body.

The vaccine succeeded in doing that—in getting an immune response. But inexplicably, it may also somehow have increased the risk of infection in the highest Ad5 group. This was contrary to the two main goals of the study—to decrease the risk of HIV infection or lower viral load if infected. The study continues.—*Enid Vázquez*

THE BIOLOGICAL MECHANISM FOR THE INCREASED RISK REMAINS A MYSTERY.

Several of the variables were associated with an increased risk of infection; however, when comparing the vaccinated group to the placebo group, only two of them were associated with increased risk. Furthermore, participants had to have both variables for a statistically significant difference. There was no increased risk if the individual had one or the other risk factor.

The two factors were lack of circumcision and having high levels of immunity to adenovirus-5 at the start of the study (see sidebar for details of the trial).

The other variables examined were age (30 or under), race, region (this is an international study in the U.S., the Caribbean, and Brazil), number of male sex partners, unprotected receptive anal sex, unprotected insertive anal sex, substance use, or self-reported sexually transmitted infection. The study continues to look at other variables that may have been associated with increased risk of infection.

The biological mechanism for the increased risk remains a mystery. For more information, see October 1, 2007 Exclusive Online News Briefs at www.positivelyaware.com.

Editor's note: The author is a member of the Community Advisory Board (CAB) of the STEP Study at the University of Illinois at Chicago site.

The Price of Surviving HIV

Aging and complications

by Matt Sharp

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This past January, the *New York Times* published a front page story about the downside of living longer with HIV. Despite the fact that people with HIV are living longer, the story described survival issues and other health complications that are predisposing people who have been able to control their HIV for years. Effective antiretroviral therapy has most certainly extended the lives of people with HIV, but at what cost? Clearly, more research is needed to determine what exactly is going on in the HIV aging population. There is still a lot we do not understand about long-term HIV infection and long term side effects from antiretroviral therapy.

According to the U.S. Centers for Disease Control and Prevention, the number of people living with HIV over 50 has increased 77% from 2001 to 2005, representing more than a quarter of all cases in the U.S. Data from the 33 names-reporting states showed that the number of people with HIV/AIDS over 50 went from 64,445 in 2001 to 115,871 in 2005. The number most certainly is going to rise as more people survive due to the recent advances in antiretroviral treatment. This accumulating data is compelling because it proves that survival is achievable for people with HIV, but again, at what cost?

For the first time at CROI, there was a symposium on aging and AIDS. Several presentations provided a degree of information as to what is happening to people who are living longer and aging with HIV. There were also presentations of how to study and prevent the complications related to aging with HIV disease—not just the complications related to the virus itself. It is also clear that antiretrovirals are having a distinct impact, and that doing without them can cause harm, as was shown with several treatment interruption studies. But at the same time, there was more information about long-term heart, kidney and bone toxicities linked to the drugs.

Aging complications

There were several cohort studies on aging and HIV that were not mentioned in the *New York Times* article, and they looked retrospectively at the underlying causes of complications during long-term survival. There is more evidence that loss of CD4 cells in the gut contribute to immune dysfunction and progression to AIDS (called gut-associated lymphatic tissue or GALT), as well as loss of epithelial tissue in the mucosa, general immune activation and lymphatic fibrosis. There is ongoing chronic inflammation that leads to cancer and long-term antiretroviral therapy that may lead to kidney damage. HDL cholesterol elevations seen in HIV as well as inflammation can lead to cardiovascular problems. Bone density loss (osteopenia), bone loss (osteoporosis), and bone death (osteonecrosis) are related to old age and now are being seen in people with HIV. All of these issues come together like a perfect storm to wreak havoc on survivors.

Ziagen and the heart

Cardiovascular events in HIV are continuing to be a major concern as people are living longer, but thus far have been linked to risk factors such as smoking and diet. One of the hottest news items of the conference was further evidence that long-term antiretroviral therapy may help to cause heart attacks. The D:A:D study (Interna-

tional Data Collection of Adverse Events of Anti-HIV Drugs) is a large, seven-year observational study from 11 cohorts from Europe, Australia, and the U.S. At CROI, a sub-study analysis from D:A:D was important enough that many activists felt it should have been in a late breaker presentation, rather than a less significant poster discussion. It showed that people using Ziagen had a 90% increased risk of having a heart attack, although the overall number of heart attacks was very small. There was also a 49% increased risk with use of Videx but not the other nucleosides studied, such as Retrovir and Zerit, which have been the usual suspects with increased lipid levels and insulin resistance—risk factors associated with heart attacks. The risk was only associated with people currently taking Ziagen and Videx, not with those who had a history of using these medications more than six months, suggesting that it is reversible upon stopping the drugs. One caveat with this study is that those subjects using Ziagen or Videx also had higher rate of cardiovascular risks such as smoking, diabetes, or high blood pressure. This was also not a randomized controlled study, so results should be weighed with that in mind. However, the authors concluded that there was no inherent bias. Medical providers are waiting for more information. HIV specialist Joel Gallant, M.D., from Johns Hopkins University, told TheBody.com, "If there's a risk of a heart attack from the drug [abacavir], it's small in comparison with the risk of smoking cigarettes or sitting on the couch eating potato chips. You have to be realistic and put this all in perspective."

Photo © Jeff Berry

SMART study

On the other hand, the pros of staying on treatment are being proven in SMART sub-studies. The SMART study was a large randomized, controlled treatment interruption study closed in January 2006 because there were more complications and deaths in those discontinuing treatment than those randomized to stay on treatment. 85 out of more than 5,000 people died in the SMART study, which is providing a wealth of data regarding the effectiveness of antiviral therapy and the harms of stopping treatment. At CROI there was information looking at what occurs when people restarted therapy after treatment interruption. Those

who resumed therapy reduced their risk of AIDS-related opportunistic infections by half.

Interestingly, 8% of the deaths in the SMART study were AIDS-related. The rest were due to other complications related to cardiovascular, kidney or liver disease in the discontinuation therapy arm. A SMART sub-study presented at CROI provided insight as to which inflammatory and coagulation markers might be related to cardiovascular deaths. Two markers, IL-6 and D-dimer, linked to inflammation and coagulation may explain the risk of cardiovascular deaths in the treatment interruption arm of the study. (These markers are only measured in research, not in the clinic.) Even those who resumed HIV treatment after stopping it do not respond as well with lower viral loads and increased CD4 cells as those who stayed on treatment. All of this leads doctors to begin considering HIV therapy even earlier, perhaps at 500 CD4 cell count, or certainly remaining on treatment. But when we start considering life-long therapy, the implications of longer-term toxicities still must be taken into consideration. In another treatment interruption study there were increases in these cardio risk markers independent of cardiovascular events.

Bone problems

Bone disorders continue to be a concern for people living longer with HIV. Not only does aging have an effect on our bones, as evidenced by hip fractures seen in the elderly, but HIV and antiretrovirals may also play a role. Several studies at CROI showed more evidence of bone disorders. One study showed over 50% had osteopenia and 13% had osteoporosis. These conditions were not related to antiretroviral therapy, except for Viread, but correlations were seen with low physical activity, alcohol, older age and low CD4 counts. There remains to be conflicting information as to which drugs may cause bone disorders, but it is obvious as more people age with HIV that there will be more problems.

Metabolics

There have been few treatment advances in metabolic complications of HIV related to long-term antiretroviral therapy, but there were some studies looking at the management of metabolic complications, lipodystrophy, or body fat changes presented at CROI. Several treatments such as rosiglitazone, pioglitazone, metformin, fish oil, and fenofibrate have all generated interest over the years to help with the metabolic problems associated with long-term HIV therapy. Unfortunately, all the effects studied of these agents were not clinically relevant and had a minor impact in studies at CROI. Any new treatment breakthroughs for metabolic abnormalities and lipodystrophy remain to be seen.

Summary

Overall, the information is accumulating as HIV gets older and longer studies can confirm suspected causality of complications. One take-home message is to remember that growing older and unhealthy lifestyle choices are major factors in illness and death anyway. Despite HIV, we can make healthier choices and take advantage of our survival in the near and distant future.

Prevention Updates from CROI

Suppression of genital herpes, circumcision, and serosorting as prevention

by Keith R. Green

Suppression of genital herpes may not prevent HIV infection after all

A study presented at CROI 2008 found that suppressing HSV-2 (also known as genital herpes) with a currently available therapy was not effective at preventing HIV seroconversion among participants.

The study enrolled large numbers of heterosexual women from Africa and men who have sex with men (MSM) from the U.S. and Peru (3,277 participants in total), who were all HIV negative but positive for HSV-2. Participants were randomized into two different groups, with one group receiving a standard treatment for HSV-2 (400 mg of acyclovir twice daily) and the other receiving a placebo (or dummy pill), and then followed for 18 months.

Aside from receiving their study drugs during routine monthly visits, participants were given adherence and risk reduction counseling and were tested for HIV on a quarterly basis.

There was no significant difference found in HIV incidence between the two groups, with participants in the acyclovir arm actually experiencing a slightly higher incidence rate than those receiving placebo (75 events versus 64, respectively). Reported and observed adherence between the two groups was relatively high, ruling adherence out as a possible cause for the unexpected outcome.

Overall reduction of genital ulcer disease (GUD) associated with HSV-2 was reduced by 35 percent in the acyclovir arm, leading researchers to conclude that the drug is effective at suppressing HSV-2 but not at preventing HIV in those infected.

Connie Celum M.D., a researcher at the University of Washington who presented the study at CROI, explained that these findings are "surprising, disappointing, and important results for HIV prevention," and that they "underscore why it is important to do clinical trials to move from epidemiological data."

Celum suggested, as a possible interpretation of the data, that perhaps HSV-2 is not the risk factor for HIV that we have come to believe it is. Given the plethora of data to the contrary however, which estimates that 38-69% of new HIV infections in men and 8-49% in women are due to prevalent HSV-2, she contends that this conclusion is highly unlikely.

She goes on to suggest that "there is [also] a possibility that we have underestimated HSV-2 in terms of the frequency of reactivation, based on some recent studies, as well as the potential importance of the genital immune response. [This leads] to the possibility that we need either higher doses [of the drugs that we are currently using to suppress HSV-2], new drugs, or combination therapy."

Circumcision also decreases the risk of HSV-2 infection in men, as well as other STIs in their female partners

Recent studies have proven the effectiveness of circumcision in preventing HIV infection, particularly among heterosexual men in African countries. Building on that knowledge, data was presented at CROI 2008 on a study that was conducted to explore the effect of the procedure on HSV-2 acquisition in heterosexual men and vaginal infections among their female partners.

Nearly 2,800 HSV-2-negative men were randomized into two groups, one group receiving immediate circumcision and the other receiving the procedure later in the study. Both groups were followed for two years.

Subsequently, more than 1,600 of the wives of the participating men were recruited and randomized into two groups, depending on when their husband was circumcised in the trial.

The overall incidence of HSV-2 infection decreased by 25% in men who were circumcised immediately, compared to those whose circumcision was delayed. Moreover, there was a 50% reduction in men who reported consistent condom use.

For the women, there was a significant decrease in reported genital ulcer disease (GUD), and a significant reduction in trichomonas (about 50% for those who were married to men who were circumcised immediately). Significant decreases in bacterial vaginosis were also observed.

Researchers concluded that male circumcision is also effective at preventing infection with HSV-2 in men, and further reduces rates of sexually transmissible infection in their female partners. These effects of circumcision may have an impact on the protective effect of the procedure on HIV acquisition.

Serosorting decreases risk for HIV infection, but not seropositioning

Serosorting and seropositioning have become buzz words in HIV prevention in the U.S., particularly as it relates to men who have sex with men (MSM). With increasing rates of HIV infection among this population, however, the effectiveness of such practices remains questionable.

Looking at data from more than 3,000 participants in the EXPLORE study, a randomized trial of an individual behavioral HIV intervention in HIV-negative men who have sex with men in the U.S., researchers were able to ascertain that a sizable minority of MSM in all demographic categories do in fact engage in these practices.

They found that the most common of the two practices among those surveyed was serosorting, defined in this study as the preferential use of condoms with partners whose HIV status was either positive or unknown. Serosorting was associated with a 12% decrease in risk for HIV seroconversion, even in those reporting 10 or more sex partners.

Seropositioning, however, which is defined as the practice of insertive rather than receptive anal sex with a partner whose HIV status is either positive or unknown (which may or may not include the use of condoms), was less common and significantly less effective. In fact, researchers found no evidence that seropositioning had any effect against HIV acquisition.

A separate poster session at CROI presented data from a study of HIV serosorting practices among HIV-negative gay and bisexual men in the San Francisco Bay area. This study supported the notion that serosorting practices were common among both Bay area residents in general and among circuit party attendees (with more of the circuit party attendee participants reporting that they were more likely to have practiced serosorting than those in the general population).

Serosorting, however, was defined differently in this study than the above one. Participants, who were all HIV-uninfected, were asked if their decision to have sex with a potential partner was impacted by his HIV status. This definition is consistent with the traditional use of the term, which basically means selecting sexual partners of like serostatus.

The take-home message, offered by Susan Philip of the San Francisco Department of Public Health who presented the EXPLORE study data, is to continue to promote condom use among MSM, in support of serosorting as an effective HIV prevention strategy. Philip also pointed out that promoting frequent HIV testing among MSM and ensuring that access to the most advanced testing technology is available is also critical.

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Tesamorelin for Fat Accumulation

52-week effects and safety of tesamorelin (growth hormone releasing factor) in HIV patients with fat accumulation

by Dan Berger, M.D.

Body fat changes (lipodystrophy) are relatively common among HIV patients, especially in those who have been on longer treatment, who are older, and have had fluctuations in weight. Also, there are particular antiviral medications that are associated with these body changes. At CROI, 52 week, long-term safety and efficacy of tesamorelin was reported. Tesamorelin or placebo was given (randomized) to patients with increased abdominal fat—lipodystrophy, daily by subcutaneous injection for 26 weeks. This phase was followed by another 26 weeks by which placebo patients received tesamorelin and the previous tesamorelin-treated individuals were re-randomized to continue for an additional 26 weeks or change to a placebo. At 52 weeks, from the study population of 275 men and 40 women there was a highly significant improvement in patients continuing on the drug, showing loss of 17 and 23% of abdominal fat respectively. Also, observed at 52 weeks was a sustained increase in body mass. Importantly, the drug did not alter glucose (blood sugar) metabolism or contribute to other adverse events, unlike growth hormone (Serostim). An added benefit was a loss of triglycerides (blood fats, associated with increased cardiovascular risk).

Tesamorelin is a growth hormone releasing factor analogue. When tesamorelin is administered, the bio-feedback system of growth hormone release by the pituitary gland is still intact, avoiding excessive growth hormone levels and potential side effects. This distinguishes tesamorelin from Serostim. The reduction in both belly fat and triglycerides, without significantly effecting sugar levels, seen with tesamorelin use has the overall potential of reducing cardiovascular risk to patients with HIV disease (but individuals should also consider smoking cessation), as well as improving and enhancing their quality of life.

Dr. Dan Berger (Medical Director, Northstar Healthcare, Chicago) is an author of the article published in The New England Journal of Medicine *on tesamorelin and an author of the abstract presented at CROI.*

Co-infection at the 2008 Retrovirus Conference

Liver fibrosis, hep c treatment, and the role of ART

by Liz Highleyman

This year's Conference on Retroviruses and Opportunistic Infections (CROI), held February 3-6 in Boston, featured numerous reports on hepatitis C virus (HCV) co-infection in people with HIV.

Liver fibrosis progression

Past research has shown that HIV/HCV co-infected individuals tend to experience more rapid liver disease progression than HIV-negative people with HCV alone, though there is conflicting data about whether this is true for co-infected patients with well-controlled HIV disease and well-preserved immune function. Most presentations at CROI supported faster progression—with the notable exception of the SLAM-C study described below in the treatment section.

THESE FINDINGS ARE A CONCERN GIVEN RECENT OUTBREAKS OF APPARENTLY SEXUALLY TRANSMITTED HCV AMONG MOSTLY HIV-POSITIVE MEN WHO HAVE SEX WITH MEN IN SEVERAL CITIES IN EUROPE AND AUSTRALIA.

Juan Macias and colleagues (Abstract 1055) assessed fibrosis progression in 83 HIV/HCV co-infected patients in Spain who underwent paired liver biopsies separated by at least one year; those with pre-existing cirrhosis were excluded. Most were on HAART and 76% had undetectable HIV viral load. About half received interferon-based therapy, and half of these achieved an end-of-treatment response. Between the two biopsies, 16% experienced fibrosis regression by one or more stages, 43% had no change, and 41% progressed by at least one stage—higher than the rate for HIV-negative hepatitis C patients. Co-infected individuals who responded to anti-HCV treatment, however, had a lower risk of progression.

More disturbing data came from a study (Abstract 1050) suggesting that people who are already HIV-positive when they contract HCV may experience unusually rapid liver disease progression. At last year's CROI, Daniel Fierer and colleagues from New York's Mt. Sinai School of Medicine reported that four out of five HIV-positive men infected with HCV for six months or less already had moderate fibrosis. This year, they presented further data showing that among 11 HIV-positive men with acute hepatitis C who underwent liver biopsies, nine already had stage F2 (moderate) and one had stage F1 (mild) fibrosis, for an average fibrosis progression rate of 4.5 units per year. The researchers concluded that HIV-positive people with acute HCV showed progression rates "far in excess of other settings of HCV infection."

These findings are a concern given recent outbreaks of apparently sexually transmitted HCV among mostly HIV-positive men who have sex with men in several cities in Europe and Australia. British researchers (Abstract 61LB) reported results from a viral genetic analysis showing that the re-appearance of HCV infection observed in several HIV-positive men was due to re-infection—indicating continued unprotected sex—rather than late relapse.

Another research team from Mt. Sinai (Abstract 57) revealed a possible mechanism for accelerated fibrosis in HIV/HCV co-infected individuals, demonstrating in a laboratory study that HIV enters and actively replicates within hepatic stellate cells, a type of support cell in the liver that produces collagen and other scar tissue proteins responsible for fibrosis.

Response to hepatitis C treatment

Along with accelerated liver disease progression, HIV/HCV co-infected people also typically respond less well to treatment with pegylated interferon alpha plus ribavirin. When treatment works, however, it can slow or halt fibrosis progression, according to the Spanish GESIDA 3603 study (Abstract 60). Investigators looked at about 700 co-infected patients with well-controlled HIV disease overall (median CD4 count of 544 cells/mm3). Six months after finishing treatment with pegylated interferon (Pegasys or PegIntron) or the older conventional interferon plus ribavirin, 14% with hard-to-treat HCV genotypes 1 or 4 and 46% with genotypes 2 or 3 achieved sustained virological response (SVR), or continued undetectable HCV viral load. After 20 months of follow-up, sustained responders were about nine times less likely than non-responders

to develop liver cancer, progress to decompensated liver disease, or require a liver transplant.

Two other research teams looked at treatment of acute hepatitis C in HIV-positive individuals. A team of British, French, and German investigators (Abstract 1071) studied HIV-positive men involved in the previously mentioned acute hepatitis C outbreaks. Among 101 men who started treatment with pegylated interferon with or without ribavirin within 6 months after HCV infection, 64% achieved SVR, and response did not differ based on HCV genotype. In a related study, researchers with the Australian Trial in Acute Hepatitis C (Abstract 1070) found that rapid virological response at week 4 predicted which patients would go on to achieve SVR; however, co-infected individuals were slightly less likely to achieve rapid response than those with HCV alone (39% vs. 49%).

Given that many people do not respond to standard combination hepatitis C treatment, researchers have studied whether long-term interferon maintenance monotherapy might reduce the risk of liver complications even without HCV clearance. Kenneth Sherman and colleagues (Abstract 59) presented results from the SLAM-C study (ACTG 5178), which included 329 HIV/HCV co-infected participants with mostly well-controlled HIV disease (median CD4 cell count 498 cells/mm3). Participants first received combination treatment with 180 mcg once-weekly Pegasys plus 1,000–1,200 mg/day ribavirin. The 86 patients (44%) who did not achieve early virological response at 12 weeks were randomly assigned to either continue on Pegasys maintenance monotherapy at the same dose or undergo observation without further treatment for 72 weeks. An interim analysis of paired liver biopsies from 45 participants who completed follow-up showed that there was no significant change in fibrosis in either the Pegasys maintenance arm or the untreated observation arm. But the maintenance arm (which was halted in April 2007 due to lack of efficacy) was unable to demonstrate any benefit because the fibrosis progression rate in the untreated group was so unexpectedly low—in contrast to the aforementioned research indicating that co-infected individuals tend to experience rapid progression.

Role of antiretroviral therapy

Several conference presentations looked at the role of antiretroviral therapy in HIV/HCV co-infected people. Assessing risk factors for fibrosis progression in 323 co-infected Spanish patients, Ana Moreno and colleagues (Abstract 1056) found that neither exposure to non-nucleoside reverse transcriptase inhibitors (NNRTIs) nor to protease inhibitors (PIs) were associated with advanced fibrosis or cirrhosis; however, those who used PIs tended to have a higher fibrosis progression rate.

Other studies suggested that choice of nucleoside reverse transcriptase inhibitors (NRTIs) may influence response to hepatitis C treatment. A retrospective analysis by researchers with the GESIDA 50/06 study (Abstract 1076) showed that patients who used tenofovir (Viread) as part of their HAART regimen were significantly more likely to achieve SVR with pegylated interferon plus ribavirin than those who used AZT (Retrovir, zidovudine), d4T (Zerit), or abacavir (Ziagen). Those who used AZT, by contrast, had a 40% lower sustained response rate, attributable to adverse events such as anemia. Another Spanish study (Abstract 1074) revealed that co-infected patients taking abacavir plus 3TC (Epivir) were less likely to achieve SVR than those using tenofovir plus 3TC or emtricitabine (Emtriva; also in the Truvada and Atripla combination pills), which they suggested may be due to a negative interaction between abacavir and ribavirin.

THOSE WHO USED AZT, BY CONTRAST, HAD A 40% LOWER SUSTAINED RESPONSE RATE, ATTRIBUTABLE TO ADVERSE EVENTS SUCH AS ANEMIA.

Finally, research with the large EuroSIDA study (Abstract 1069) presented encouraging data showing that HCV co-infection does not appear to impair CD4 cell recovery on antiretroviral therapy, which conflicts with some prior studies. Similarly, other researchers (Abstracts 1029, 1030, and 1031) reported that hepatitis B virus co-infection does not have a detrimental effect on virological or immunological response to HAART.

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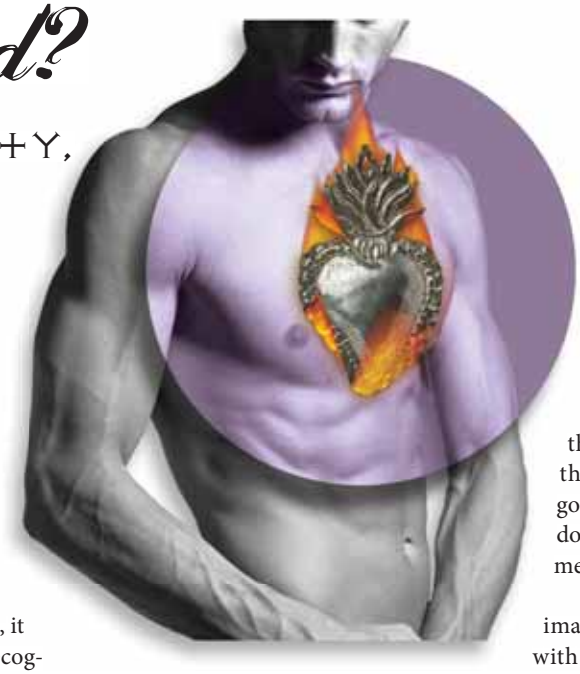
What is Sacred?

SACREDNESS AND SEXUALITY, SIDE BY SIDE

BY TONY HOLLENBACK



What is sacred?

This is a question that I have asked since I was a little boy. Growing up Catholic, the answer usually came from nuns, priests, parents, and other folks who I thought would have the "answer."

The dictionary defines sacred as dedicated or set apart for the service or worship of a deity, or devoted exclusively to one service or use (as of a person or purpose). It is also defined as worthy of religious veneration or highly valued and important.

However sacred was defined, by whoever defined it for me, it was clear that it was something important to acknowledge, recognize, and respect. Although used most often in religious contexts, I found myself with a hunger for the "sacred" in my own life—a sense of connection with something bigger than myself, such as the beauty of nature, the birth of a child, the death of a loved one, or a connection to a partner/beloved.

Coming out as a gay man in my early 20's, and being very new to the whole "gay thing," I was awestruck by how gay people connected with each other. Conversations and dialogue from my earliest experiences with gay men were purely sexual in nature.

"What do you get into?"

"Are you a top or a bottom?"

And, one of my all time favorites, "What *tricks* do you do in bed?"

Naïvely, I replied that I knew magicians who could do things like pull a bunny out of a hat, but I didn't know of any "tricks" I could do in the bedroom.

My "initiation" into the tribe focused on my sexual resume and nothing else. I found this to be a very empty, disappointing, and somewhat limiting way to connect with someone, although it was commonly accepted (so it appeared) by many other gay men at bars, parties, social functions, etc.

Fast forward some time, and I have been a clinical social worker for the past 17 years. I have had the privilege of working with clients of every age (from 2 to 98) and continue to be in "awe" of those who I provide service to.

Working with the gay community has been a gift to me, including my work with HIV impacted youth, couples, and adults. When I meet a new client, the first thing I do is to ask them to tell me their *story*. This goes deeper than doing an "assessment."

I listen to the images they share with me, the memories of how they came to be here and what matters to them the most. When discussing sexuality and sexual relationships, I also hear a similar yearning and longing for meaning and connection that is familiar to me. When I ask folks how they decide who they share their bodies with, or what is "sacred" in their relationships with their partners, I usually get a curious expression and one of two questions: "What do you mean?" or "No one has ever asked me that before."

It's healthy to be selective about who we share our bodies with. One of the most powerful experiences we have as human beings is our ability to connect with each other sexually. It amazes me how little time we spend in our lives learning about the wonders of the human body and the gift of our sexuality, before we are ready to share them.

Our bodies are temples and we can share them with whomever we wish. When we allow ourselves to go deeper than having "sex" with someone, we can explore the "sacred" within a sexual union.

Recently I attended a Sunday morning service at Trinity United Church of Christ with a close friend of mine. During one point in the service, we were asked to share our intentions and prayers with each other. A gentleman sitting next to me engaged me in conversation and asked me, "What's in your heart?"

I found myself smiling, since I can't remember any other gay man asking me that question in a very long time.

My response was, "A hunger for the sacred and for love."

Where is the "sacred" in your life? Imagine sacred sexuality where you can connect with your mind, body, and spirit. What would this look like for you? If you can think even for a moment about this possibility, you can make it happen!

Tony Hollenbach is the Manager of Clinical Social Work/Behavioral Health for Access Community Health Network. He created the Healing Center of Chicago to integrate faith and hope into clinical work. He is available for consultation, workshops, retreats, and "healing" work with children, teens, and adults, and is also experienced in grief/loss and working with the GLBT community. E-mail Tony at soulandspirit@hotmail.com.

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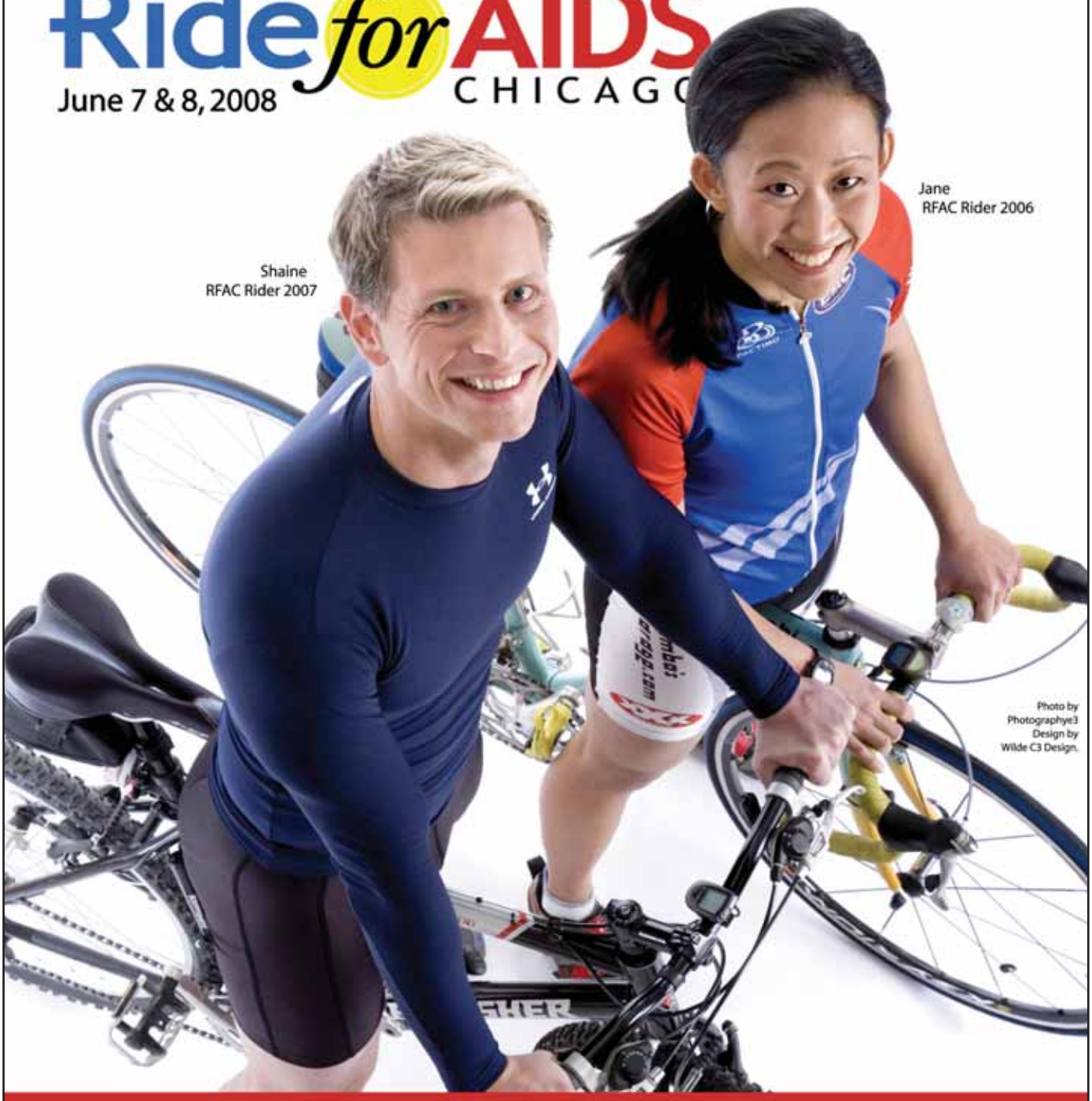

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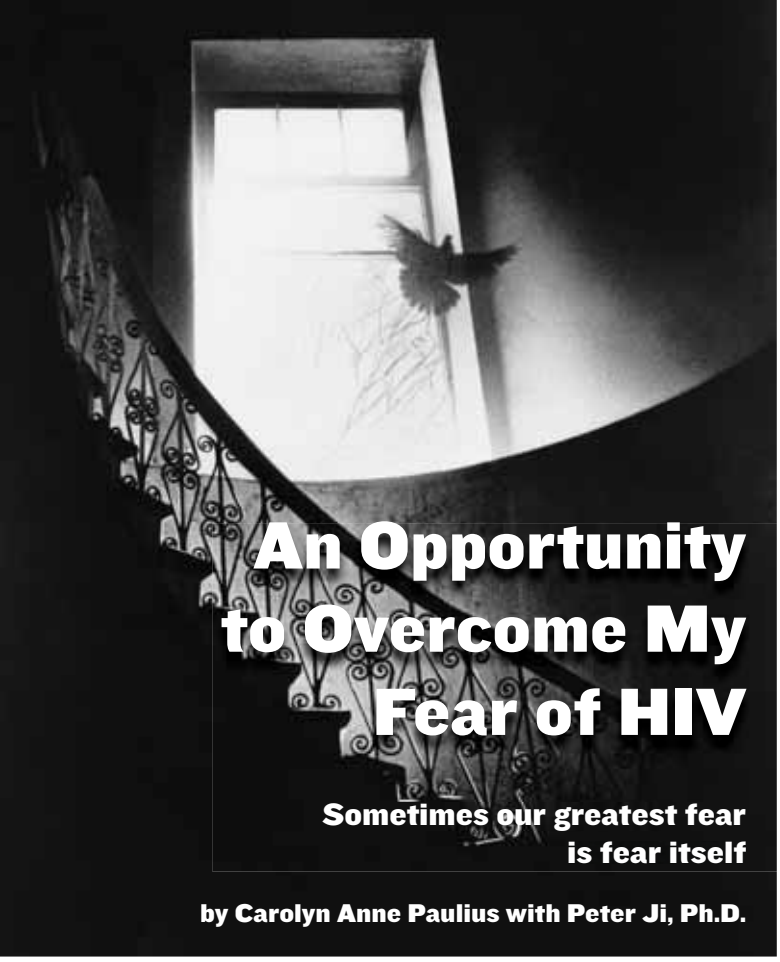

An Opportunity to Overcome My Fear of HIV

Sometimes our greatest fear is fear itself

by Carolyn Anne Paulius with Peter Ji, Ph.D.

While registering for my fall 2007 Honors class at the University of Illinois at Chicago, I stumbled upon a seminar titled "Becoming a Straight Ally to the Lesbian, Gay, Bisexual, and Transgender (LGBT) Community," and knew right away that I should take that class. I realized that becoming an ally was not such an easy process, but I needed to start somewhere.

Throughout the following weeks, I met and listened to various speakers, such as a gay psychologist, a transgender person, a bisexual person, and parents of lesbians and gays. I became well aware of the struggles that some of the members of these communities face and really became motivated to help.

In the class, students are required to participate in an LGBT themed activity. I decided to attend a Test Positive Aware Network (TPAN) meeting. My reason for attending TPAN was quite simple, but difficult to admit. I have always had a fear of making contact with HIV-infected people. I found this out after learning that my friend's partner had the virus. I was always filled with anxiety when I was around him. I knew the facts of how HIV is transmitted but somehow still thought that I could catch it. It was as if HIV was an airborne virus or could be contracted by shaking hands. After spending countless times with this couple and being around someone with HIV, I could not get these worries out of my head. These worries got me depressed because I was concerned that I might have contracted it, and no matter how I tried to rationalize it, the worries persisted.

After a year I finally got the strength to put worry to an end and got tested for HIV. Part of me knew I was not at any serious risk of testing positive, but I still had to do it. My results came back negative, but the experience still taught me a valuable lesson. The counseling showed me that even though I am a Caucasian heterosexual female, I am still at risk of contracting HIV. Because of this, I apply extra precautions in my dating life as well as at my job at a hospital. I still needed to resolve my fears of contracting HIV for my own mental health. I needed the knowledge and confidence to help myself and others who were afraid of acquiring the virus.

TPAN seemed like a safe place where I could go and meet counselors and educators who could provide me with what I needed to overcome my fear. Prior to the meeting, I called TPAN to confirm my visit. Driving there, I started to become anxious the closer I approached.

So many thoughts were rushing through my head. Were they going to think that my motive for wanting to know how infected people deal with HIV was an invasion of privacy? My stressful thinking was interrupted by the staff member who greeted me, shook my hand and then escorted me into a tiny office. I sat next to him and he passed to me some paperwork that I was asked to fill out. The paperwork asked me various questions about my basic information and sexual orientation. Wait… sexual orientation? Did he not know I was straight? He asked me if I needed to get a test done. A test, what was he talking about?

Now, not only was I in doubt about being here, but also extremely nervous. Fortunately he smiled, which assured me that everything was okay. I said that I do not, and know that I do not, have HIV. We both laughed and I started to explain exactly why I came to TPAN. I carried on and on about my fears about contracting HIV that I knew were not true, but my attempts to use my rational thoughts were not enough to resolve my fear.

While we talked, he told me that he has been living with HIV for 20 years. I have to admit my heart wanted to jump out of my chest. My fear was right in front of me! Not only did I shake his hand but I was sitting and breathing the same air as him! And then it hit me—I was confronting my fear. I told him exactly how I was feeling at that point and was soothed by his kind words. He explained that this was a common fear and that it really was not that big of a deal. I smiled, and finally for the first time realized firsthand at a deep emotional level that people with HIV are people too, and that my fear was extremely ridiculous. I had officially confronted my fear!

TPAN accepted me and he shared events that I could attend, and interested me in some volunteer activities. I gave him my email address, and before I knew it my great experience at TPAN was over.

Driving home, I realized what an incredible experience I had. I learned firsthand how it felt to have someone question my sexual orientation, and how when a person has HIV it is like having to "come out" again to society. Not only did my interaction with an HIV-positive staff person enable me to overcome my fear, but he also made me realize that having HIV is not a death sentence. I am ever so grateful for attending TPAN and meeting that man.

Carolyn Paulius is a third year senior at the University of Illinois at Chicago. She is a nursing major and enrolled in the Honors College.

Peter Ji, Ph.D. is a Research Assistant Professor at the Department of Psychology at the University of Illinois at Chicago. He is the leader of the PFLAG (Parents, Families, and Friends of Lesbians and Gays) Chicago Metro chapter, serves on the board of the Hinsdale, IL PFLAG Chapter, and president of the Northern IL Council of PFLAG.

That Hump

Reflections on the rising rates of STIs African American teenage girls

by Keith R. Green

Because I am genuinely passionate about my work, it is sometimes really difficult for me to not take it personally. Hearing that one in two African American teenage girls may be infected with at least one sexually transmissible infection (STI) was one of those times.

The data is from a study that was released at the 2008 National STD Prevention Conference. It was held here in Chicago this year, so I was able to ride the train to and from the sessions listening to Erykah Badu's politically charged new CD, *New Amerykah*, on my iPod.

There's a song on the CD called The Hump. It's sung from the perspective of a drug-addicted single mother of two who is certain that if she could just "get over that hump," things would be better. But you can tell from her words that she knows that even if she is able to miraculously get over the hump that she's faced with today, another one awaits at tomorrow's sunrise.

It's the circle of life that traps, I mean, moves us all, right?

So, though I have no idea what it feels like to be in her shoes, on the train ride home following the first full day of the conference, I could certainly relate to her pain.

Fully aware of the relationship between STIs and HIV (infection with any of the former makes one considerably more susceptible to the latter), what I saw developing was yet another hump in the work that I have signed on to—the work of eradicating HIV from communities of color and other marginalized populations.

Lucky for me, the car that I ended up on for the train ride home was practically empty. Usually, I can hold it until I get home, but the combination of those statistics and the shrill of Badu's voice towards the end of that song brought me to tears right on the train.

My brother's sleepin' on my flo'
A bitch could use a little mo'

If I could get over that hump
Then maybe I will feel better

I cried because I knew that relief for her pain, the other side of the hump, would be a long time coming.

In the five years that I have worked in HIV, the one thing that I know for sure is that it is not a lack of resources necessarily that allows this virus to continue to disproportionately affect African Americans. Rather, it is a lack of collective human will to sincerely address and correct the myriad of social ills that have impacted African Americans since there was such a population.

I recently heard one-time presidential hopeful Mitt Romney give a speech to his campaign supporters. In that speech, he suggested that the one thing that all Americans have in common is the fact that all of our ancestors came to this country in search of better opportunity. I believe he was speaking about immigration and the need for policies that would reward people for doing it the "right way," while severely penalizing those who did not.

Sitting in my living room in complete awe, I nearly jumped through the screen to pull him off that stage by his ear to give him a piece of my mind.

I wanted to tell him that my ancestors, Mr. Romney, did not come to this country in search of anything. In fact, they didn't even come by their own volition. And until you and others like you recognize this, and that this very critical historical fact has given you and others like you an incredible advantage for survival, both economically and emotionally, people like me and the woman in Erykah's song will continue to live our lives struggling to get over "that hump."

I want it to be clear that I am not blaming anybody for the current situation of Black people in America. We have a responsibility to ourselves to relentlessly fight the uphill battle and to not prove ourselves to be the inferior human beings that we were once "scientifically validated" to be. Often times, as Bill Cosby once said, we are not holding up our end of the bargain.

But I also want it to be clear that until we acknowledge and make a sincere effort to correct the psychological effects that the years of oppression of Black people in America has had on *all* of America, but African Americans in particular, none of us will get over the hump.

Taxes for the rich will continue to increase. The gap between the haves and the have nots will continue to widen. Our schools will not be safe. Teenage girls will continue to contract STIs at astronomical rates. And African Americans will always be disproportionately impacted by HIV/AIDS.

But if I could get over that hump, maybe I will feel better.

Photo © Russell McGonagle

The Setpoint Study (Study A5217)

A randomized study comparing immediate treatment vs. treatment as indicated in newly-infected HIV-positive patients

by the A5217 Study Team

Why is this study being done?

This study is being done by the AIDS Clinical Trials Group (ACTG) to learn if treating people during early HIV infection is beneficial. Researchers want to know if taking anti-HIV medication immediately following infection is better than waiting to start medications until the HIV infection has progressed.

Studies have shown that treatment of HIV lowers the chance of death, improves quality of life and lowers the chance of opportunistic infections for HIV-infected patients. However, the use of these medications also has side effects such as raising cholesterol, raising the sugar level in your blood, a possible abnormal fat distribution and possible liver damage. These side effects are always considered when people decide whether or not to begin anti-HIV treatment. Most people infected with HIV wait to start treatment until after they have been infected for a while.

Based on recent studies, there are some data to suggest that treating people early after their infection may be of some benefit. The part of the immune system that fights HIV infection may stay healthier if treatment is begun early. People who are treated early and then stop treatment may be able to control the virus better than if they had not been treated early. Early treatment may also lower the chance of spreading the infection to another person.

However, early treatment also poses risks. People may be exposed to medications and their side effects and inconveniences for a longer period of time. Also, if medications are not taken correctly, resistance to the medications can occur, making it less likely that medications will work as well later in one's life.

We do not know if beginning treatment earlier than normal outweighs the risks. We do not know whether or not treating early HIV infection makes a difference in the long-run in terms of keeping you healthier longer. That is what this trial will try to discover.

What will happen in this study?

During this study, one group of people will immediately begin taking anti-HIV drugs (Truvada once daily plus Kaletra twice daily) for nine months. The second group will start treatment only when their CD4 T-cell count goes low or their viral load stays high, or if they develop certain symptoms related to HIV disease.

At the end of the study, the amount of HIV in persons who received anti-HIV drugs at the beginning of the study and then stopped the anti-HIV drugs will be compared to the amount of HIV in persons who did not start anti-HIV drugs, to see if the persons who received the nine months of treatment have a lower amount of HIV. We do know that persons who have less HIV in their blood tend to do better than persons with higher amounts of HIV.

Some rules

In this study, you cannot choose to start treatment or wait. You will have a 50/50 chance, as if by the toss of a coin, to immediately begin treatment for nine months, or to delay treatment until your HIV disease has progressed (which is when most people start treatment). You must also be willing to stop treatment after nine months if you are in the treatment arm.

It is very important for you to know that during the study, anyone who needs treatment for HIV because of high viral load, immune system decline or symptoms related to HIV infection will be offered treatment.

For more information on the study, please contact Dr. Christine Hogan at 1–414–223–6843, or send her an e-mail at ch358@columbia.edu. Visit www.clinicaltrials.gov for more information, including a list of study sites.

Kaletra tablet (lopinavir/ritonavir)

Truvada tablet (emtricitabine/tenofovir DF)

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