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AIDS ALERT®

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Adolescent sexual trauma screening is urged for HIV-infected women

1 in 2 women with HIV have sexual abuse history

Childhood sexual abuse appears to be a common experience among American women who are infected with HIV, and the trauma resulting from this abuse could have a negative impact on HIV treatment unless it is addressed specifically, according to a recent study of HIV-infected women of various ethnic backgrounds.

"We looked to see what predictors of HIV serostatus were the most salient for women," says **Gail Wyatt**, PhD, associate director of behavior sciences at the University of California-Los Angeles (UCLA) AIDS Institute.

"And a number of studies have reported that ethnic minority women are at greater risk for HIV," Wyatt says. "But when we looked at predictors for risk for HIV-positive women, we looked at demographic statistics, and we found that a history of child sexual abuse was more likely to predict HIV serostatus than ethnicity."

UCLA researchers found that among a community sample of 490 women, those who were HIV-positive were significantly more likely to report having had a pattern of child sexual abuse.[1]

HIV-positive women were recruited from HIV and service agencies, flyers, radio and print advertisements, personal contacts, and a random sample of women who were HIV-negative were recruited with random-digit dialing and 1990 U.S. census track data.[1]

"If you had at least one incident of sexual abuse before age 18, you were twice as likely to be HIV-positive as were women with no history," Wyatt says.

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- U.S. pays closer attention to HIV epidemic in prisons: State bills and new studies demonstrate need for more prevention

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Editorial Questions

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"These findings have implications because we have normally talked about high-risk behavior that is current or in the recent past for a person who is at risk for being infected or who is infected," Wyatt notes.

"This was one of the first studies that documented that not only do current practices have to be discussed," she says, "but also experiences in life that could have happened long ago that might have been equally traumatic, if not more so."

The study found that one in two HIV-positive women had a history of childhood sexual abuse, compared with one in three women among those who were HIV-negative, she says.

This abuse involved rape and other nonconsensual sexual trauma before the age of 18, and the study found that the typical age gap between the victim and perpetrator was five years, Wyatt says.

"This is a common occurrence, and the findings stress the need for HIV providers to ask about past histories of sexual trauma and not to just ask traditional questions about the woman's current partner and the last three months of sexual activity," she explains. "There are many experiences in one's life that can influence what we do today."

The UCLA research highlights a little discussed problem with treating women who are HIV-positive. Unless an HIV clinic provides psychosocial support or unless a clinician builds rapport and specifically asks female patients about sexual abuse in their past, their history of sexual trauma may never be identified.

Often, a woman who has experienced sexual abuse will engage in self-destructive behavior that both contributed to the HIV risk and that causes her to sabotage her antiretroviral therapy treatment.

"This is a pattern of self-destructive behavior of people who do not know how to do self-care," explains **Ellen Kahn**, MSW, director of Lesbian Health Services for the Whitman-Walker Clinic in Washington, DC. Kahn had worked with HIV/AIDS patients for 11 years.

As women who have these histories of sexual abuse begin to receive psychosocial treatment, they begin to value themselves more and are more likely to adhere to their medication regimens and attend support groups, as well as change their self-destructive behaviors of abusing drugs and alcohol, she says.

"Your expectation as a medical provider is that people will understand what it means to be HIV-positive and that they've invested in their treatment and will be cooperative," Kahn says. "But it's few and far between that you can get a patient who will comply."

Other studies also have shown a relationship between sexual abuse and high-risk sexual and drug behavior, says **Denise Paone**, EDD, a researcher who was formerly the associate director of research at the Chemical Dependency Institute of Beth Israel Medical Center in New York City.

"Most studies show there is definitely a high prevalence of sexual abuse histories in childhood among women who use drugs, and that was also true in a study that I conducted," she says. "It's also true that women who have sexual abuse histories often go into sex work, and that puts them at higher sexual risk if they're not using condoms."

When Paone was conducting focus groups a few years ago, she often had women, who were sex workers and injection drug users, in her groups talk about how they were going to get off of their drugs, but whenever they thought about quitting, they'd remember their past trauma.

"They'd recreate that behavior and other high-risk situations," Paone says.

Years of doubt and depression take a toll

It's not that women go directly from childhood sexual abuse to drug use and sexual risk taking, but they may spend years of being depressed, feeling as though they were at fault and are worthless, and this sort of emotional impairment makes them more susceptible to self-medication through drugs and devaluing their bodies and self-worth, she explains.

"I think child sexual abuse as a risk factor for HIV exposure among men and women needs to be looked at a lot more in research," says **Claire Siverson**, LCSW, who is a clinical social worker with the Women's Specialty Program and University of California-San Francisco (UCSF) Medical Center and is a psychotherapist, who works with sexual abuse survivors, in private practice.

"A lot of women with a sexual abuse history have problems with risk taking and inaccurate perceptions of risk, and then as a clinician, I have to gently confront some denial and misperceptions about sexual risk and safety," Siverson says.

Since childhood sexual abuse is so common and may negatively impact HIV treatment, it's probably a good idea to screen new HIV patients,

as well as at-risk populations, for such abuse.

"We screen for this all the time," says **Andy Epstein**, RN, MPH, nurse manager for Cambridge (MA) Hospital's Zinberg Clinic.

"There is a large social-service component to our patient care," he says. "Thirty-four percent of our folks are injection drug users, and we know injection drug use is connected to early abuse."

A majority of women seen by the Zinberg Clinic have had some form of abuse in their past, and many have long histories of abuse, as well as mental health problems, homelessness, and addiction, Epstein says.

"Once it's identified that they have mental health issues, they are seen by a psychiatrist and followed up by a social worker," he says. "We take care of the physical and mental health aspects, and we have a nurse practitioner who specializes in medical adherence."

A woman's history of sexual abuse might be identified at the intake session with a social worker or nurse, or it might take the woman a few visits longer before she is comfortable disclosing her past history, Epstein says.

"We have close ongoing relationships with our patients, so people feel comfortable talking with us about these issues," Epstein adds.

Trust is a crucial component of identifying and treating HIV-infected women who have a history of sexual trauma, Siverson notes.

"If you're someone who has survived sex abuse or any kind of trauma, trust is already shaky because the person who did this against you has betrayed your trust," she says.

"Some women have medicated their pain and abuse with drugs, and I have to find out first if they are using before I can do any work with them and before I am able to demonstrate that I'm trustworthy," she adds. "Once I'm able to establish that trust, the women tend to find it a relief to be able to unload the years of pain that they've stored inside, and their shame and guilt."

Ironically, it might be the very fact of a positive HIV test to wake these women up to how their self-destructive behaviors and their need for good health care, Siverson adds.

One factor that contributes to building that trust is that the clinic's staff reflect the client population with professionals who are of Puerto Rican, Haitian, and Brazilian cultural backgrounds, Epstein says.

"We have a multilingual and multicultural staff," he says. "Social workers do financial counseling and also have a therapeutic relationship with patients and see them in ongoing therapy to work with them through the abuse issues."

Other ways to screen for sexual trauma among HIV-infected women is to include a question about past sexual abuse on an assessment form because some women might be more comfortable with this sort of impersonal reporting method, Siverson says.

Siverson suggests that clinicians also may ask these questions in person, perhaps making a neutral and open-ended statement, such as: "A lot of women with HIV have been hurt in the past, either physically or sexually, and it's very understandable to feel that nobody really cares or that your life is not worth saving when it comes to taking your medications and taking care of your HIV, and I wonder if you've ever felt like that?"

Reference

1. Wyatt GE; Myers HF; Williams JK, et al. Does a history of trauma contribute to HIV risk for women of color? Implications for prevention and policy. *Am J Public Health* 2002; 92(4):660-665. ■

Is atherosclerosis connected to PI therapy?

Study discovers direct toxicity from PIs

In a breakthrough study, researchers at the Columbus (OH) Children's Research Institute Center of Developmental Pharmacology and Toxicology have discovered direct toxicity of protease inhibitors to the cells that line blood vessels.

"Basically, what we were trying to do is something very simple, but it's the first time it's been done," says **John Anthony Bauer**, PhD, associate professor of pediatrics at Ohio State University and an investigator at the Columbus Children's Research Institute, both in Columbus.

"There has been evidence in the last year or two that particularly associated with protease inhibitor [PI] drugs there seems to be a form of aggressive atherosclerosis, artery coronary disease," he says. "These are young patients with cardiovascular disease, and that is abnormal."

HIV investigators had speculated that HIV drugs affected lipid levels, and that was the cause of the problem. The question unanswered in the literature was whether PI drugs have direct action

on endothelial cells or direct toxicity on endothelial cells.

"No one had really asked that question," Bauer says. "What we found was, yeah, these drugs actually had quite striking effects on endothelial cells."

The findings could have an important impact on future therapies, Bauer predicts. "The only fighting chance we have of having good therapy is to find out how these problems go and try to fix them, and this is more information."

Another clinical implication may involve PI treatment of pregnant women because placentas are made up of endothelial cells, which help the placenta maintain its integrity, he says.

Other recent research has shown that while, in general, antiretroviral drugs given to pregnant women do not appear to have a negative impact on their newborns, there is an association between protease inhibitors and very low birthweight babies, according to a National Institutes of Health-sponsored study published in the June 2002 issue of *The New England Journal of Medicine*.

"The endothelial cells are the Teflon coating of blood vessels, a single cell lining of all blood vessels, and they modulate and control the extent of the constriction of blood vessels," he explains. "The second thing it does is prevent stickiness, prevents clotting, and keeps the surface smooth so blood products don't clot and form clots on the inside of the blood vessel."

Researchers have found in recent years that an impairment of that function in the endothelial cells promotes atherosclerosis, and it's now considered an early event of atherosclerosis, Bauer says. "In the last five to 10 years, there has been overwhelming evidence that this matters."

With the knowledge that PIs impair the process of endothelial cells, the next step is to find out what exactly goes wrong, he adds. "We think there are fairly specific events that influence very specific proteins that are important for endothelial survival."

Also, further research could explore whether this effect is specific to PI drugs or whether other antiretroviral drugs also have a negative impact on endothelial cells.

Finally, investigators will want to devise strategies to prevent the problem, and they'll need to explore what factors make a person more susceptible to this damage, Bauer suggests.

"That's an important part of what we're interested in, the genetic aspects that play a role in cardiovascular disease in general," he says. "Are there people particularly vulnerable to this type of toxicity? We're just getting to the point of asking these questions, and it's probably important for understanding cardiovascular disease."

Until more answers are available, the best strategy for clinicians is to continue to monitor patients' cardiovascular status. Since there is no easy marker for endothelial injury, it's important that clinicians know about the side effects of PI drugs, such as increased lipid levels.

Also, clinicians should keep in mind that separate from any antiretroviral-related cardiovascular toxicity, HIV patients appear to have a variety of cardiovascular problems that are unrelated to the drugs, Bauer says.

"How does HIV promote cardiovascular disease itself?" he muses. "It turns out to be an interesting story because it seems that many HIV patients are becoming cardiovascular patients, independent of their treatment." ■

CDC prevention project one of few for young MSM

First outcome data will be out next year

Prevention interventions geared toward young men who have sex with men (MSM) are few and far between, so clinicians and researchers will be watching with interest next year when some outcomes data are released for one of the most comprehensive prevention projects aimed at this population.

The Community Intervention Trial for Youth (CITY), a research project of the Centers for Disease Control and Prevention (CDC) in Atlanta is an intervention that was developed specifically for MSM in the age range of 15 to 25 years.

"What is unique about this study is there have not been that many interventions evaluated in the literature developed specifically for young men who have sex with men," says **Carolyn Guenther-Grey**, MA, health communication specialist with the CDC. Guenther-Grey is the co-project officer for the CITY project.

The research study includes 13 communities. Through randomization, six were assigned to receive the intervention, and six were assigned to the comparison condition. One additional community is serving as a case study. The study communities target various racial and ethnic

populations, Guenther-Grey says.

These populations are divided as follows:

- A CITY intervention being implemented in Seattle and a comparison group in San Diego target Asian and Pacific Islander young MSM.
- Four communities are targeting young Hispanic and Latino MSM. Of these, the intervention communities are Washington Heights and South Bronx in New York City, and Orange County in Los Angeles. The comparison communities are in Jackson Heights in Queens, NY, and the San Gabriel Valley in California.
- Communities targeting young African-American MSM include an intervention community in Birmingham, AL, and a comparison community in Atlanta, as well as a case-study community in Chicago.
- Also, four communities target young MSM of all races and ethnicity. These include intervention communities in Milwaukee, West Hollywood, CA, and Los Angeles, and comparison communities in Detroit and Minneapolis.

The CITY project began in October 1996, with formative research in 1997 and 1998. Investigators collected pre-intervention data from the intervention and comparison communities in the summers of 1999 and 2000, midintervention data in the summer of 2001, and end-of-the-intervention data this year.

"Basically, they do data collection using a time-space sampling design where interviewers go to venues in the study communities where we've determined through formative research that young men can be found," Guenther-Grey says.

These places include coffee houses, bars, clubs, and parks. Interviews are conducted in those places.

"At the end of the interview, individuals in the intervention and comparison communities are given referral information about small group workshops on HIV prevention in the community, lists of HIV prevention and social service providers, and the interviewers answer any questions they have," she adds.

"Currently, there are HIV prevention activities in all of the intervention and comparison communities, so we are evaluating the effectiveness of an additional collection of HIV prevention activities in the intervention communities," Guenther-Grey continues.

"At the end of the study, it is our intention to provide resources to the comparison communities to do additional HIV prevention activities, and if the intervention proves to be effective, we will develop replication materials that will then be given to the comparison communities or to other communities, as well."

The interventions were based on components shown to be effective in previous intervention studies, such as Mpowerment and Popular Opinion Leader, she says.

General overview

Until the project is complete, Guenther-Grey says she is unable to provide much detail about how the interventions work, but she does offer this general overview:

- Each intervention community develops a community health advisor (CHA) network of young MSM and their peers who receive a multisession training about HIV prevention.

These CHA then talk with other people they know in the community, serving as opinion leaders and linking men to services. The community health advisors also become actively involved in other aspects of the intervention through the network.

- Intervention communities have small group workshops based on different topics, including negotiation of condom use and how to use condoms; and on the triggers for unsafe sex, including alcohol and drug use, and how to overcome trigger pressures.

"These are sometimes led by staff and sometimes led by community health advisors," Guenther-Grey says.

- Social events are held with an HIV-prevention component, although the HIV focus might not be the primary reason for the event. "The HIV prevention activity might piggyback on other activities going on in the community, like a gay pride event or a poetry reading cosponsored by another organization," she says.

"At one event, we had a poet reading poems and talking about HIV and HIV prevention as part of the evening event," she adds. "So we're trying to find fun ways to build in HIV prevention and also giving young men a safe place to go to learn about HIV prevention."

- Intervention activities also include the distribution of brochures, posters, and fliers about HIV prevention.

Guenther-Grey says the goal is to complete data collection by September 2002, clean the data, and begin to analyze the results in December with a possible release of study outcomes in the spring of 2003. ■

First comprehensive HIV data several years away

All but three areas are collecting HIV info

Since the Centers for Disease Control and Prevention (CDC) in Atlanta asked that each state and territory add HIV surveillance to their AIDS surveillance, all but three have complied.

"California is supposed to implement HIV surveillance on July 1 this year, and Pennsylvania is still going through the process to implement this year," says **Robert Janssen**, MD, director of the division of HIV/AIDS Prevention — Intervention, Research, and Support.

"And Georgia has not announced any plans to implement surveillance," he adds.

The fact that some of the biggest states have been the longest holdouts on HIV data collecting is one of the reasons the CDC does not anticipate having any additional information about HIV prevalence and incidence for several more years, Janssen says.

In recent CDC surveillance reports, the HIV data are from 25 states that have been collecting the information for quite a while and, therefore, their data are very stable systems, he says.

"So the people being diagnosed in 2001 with HIV are reported in 2001," Janssen explains. "While in new states that are just beginning to conduct HIV surveillance, some states are asking for reports on everyone who is diagnosed with HIV, but not AIDS, so that means in 2001 they might be getting people who were diagnosed with HIV in 1997."

This backlog of HIV-infected people who need to be reported will create less-than-perfect data for at least the first two or three years of a state's new HIV surveillance.

Then there is the problem that while the majority of states and territories were collecting HIV data by Jan. 1, 2001, there were some major gaps. For instance, New York had problems when the reporting began, and, of course, any national HIV surveillance report that is missing data from Pennsylvania and California will be far from complete.

"We can tell whether a system is stable because some problem has occurred, or you will look at the data and they don't make sense," Janssen says.

Meantime, Congress has directed the Department of Health and Human Services to do a review of HIV reporting and the quality of HIV reporting in each state, and that report is due to be released next year, he says.

"We're doing an evaluation in 10 states of HIV reporting, including those where it's reported by name and those where it's reported by coded identifier," Janssen says. "We'll do the evaluation from July through December 2002, and if everything goes OK, we'll have data early next year."

The report will evaluate the quality of the data-collecting systems, the completeness of reporting, the timeliness of reporting, whether people are reported multiple times, and other issues.

"What we're beginning to do in states with HIV reporting is we are beginning to move to a national HIV incidence surveillance, and we have funded five states to pilot the approach, which is the Detuned Assay," he says.

The Detuned Assay, developed in 1998, is an enzyme immunoassay that is less sensitive than the more commonly used EIA and Western Bloc assays.

Since a newly-infected person's antibodies generally peak and stabilize about six months after the infection date, the Detuned Assay only is sensitive after the stabilization.

"So if you have blood from someone that is positive in the other tests but nonreactive on the Detuned Assay, then you know you're within that six-month time period and the person has an early infection," Janssen explains.

"No what we want to do is use that method for when a specimen from an individual goes to the diagnostic lab for the HIV test and the specimen tests positive on the EIA and Western Bloc, we want it tested with the less-sensitive test, so we can identify when they are reporting that this person is in early infection," he says.

"We will identify people who were just infected and use it to make estimates of incidence rates," he says.

In all, 32 health departments will receive funding to conduct this surveillance in Alabama, Michigan, Colorado, New Jersey, and Washington state. ■

NCI investigators find CD4 t-cell protectors

Researcher describes the findings

(Recently released research has shown that a novel human antibody is effective in preventing some strains of HIV from entering CD4 t-cells. The researchers, led by ***Dimiter S. Dimitrov****, PhD, SCD, senior investigator with the National Cancer Institute in Frederick, MD, named the newly identified antibody X5 and found that it reacts strongly against a highly conserved region of the viral glycoprotein gp120.*[1] *The findings were published in the* Proceedings of the National Academy of Sciences *in the May 14, 2002, issue. In this interview, Dimitrov discussed the discovery.)*

AIDS Alert: How did your team's discovery of X5 come about?

Dimitrov: In 1996, immediately after Eduard Berger described in his *Science* article[2] the discovery of the HIV fusion co-factors, I hypothesized in a *Nature Medicine* article that the role of the fusion co-factors is to form complexes with the HIV envelope glycoprotein (ENV) and CD4, i.e., to serve as co-receptors. And I thought that interactions of receptors (CD4 and co-receptors) with the ENV can induce exposure of conserved ENV structure, which otherwise could be partially hidden as part of the HIV strategy to avoid immune responses.

Several years ago my group was able to produce relatively large amounts of complexes between gp120, CD4, and CCR5, and I contacted Dennis Burton, who was interested to screen these complexes against a human phage display library. Maxim Moullard from Burton's laboratory selected X5 by using our antigen two years ago. Then, in my lab and in Burton's lab, we characterized extensively the properties of this antibody Fab and found its potent and broad neutralizing activity against a total of about 30 primary isolates.

AIDS Alert: How does the X5 interrupt HIV progression?

Dimitrov: By inhibition of HIV entry into cells.

AIDS Alert: What type of research needs to be done before it is possible to develop a treatment using X5 or a similar mechanism?

Dimitrov: Tests in animal models, e.g. in monkeys.

AIDS Alert: How would any such future treatment differ from the therapies currently being used to treat HIV patients?

Dimitrov: X5 is an entry inhibitor, while the most widely used inhibitors affect other stages of the HIV life cycle — reverse transcriptase and maturation; recently there are several entry inhibitors, including other human monoclonal antibodies, which are at different stages of clinical testing but not yet for general use.

AIDS Alert: Is there a potential use of this knowledge in creating a vaccine?

Dimitrov: Yes, if we find an antigen able to elicit X5-like antibodies in humans, and we are currently performing such experiments.

References

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2. Feng Y; Broder CC; Kennedy PE; Berger EA. HIV-1 entry cofactor: functional cDNA cloning of a seven-transmembrane, G protein-coupled receptor. *Science* 1996; 272 (5263):872-877. ■

New viral fitness test helps determine regimens

Test is offered along with resistance testing

The enigma of failing antiretroviral regimens and rising viral load in patients who are not progressing to AIDS now has an explanation and a tool that will help clinicians determine which patients will experience this phenomenon.

It appears that at the same time HIV mutates and becomes resistant to antiretrovirals in some patients, the virus also has a reduced ability to replicate.

"This is something completely different from the resistance of the virus," says **Nick Hellmann**, MD, vice president of clinical research for ViroLogic Inc. in South San Francisco, CA.

"We have some data already presented and some upcoming data that suggest when you have a virus that can't replicate as well, it is associated with a better outcome as far as CD4 cell counts are concerned," he says. "The CD4 cell counts don't decline as rapidly as they would if you had a wild-type virus that was not mutated."

This apparent silver lining in drug resistance now can be accurately measured in patients who

require resistance testing. ViroLogic, which has developed the PhenoSense tests for phenotypic resistance testing, now has launched a replication capacity (RC) test that will give clinicians an indication of the viral fitness of drug-resistant HIV.

"Each patient has a unique strain of virus, and wild-type virus means it has no classically defined resistance mutations," Hellmann says. "You find there's a broad range of replication capacities in those viruses, which can go as high as 200% compared with the reference virus we use, and as low as 10% of the reference virus."

ViroLogic's RC test uses 100% as the median of wild type viruses for comparison, he says. Below that the virus has diminished ability to replicate and over that median, the virus can replicate more effectively than wild-type HIV. "When we perform our assay, we developed things called resistance test specters, a molecular copy of HIV that we insert in protease and reverse transcriptase virus. We run a parallel test with the assay, using the patient's virus and then reference viruses, as well, and that gives us a constant point of comparison across viruses."

In ViroLogic's studies, the variability in the reference test has been less than 0.2 logs. All of the RC testing is done within ViroLogic's lab because the process is complex and would not be easy to put into a kit for other labs to reproduce, Hellmann says. "We are considering licensing out the test to other labs, but the decision to do that will rest on the quality of the lab that will perform the testing. We have agreements with all of the major national and regional labs around the country."

Since ViroLogic already provides both phenotypic and genotypic resistance testing, clinicians may send a sample to be simultaneously tested for drug resistance and for replication capacity. There is a two-week turnaround on test results.

This type of information would be especially useful clinically in instances in which a patient has been on a variety of therapies and is failing those regimens, he says. "The physician is in a quandary about what to do with the patient, whether he should evaluate the patient and switch therapy or continue therapy on the patient or stop therapy altogether. That's a scenario where looking at replication capacity or the fitness of the virus may be helpful because if the physician finds out that the patient's virus is unfit and there are no treatment options left to the patient, then the patient might do better to stay on the current therapy and not change."

Recent data show that this strategy would lead to slower disease progression. However, if the RC test shows the opposite, that the virus has a high replication capacity, then the physician would want to switch the patient to some new treatment to make the virus less fit and to slow down the pace of disease progression, Hellmann says.

ViroLogic will continue to improve the RC test, working toward a second-generation fitness test that would be able to identify which drugs in a treatment regimen contribute to poor viral fitness, he says. "Eventually, we would like to get to the point of helping the physician select which is the best drug from a therapy standpoint and from a fitness standpoint, as well," Hellmann says. "At this point in time, we can measure that, but we haven't done enough testing to validate that type of drug-fitness testing, and we need to do more work before we can find the best strategy."

[Editor's note: For more information about replication capacity testing, call (800) Pheno-AID.] ■

FDA Notifications

Watch out for counterfeit Procrit, 2 lot numbers

Ortho Biotech Products, L.P., with the knowledge of the Food & Drug Administration, notified pharmacists, health care providers, and wholesalers/distributors of counterfeit Procrit (epoetin alfa). Vials of Procrit labeled as 40,000 U/mL in four-pack boxes, lot number P002641, expiration date: 9/03, have been found to contain active ingredient that is approximately 20 times lower than would be expected for Procrit in 40,000 U/mL vials. Based on inventory and historic use patterns, it is thought that all existing inventory of authentic lot number P002641 may have been used.

Any product bearing this lot number should be considered suspect and be closely examined. A brief description of the differences between the actual product and the counterfeit, with comparative photographs, is provided in the Ortho Biotech letter.

In addition, lot number P002384, expiration:

03/2003 also has been determined to be counterfeit. Distinctions between this counterfeit lot and authentic Procrit still are being analyzed.

Distinctions may not be the same as those identified in the Dear Healthcare Professional letter dated June 6, 2002. Thus, any product bearing this lot number in particular should be considered suspect.

Procrit is used primarily for the treatment of anemia associated with chemotherapy, chronic renal failure (pre-dialysis), zidovudine treatment in HIV patients, and patients undergoing elective, noncardiac, nonvascular surgery.

For more information, check these web sites:

- www.fda.gov/medwatch/SAFETY/2002/procrit.htm.
- www.fda.gov/medwatch/SAFETY/2002/ProcrittamperDDL.PDF.
- www.fda.gov/medwatch/SAFETY/2002/procrit2.htm. ▼

Product tampering labels Ziagen as Combivir

GlaxoSmithKline has received four reports of suspect bottles containing 60 tablets of Combivir (lamivudine plus zidovudine) that actually contained another medicine, Ziagen (abacavir sulfate) Tablets.

The company has determined that counterfeit labels for Combivir Tablets were placed on two bottles of Ziagen and labels on another two bottles are suspect. Both medicines are used as part of combination regimens to treat HIV infection.

Pharmacists, physicians and patients should immediately examine the contents of each Combivir bottle to confirm they do not contain Ziagen tablets. The two kinds of tablets are easily distinguishable. Combivir is a white capsule-shaped tablet engraved with "GX FC3" on one side; the other side of the tablet is plain. Ziagen is a yellow capsule-shaped tablet engraved with "GX 623" on one face; the other side is plain.

The risk to patients is primarily because about 5% of individuals who receive abacavir sulfate in Ziagen or Trizivir (abacavir sulfate, lamivudine, and zidovudine) tablets have developed a potentially life-threatening hypersensitivity reaction. Symptoms generally resolve after discontinuing the medication, however, patients who have had a hypersensitivity reaction to Ziagen are advised to never take the medication again.

Patients taking Combivir would not have been advised about the hypersensitivity reaction and how to take Ziagen safely because Combivir does not contain abacavir sulfate. Patients who have had a hypersensitivity reaction to abacavir yet take Ziagen or Trizivir again experience more severe symptoms within hours that may include life-threatening hypotension (lowering of the blood pressure) and death. In addition, the replacement of Combivir which contains two antiviral drugs with Ziagen, a single antiviral, may decrease the effectiveness of a patient's treatment regimen.

Read the MedWatch 2002 Safety Information Summary including links to the GlaxoSmithKline press release at:

- www.fda.gov/medwatch/SAFETY/2002/safety02.htm#comb. ▼

Watch for counterfeit lot of Serostim

Serono Inc. has become aware of a counterfeit lot of Serostim [somatropin (rDNA origin) for injection]. The counterfeit material has been packaged to appear as drug product lot number S810-1A1. This is not a legitimate Serostim lot number. Preliminary information indicates that the counterfeit material may have been distributed via the Internet. However, pharmacists should examine Serostim prior to dispensing to ensure that the package does not bear lot number S810-1A1. Patients should check the product in their possession to ensure it does not bear the lot number S810-1A1. Access the MedWatch 2002 safety information summary, including links to the current press release, Dear Doctor Letter, and past MedWatch alerts regarding serostim at:

- www.fda.gov/medwatch/SAFETY/2002/safety02.htm#serost. ▼

FDA warns about counterfeit Epogen

Amgen, in cooperation with the Food and Drug Administration, notified pharmacists and health care providers of counterfeit Epogen (epoetin alfa). Epogen is used to treat the anemia that some patients with HIV/AIDS experience while taking zidovudine, commonly called AZT.

Epogen 40,000 U/mL vials in 10-pack boxes,

lot number P002970, expiration date: 7/03, has been found to contain active ingredient that is approximately 20 times lower than would be expected for Epogen in 40,000 U/mL vials. Pharmacists and health care providers should carefully examine all vials of Epogen before use. A brief description and pictures of the differences between the actual product and the counterfeit are provided.

For more information, read the MedWatch 2002 Safety Summary, including photos and a link to the Dear Healthcare Professional letter, at:

- www.fda.gov/medwatch/SAFETY/2002/safety02.htm#epogen. ■

Program targets HIV+ injection drug users

Study is designed with 10-week intervention

A large intervention program designed specifically for HIV-positive injection drug users (IDUs) may provide HIV programs with a workable way to teach this population about safety measures once the study concludes and outcomes data are available within the next two years.

"There have been no interventions for HIV-positive IDUs, and interventions with [other] seropositive HIV folks are relatively new," says **David Purcell**, JD, PhD, a behavioral scientist with the Centers for Disease Control and Prevention (CDC) in Atlanta. Purcell also is the team leader for the Behavioral Intervention Research Branch of the CDC and is the project officer for the Interventions for HIV-SeroPositive IDUs — Research and Evaluation (INSPIRE) project.

INSPIRE aims to help IDUs take a peer-oriented role through an intervention that might help them change their own behaviors and also encourage other IDUs to change their risk behaviors, Purcell says.

This is done through 10 intervention sessions, including seven individual sessions, two group sessions, and a community outreach session where participants work and participate in a community-based program or with an AIDS service organization, he adds.

The first four sessions of the intervention focus on adherence to HIV medications and access to medical care; the next four sessions address reducing sex and drug-use behaviors that might transmit HIV or lead to infection with sexually-transmitted disease; the ninth session has participants working two to four hours in an agency that serves HIV-positive IDUs, and the 10th session provides a reinforcement of the lessons of intervention, along with a graduation.

"The content is on helping people with primary things that concern HIV-positive IDUs, such as getting into care, utilizing care at the appropriate

CE/CME *questions*

5. A recent study conducted in Los Angeles found that the incidence of nonconsensual sexual trauma/ abuse before age 18 among adult HIV-infected women was which ratio?
   A. one in four
   B. one in three
   C. one in two
   D. one in five

6. A Columbus Children's Research Institute Center study recently discovered that protease inhibitors can lead to an aggressive form of atherosclerosis due to what process?
   A. PIs can cause hyperlipidemia.
   B. PIs have a direct toxicity on endothelial cells.
   C. PIs can cause hypertension.
   D. none of the above

7. The CDC still is several years away from reporting comprehensive HIV surveillance data, partly because three states have been late in beginning HIV surveillance programs. Which three states have been holdouts?
   A. Florida, California, and New York
   B. New Mexico, New Hampshire, and Utah
   C. Ohio, Arizona, and Pennsylvania
   D. California, Pennsylvania, and Georgia

8. A new test, developed by ViroLogic Inc. of South San Francisco, CA, will allow clinicians to find out whether a patient's HIV infection, when drug resistance has occurred, has replication capacity/viral fitness. What does this mean?
   A. This will measure whether an HIV patient's immune system has rebounded against the virus during the use of standard antiretroviral therapy.
   B. This will measure whether the CD4 cell counts don't decline as rapidly as they would if the person was still infected with a wild-type virus that had not mutated, resulting in a slower progression to AIDS.
   C. This will measure whether the mutated virus is fit against protease inhibitor drugs.
   D. none of the above

rate, adhering to medications if they're on them, and working with the doctor to decide if they should be on medications, and reducing risk behavior and drug use," Purcell explains.

Based on previous prevention programs that have proven success, the program is designed to designate participants as peer mentors, although it's an informal label that doesn't mean they have passed any type of special training or certificate course.

This idea came out of research intervention projects that targeted gay and bisexual men by having researchers visit gay bars and ask clients to nominate the five most visible people in the community. These are the popular opinion leaders who are targeted to help change other people's behavior, Purcell says.

"What researchers found was that the peer opinion leaders also changed their own behavior, and that's what we are going for," he explains.

"What we're focusing on is content and activities between each session of talking to peers about their medical care and listening before you talk and not being opinionated about it," Purcell explains.

"If you get folks together to talk about sex and drug risk behavior, that turns off people. We hook people into the program with statements like, 'Even though you're not engaging in risk behavior, you know folks who are.'"

The study includes a control group that receives eight sessions on prevention, led by two group leaders. These sessions include videos and discussions about substance use, disclosure of HIV status to children, prejudice, and other relevant topics.

At baseline, the study enrolled about 1,500 people in four cities, and there will be about 1,000 who will go through the intervention and control group. Each participant is followed at three months, six months, and 12 months.

The five-year intervention study, which began in late 1999, involves Johns Hopkins University in Baltimore; the University of Miami in Miami; the New York Academy of Medicine in New York City; and the University of California-San Francisco.

About 80% of the participants have been African-Americans, Hispanics, and other people of color. The median age is about 40 years, and there are more men than women participants.

One of the drawbacks of the intervention study is that because it involves a lengthy follow-up of participants and is for research purposes, participants are being paid for their time, and this sort of incentive would not be practical if the intervention were used in a nonresearch, community setting.

"For studies we have to do this," Purcell says. "It's expected that you pay people for their time and effort, and so we do, and the people also like the program — they come for the money initially, but then they like it." ■

CE objectives

After reading this issue of *AIDS Alert*, CE participants should be able to:

- identify the particular clinical, legal, or scientific issues related to AIDS patient care;
- describe how those issues affect nurses, physicians, hospitals, clinics, or the health care industry in general;
- cite practical solutions to the problems associated with those issues, based on overall expert guidelines from the Centers for Disease Control and Prevention or other authorities and/or based on independent recommendations from specific clinicians at individual institutions. ■

AIDS GUIDE
For
Health Care Workers®

CDC releases new guidelines for OI exposures

Here's help in knowing what to teach patients

The revised *Guidelines for Preventing Opportunistic Infections Among HIV-Infected Persons-2002* contain several changes from the 1999 guidelines, as well as an appendix with recommendations for helping patients to avoid opportunistic infections (OIs).

Recently published by the Centers for Disease Control and Prevention, here is a summary of what the guidelines contain and what health care workers need to know about OIs and teaching HIV/AIDS patients about limiting exposure to OIs and avoiding infection:

Major changes in OI treatment recommendations:

• The new recommendation is to discontinue primary toxoplasmosis prophylaxis when the CD4 t-cell count has increased to greater than 200 cells for three or more months.

• Prophylaxis for *Pneumocystis carinii* pneumonia (PCP) may be discontinued when the CD4 t-cells have increased to greater than 200 cells for three or more months after initiation of highly active antiretroviral therapy (HAART).

• Prophylaxis for *Mycobacterium avium* complex (MAC) may be discontinued when CD4 t-cells have increased to more than 100 cells for three or more months. Secondary prophylaxis for disseminated MAC can be discontinued after a six month or greater increase in CD4 t-cells count to greater than 100 cells in response to HAART, if the patient has completed 12 months of MAC therapy and has no signs or symptoms of MAC.

• Clinicians may discontinue secondary prophylaxis for toxoplasmosis and cryptococcosis when patients have had a CD4 t-cell count of greater than 200 cells and greater than 100 cells, respectively, in response to HAART, for six months or greater. This is dependent upon their having completed their initial therapy and having demonstrated no signs or symptoms.

• Screen all HIV-infected patients for hepatitis C.

Advice to give HIV-infected patients about preventing OIs:

• Use a latex condom during every act of sexual intercourse to reduce the risk for acquiring cytomegalovirus, herpes simplex virus, and human papillomavirus as well as other sexually transmitted pathogens. Using a condom also will reduce the risk for acquiring human herpes/virus 8, as well as superinfection with a strain of HIV that has become resistant to antiretroviral drugs and will prevent transmission of HIV and other sexually transmitted pathogens to others. Female condoms are recommended to reduce risk strategy.

• Avoid sexual practices that might result in oral exposure to feces (e.g., oral-anal contact) to reduce the risk for intestinal infections (e.g., cryptosporidiosis, shigellosis, campylobacteriosis, amebiasis, giardiasis, and hepatitis A). Even using a latex condom might not be enough to

reduce the risk for acquiring these fecal-orally transmitted pathogens, chiefly those that have low infectious doses. Other risk-reduction strategies include using dental dams or similar barrier methods for oral-anal and oral-genital contact, changing condoms after anal intercourse, wearing latex gloves during digital-anal contact, and washing hands frequently with warm soapy water during and after activities that might bring these body parts in contact with feces.

• All HIV-positive people who are susceptible should be vaccinated for hepatitis B, using the antihepatitis B core antigen-negative. Some, including those who inject drugs, also may need to be vaccinated for hepatitis A.

• Patients who inject drugs and are not ready to change their behavior should be advised to never reuse or share syringes, needles, water, or drug-preparation equipment, or to at least clean equipment with bleach and water.

• Injection-drug using patients also should obtain their syringes from pharmacies or needle-exchange programs, and they should use boiled or sterile water to prepare their drugs, clean the injection site with a new alcohol swab before injection, and safely dispose of syringes after one use.

• HIV-infected patients who work or volunteer in certain settings may place themselves at greater risk for exposure to tuberculosis. These settings include health care facilities, correctional institutions, homeless shelters, among others identified by local health authorities.

• HIV-infected patients who live with children in child care or work in child-care settings are at greater risk of acquiring cytomegalovirus infection, cryptosporidiosis, and other infections (e.g., hepatitis A and giardiasis) from children. This risk can be reduced through vigilant hand washing after contact with diapers, urine, or saliva.

• Another occupational risk factor is veterinary work and employment in pet stores, farms, or slaughterhouses, where HIV-infected persons may be exposed to cryptosporidiosis, toxoplasmosis, salmonellosis, campylobacteriosis, or *Bartonella* infection.

Patients should wash hands after contact with young farm animals and after gardening. Avoid exposure to surface soil dust, chicken coops, bird-roosting sites, old buildings with remodeling or cleaning projects underway, and cave exploring, particularly in areas endemic for histoplasmosis. The same advice regarding exposure to native soil, excavation sites, and dust storms, applies in areas endemic for coccidioidomycosis.

• Be aware of potential problems from pets and avoid contact with animals that have diarrhea. It's also wise to avoid stray animals, dogs less than six months old, and cats less than a year old. Use caution when buying pets to make certain the pet-breeding facility, pet store, or animal shelter is hygienic and sanitary. Also, wash hands after handling pets and before eating and avoid contact with their feces to reduce risk for cryptosporidiosis, salmonellosis, and campylobacteriosis (BIII).

• Cat ownership increases an HIV-infected person's risk for toxoplasmosis and *Bartonella* infection, as well as enteric infections. So it's a good idea to clean litter boxes daily and thoroughly wash hands afterwards. Also, keep cats indoor and do not allow them to hunt or eat raw or undercooked meat. Avoid cat scratches and bites and, if one should occur, wash the site promptly. Do not allow cats to lick open cuts or wounds. Flea control is necessary, as well.

• Contact with reptiles (e.g., snakes, lizards, iguanas, and turtles) as well as chicks and ducklings could place an HIV-infected person at greater risk for salmonellosis. Use gloves when cleaning an aquarium to reduce the risk for infection with *Mycobacterium marinum*. Avoid contact with exotic pets.

• Avoid certain foods, including all that might contain raw eggs, such as nonprocessed hollandaise sauce, Caesar and some other salad dressings, mayonnaise, uncooked cookie and cake batter, and egg nog. Abstain from raw or undercooked poultry, meat, seafood (raw shellfish in particular); and unpasteurized dairy products; unpasteurized fruit juice; and raw seed sprouts (e.g., alfalfa sprouts or mung bean sprouts).

[For more information: Contact the CDC, which is the source of this information, at the Web site: http://www.cdc.gov.] ■