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Latest STD data in United States continues to portend problems with prevention, HIV

Other research notes high STDs among HIV-infected women

The national picture on sexually-transmitted diseases (STDs) shows a positive trend of a decline in new infections of gonorrhea, while the rates of syphilis infections is increasing among men who have sex with men (MSM), and chlamydia remains a major health threat, especially to young women.

Although gonorrhea rates have dropped overall, some surveillance data suggest increasing rates among MSM.

For four years running, from 2000 to 2004, the rate of primary and secondary syphilis in the U.S. has increased, with an 8 percent jump between 2003 and 2004, according to the most recent statistics from the CDC of Atlanta, GA. (See chart on STDs, p. 136).

The syphilis rate among women remained stable, while the rate among men rose 11.9 percent between 2003 and 2004, totaling an 81 percent increase between 2000 and 2004.[1]

Syphilis increases reflect the rising number of cases among men who have sex with men (MSM), including all racial and ethnic groups, says John Douglas, MD, director of the CDC's division of STD prevention.

"Men who have sex with men accounted for 64

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percent of all cases in 2004," Douglas says.

The syphilis rates for women decreased 55 percent from 1999 to 2004, although the rates reached a plateau in 2003 and remained steady in 2004, Douglas says.

"We have good and sound information showing that since the late 1990s, we have seen increases in high-risk behaviors among sexually-active MSM," says Ronald Valdiserri, MD, MPH, acting director for the CDC's National Center for

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Editorial Questions

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HIV, STD, and TB Prevention. Valdiserri and Douglas announced the new STD data at a teleconference on Nov. 8.

"Since the outbreaks of syphilis were observed among MSM, there has been ongoing concern about whether or not that would translate into increased HIV incidence," Valdiserri says.

According to the CDC's latest available data, there are increases in HIV diagnoses in states that provide for HIV diagnoses and, while this isn't direct evidence of an increase in HIV incidence, it is suggestive of a negative trend, Valdiserri says.

"We know that syphilis diagnoses are increasing among that group, and we remain concerned that that might reflect an increase in HIV incidence," Valdiserri says.

"We do have good evidence that men are engaging in higher risk behaviors, and we do know that in several communities—first on the West coast and more recently on the East coast—epidemics of methamphetamine use among MSM are intersecting and exacerbating transmission of syphilis," Valdiserri says.

Two behavioral factors complicate any direct comparisons to rises in HIV rates and rises in syphilis rates among MSM, Valdiserri notes.

To the extent that HIV positive MSM select partners with the same HIV status and engage in unsafe sex, and some studies have suggested this behavioral trend, this could contribute to the spread of syphilis, but not increase transmission of HIV, he says.

"The other dimension of that is we've learned through some of our epidemiological investigations that some of these men are engaging in oral sex, recognizing that it is a much less risky mode of sex in terms of transmitting HIV and not realizing that it's a highly effective way that syphilis can be transmitted," Valdiserri says.

Sexual risk behaviors also appear to be a problem with other at-risk groups.

A new study found high rates of STDs among urban, minority women infected with HIV.

Specifically, the research conducted in Newark, NJ, which has among the highest HIV prevalence rate in the nation, found that 34 percent of the HIV-positive women studied had at least one STD, with the most common being Herpes (22 percent), human papilloma virus (14 percent), and syphilis (6 percent).[2]

"These are not women who found out yesterday they had HIV," says Sally L. Hodder, MD, director of HIV programs in the department of medicine at the New Jersey Medical School, University of Medicine and Dentistry of New Jersey in Newark.

The women included in the study were mostly African American with a mean age of 42.7 years, and they had a mean duration of 8.3 years of knowing their HIV status.[1]

"About 41 percent of the women reported current sexual activity," Hodder notes.

The study demonstrates a high prevalence of STDs in this population, and it raises the question of what should be done, Hodder says.

"We need to ask ourselves, 'Do we really have very effective prevention strategies and education, particularly in this population?'" Hodder says.

"I think behavioral interventions have not always been the panacea that we would like them to be," Hodder says. "I think we really need to be very creative talking to folks and perhaps looking at strategies that are effective."

Also, this urban, poor, and minority population of HIV-infected women had enormous challenges, Hodder says.

"We really need to look at risk behaviors in that group and find something that works for this group, but which may not work for all groups," Hodder says.

The Newark study highlights some of the same concerns found in the CDC's recent STD report.

"I think what this says is STDs really signify risky behaviors, and I think we need to have an aggressive prevention agenda to prevent STDs and also the transmission of HIV," Hodder says.

Even the good news in the CDC's STD report was provided with caution.

Although reported cases of gonorrhea at 113.5 per 100,000 population fell to the lowest levels since 1941, when reporting began, this STD largely is under diagnosed and under reported, according to the CDC report.[1]

Also, there is some evidence that gonorrhea rates are increasing among MSM.

"We do think the gonorrhea rates are likely to be going up among men who have sex with men, although there's so much more gonorrhea nationally than there is syphilis now that we haven't been able to tease that blip out in the national number of cases reported," Douglas says.

A gonorrhea susceptibility project involving 28 STD clinics across the country has pulled data about sexual behavior of participants, and this indicates an increase in gonorrhea among MSM, Douglas adds.

"The proportion of men involved in that study

who acknowledge same sex activity has grown dramatically," Douglas says. "We're talking upwards of 23, 24 percent at this point, whereas in the late '90s we were back in the single digit figures."

The same data indicate a growing number of fluoroquinolone-resistant gonorrhea cases—now at 6.8 percent—and this is a growing problem, Douglas says.

The CDC reports a 23.8 percent drug resistance rate among MSM, which is of particular concern, Douglas says.

Chlamydia continues to be the most widespread and largely under diagnosed of STDs, despite improved screening and testing, CDC officials say.

While the number of reported cases rose between 2003 and 2004, this likely was due to an expansion of screening efforts, Douglas says.

Young women are the hardest hit by the disease, with the greatest number of cases reported in the 15-24 age group of women.[3]

Of the total 929,462 cases, 539,785 or 58 percent are women in the 15-24 age group.[3]

Chlamydia cases and rates have risen steadily for young women in the past five years, and this includes African American, Hispanic, and white women.[3]

Although the increased cases may be attributed to better testing, they do show that there have been no positive trends of decreases in the chlamydia infection rate, Douglas says.

"We think the response to that needs to be multiple: it will include a larger proportion of the women in those age groups being tested and a better job of preventing them from getting re-infected, which is largely a better job of treating their sexual partners," Douglas says. "And once we have done a good job of covering the female population, we believe there will be incremental value in screening, testing, and treating young men as well."

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1. Trends in Reportable Sexually Transmitted Diseases in the United States, 2004; National Surveillance Data for Chlamydia, Gonorrhea, and Syphilis. Centers for Disease Control and Prevention. Nov. 2004.
2. Reilly E, et al. Sexually Transmitted Disease in an Urban Population of HIV Infected Women. Presented at the 43rd Annual Meeting of IDSA, Oct. 6-9, 2004, in San Francisco, CA. Abstract: 855.
3. Sexually Transmitted Disease Surveillance 2004. Centers for Disease Control and Prevention. Sept. 2004;1-184.

CDC reports latest STD data

Chlamydia
Total reported cases:
2003: 877,478
2004: 929,462
Estimated new cases each year: 2.8 million
National rate of reported cases:
2003: 301.7 per 100,000 population
2004: 319.6 per 100,000 population
Increase: 5.9 percent

Gonorrhea
Total reported cases:
2003: 335,104
2004: 330,132
Estimated new cases each year: More than 650,000
National rate of reported cases:
2003: 115.2 per 100,000 population
2004: 113.5 per 100,000 population
Decrease: 1.5 percent

Primary and secondary syphilis
Total reported cases:
2003: 7,177
2004: 7,980
National rate of reported cases:
2003: 2.5 per 100,000 population
2004: 2.7 per 100,000 population
Increase: 8 percent

Source: Trends in reportable sexually transmitted diseases in the United States, 2004. National Surveillance data for chlamydia, gonorrhea, and syphilis. Centers for Disease Control and Prevention, November, 2004.

New research finds possible treatment for latent HIV

Valproic acid used to deplete HIV

Researchers have discovered a possible combination therapy that will help clear HIV from resting CD4 T-cells, which may open the doors to a new approach to eliminating HIV infection.

The recent study shows that highly-active antiretroviral therapy (HAART) with subcuta-

neous enfuvirtide, the fusion inhibitor, plus oral valproic acid accelerated the clearance of HIV from resting T-cells in vivo.[1]

Investigators first found they could recover HIV in the lab from resting T-cells of patients if they were treated with valproic acid, says David Margolis, MD, professor of epidemiology, microbiology, and medicine at the University of North Carolina at Chapel Hill.

"So then we thought if you are maintaining viral suppression with HAART and gave valproic acid over time, by whatever mechanism, we thought the virus would be expressed and, hopefully, that would lead to the disappearance of those latently-infected cells," Margolis explains. "Whether it leads to cell death or virus production in immune-mediated killing, we don't know."

The approach raised a few concerns, including the possibility that if viruses were expressed, they could infect new cells and spread infection, Margolis says.

To prevent this from happening, the treatment was intensified with enfuvirtide (Fuzeon/T-20), he says.

"So, it wasn't a perfect study," Margolis says. "All I can say is from beginning to end with intensified therapy, we had significantly less latently-infected cells than otherwise."

Plus there were only four patients, he notes.

"There was much argument on how many declines and how fast the declines and whether HAART would accelerate the decline, so we turned it into a plus or minus experiment," Margolis explains. "Subjectively, we decided that if we observed more than 50 percent depletion of latent infection and resting cells during the protocol period of 3.5 to four months, then we would call that a significant decline, a plus result."

Three of the four patients had a plus result, and one of the four patients had a 29 percent decline, Margolis says.

"The results were in the right direction for the fourth patient, but not significant by our arbitrary set point," he says. "If you're willing to accept the limited accuracy of our measurements, the very small number of patients and infected cells—it's an unexpectedly large depletion."

The average depletion was 75 percent, he says.

"I'm not giving much credence to the number of 75 percent because it means 25 percent was still there, so it's clearly not a therapeutic success," Margolis says. "But the point of the paper is a conceptual point that we suggest that we can target the latent reservoir for depletion."

This strategy could lead to treatment that provides a reasonable approach to eradicating HIV in the future, Margolis says.

Although it's a preliminary study, its findings are exciting and point to a new direction for HIV treatment, he adds.

One of the drawbacks to using valproic acid is that it slows the clearance of AZT, essentially increasing levels of AZT triphosphate. One patient who received AZT treatment developed grade one anemia toward the end of the study, Margolis says.

The patient's condition was reversed when the study was stopped, Margolis says.

"We're not enrolling patients on AZT in future studies," Margolis says.

Valproic acid, which is used to treat seizure disorders, also is inadvisable for people who have liver disease and for women who are pregnant and nursing.

Its advantages are that it's inexpensive and provides a new therapeutic target, Margolis says.

Since the study never showed a complete eradication of latent HIV, the treatment obviously is not a cure, although it is an encouraging possible treatment for people in late stage HIV disease, which was the population in which it was studied, Margolis says.

"The problem with talking about eradicating HIV or using the C [cure] word is people want there to be a cure, and so do I," Margolis says. "But it's not going to be easy or soon, and we want everybody to be responsible and take care of their own health."

Scientists need to make progress toward that goal of curing HIV without raising expectations too much, and without taking away from the focus on all of the important things people can and should do today to fight the epidemic, Margolis suggests.

"We need to develop a vaccine and treat people who have infection and identify people who have infection," Margolis says. "These are huge challenges at least as big as developing an eradication therapy, but it doesn't mean that we should not try to make steps toward that goal just because it's difficult."

The next step is a study that will look at how effective valproic acid and HAART are without the addition of enfuvirtide, Margolis says.

Reference

1. Lehrman G, et al. Depletion of Latent HIV-1 Infection In Vivo: A Proof-of-Concept Study. *Lancet*. 2005;366:549-555.

Protein in St. John's Wort may suppresses HIV-1 gene expression

Research suggests interesting possibilities

St. John's Wort contains a protein that inhibits HIV-1 replication, according to new research.

Investigators who have spent more than a decade studying the mechanism of development of neurological disorders in AIDS patients decided to look at the impact St. John's Wort might have on neuronal cells, says Kamel Khalili, PhD, director of the Center for Neurovirology, professor, and acting chair of the department of neuroscience at Temple University's School of Medicine in Philadelphia, PA.

"We thought it was a good idea to see if there was any effect of the extract of St. John's Wort on viral replication," Khalili explains. "Our initial investigation showed that crude extracts of St. John's Wort inhibit HIV-1 gene expression in cells such as astrocytes in HIV-1 and in a number of other cells, including macrophages."

A protein from a callus culture of St. John's Wort inhibits transcription of the HIV-1 long terminal repeat by affecting the activity of a transcription factor that regulates expression of the HIV-1 genome in macrophages and monocytic cells, C/EBP-beta, and the viral transactivator, Tat.[1]

The findings were unexpected, Khalili says.

After purifying the protein and sequencing it, investigators found that it was a novel protein, he says.

"So we decided to clone the gene for that protein, and it turned out that when it was expressed in the cells it affected HIV-1 replication," Khalili says. "It confirmed our first observation, and instead of using a crude extract, we're using the product of a cloned gene."

Researchers used a water-soluble protein extract from culture callus tissue of the plant, which they obtained from the Institute of Botany in Armenia.[1]

"They had already set up the conditions for growth of this callus culture in the laboratory," Khalili says.

"The St. John's Wort someone might find on the [retail] shelf may not actually effect the viral replication," Khalili adds. "We did an experiment with a commercially available St. John's Wort preparation and examined its effect on HIV gene transcription in the lab, and that effect was so little, if any, that it wasn't worth pursuing."

However, researchers theorize that the culture callus tissue grown in the laboratory environment overproduces the protein and enriches the extract.

The St. John's Wort protein binds to C/EBP-beta protein, and its interaction keeps the protein in the cytoplasm, preventing it from entering into the nucleus, Khalili says.

"So when the protein is sequestered from the nucleus it doesn't effect viral genic expression," Khalili says.

The inhibition of the St. John's Wort protein is at the level of gene expression, which means that it may control the virus when it is in a latent stage, Khalili explains.

While there are similar approaches in the antiretroviral treatment pipeline, none have yet made it to market, Khalili says.

The next step is to further investigate the St. John's Wort protein and identify a minimum region of protein that has the same beneficial effect, Khalili says.

"Then based on the feature of this protein, a small molecule that would inhibit function of C/EBP-beta and Tat could be developed," Khalili says. "We could use that molecule for blocking viral replication, and that's obviously the long-term goal."

To achieve this first step, researchers will seek funding from the National Institutes of Health (NIH), Khalili notes.

"What I would suggest is this would make an additional compound in the cocktails that could be utilized for antiretroviral replication, and it could be a strong component of that cocktail," Khalili says.

"I have worked with HIV for over 20 years, and I have learned that in order to effectively block viral replication by targeting expression, you may need to target several different factors rather than a single factor," Khalili adds. "So I think this is a protein that can be utilized in conjunction with other compounds in the market or under development."

Reference

1. Darbinian-Sarkissian N, et al. p27(SJ), A Novel Protein in St. John's Wort, That Suppresses Expression of HIV-1 Genome. *Gene Ther*. 2005;[epub ahead of print].

ADHERENCE STRATEGIES

HIV pill reminder device shows some adherence improvement

Technology now switched to cell phone

Researchers studying a population of HIV patients found that a pill reminder improved adherence for those who were memory impaired.[1]

"One reason patients don't take medications is because they simply forget it, and it's more of an issue in the population we studied because some started with mild cognitive impairment," says Adriana Andrade, MD, MPH, an assistant professor at Johns Hopkins University Division of Infectious Diseases in Baltimore, MD.

"So a device that prompts your memory and tells you what to take and when to take it might over come some normal memory impairment that comes with this disease," Andrade says. "I think these findings raise a very important point, maybe not just for HIV-infected population, but for the elderly population as well."

Investigators used a Disease Management Assistance System (DMAS) device developed by Adherence Technologies Corp. of Dulles, VA. The device was battery-powered with a digital signal processor to produce a timed, programmed voice message. It also records data about when medication was taken after the person using it presses a response button.[1]

The study measured antiretroviral drug adherence using electronic drug-exposure monitoring (eDEM) caps.[1]

At 24 weeks in the study, the HIV patients with mild memory impairment who used the DMAS device had a significantly higher adherence rate than did memory-impaired subjects who did not use the device, with 79 percent adherence versus 56 percent adherence among the control group.[1]

Although the HIV patients without memory impairment also tended to have greater adherence in the DMAS device group, when compared to a control group, these differences were not significant, Andrade says.

Subjects with mild memory impairment were not HIV patients with dementia, but were those who were able to go about their daily routine and take medications on their own, Andrade explains.

"The only way to find out if they had memory impairment was to do psychological testing like I did," Andrade says. "So what we found was that among the patients who got the device, the memory-impaired subjects were the ones who benefited the most from the device."

The adherence percentages didn't raise for any group to the high levels of adherence that researchers say is necessary to obtain optimal suppression of the virus, Andrade notes.

"The point is that there might be a subset of HIV-infected patients with mild memory impairment where this high cutoff might be unachievable," Andrade suggests. "Or in order to be achieved we will have to use much more frequent monitoring and come up with ways to help these patients take their medication and improve their compliance."

The DMAS device was small and rectangular with a "play" button and "yes" key and "advice" button.

"Patients had the option to carry it in a pocket or camera case or fanny pack," Andrade says.

When the device beeps and the light on the play button blinks, the patient could press the "play" button to acknowledge the beep and to hear the recorded message that would tell the patient to take this particular medication in this dosage, Andrade says.

Then when the patient took the medication, he or she could press the "yes" button, which would record the time and date of their taking the medication. The patient also had the option of pressing the "advice" button to hear additional instructions, such as, "Take one tablet on an empty stomach," Andrade explains.

To assuage privacy concerns, the process was set up so that the verbal message did not come on unless the patient pressed "play." This way the patient could take the device to a private area before hearing the reminder, Andrade says.

Interestingly, the company that made the

device has abandoned that design and has created a cell phone reminder tool instead, which is being sold as a service for pharmacies, Andrade says.

Patients enrolled in the study were on a variety of antiretroviral regimens for a total of no more than three different regimens, Andrade says.

"We looked at very experienced in terms of exposure and at antiretroviral-naïve patients," Andrade says. "We wanted a representative sample for the study."

The main lesson from the study is that adherence interventions need to be individualized since not every approach helps each person the same way, Andrade says.

Also, as patients infected with HIV age, the prevalence of mild forms of cognitive impairment might be increasing, Andrade says.

"For this population, the message is that caregivers must be aware of the negative impact that even a mild cognitive impairment can have on HIV therapy," Andrade says. "So providers should be aware of that and explore other adherence aids that can help this patient population with antiretroviral medication."

Reference

1. Andrade AS, et al. A Programmable Prompting Device Improves Adherence to Highly Active Antiretroviral Therapy in HIV-Infected Subjects With Memory Impairment. *Clin Infect Dis*. 2005;41(15):875-882.

Drug resistance found in SE area, representing poor, rural population

Resistance screening is indicated

A recent study about HIV drug resistance among untreated HIV patients highlights the growing problem of resistance in a Southeastern region of the country.[1]

An infectious diseases clinic in Jackson, MS, had a rate of 10.5 percent in 2004 for drug resistance found in patients who were seen at their first visit upon diagnosis of HIV infection, says Harold Henderson, MD, professor of medicine at the University of Mississippi Medical Center in the division of infectious diseases in Jackson.

The 124 patients included in the study had not received antiretroviral treatment and did not represent new infections, but could be described as chronically infected, Henderson says.

"Our conclusions are that the ability to detect anti-HIV drug resistance in chronically HIV-infected persons who had never been treated before was significant," Henderson says. "The most common mutation was the mutation that confers resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs)."

Existing research data about drug resistance mostly has looked at newly-infected patients in large urban areas, and has found resistance of 8 percent to 15 percent, Henderson says.

"The major difference from what we did was we did resistance testing on patients who came to our clinic for the first time, but who weren't necessarily newly infected patients," Henderson says. "They may have been infected for quite a while before the time they ever came to our clinic."

HIV clinicians and researchers long have discussed whether drug-resistant strains remain detectable in the absence of drug therapy, with many theorizing that wild type virus is more dominant in this untreated population.

"Some people have questioned whether such strains would remain detectable for a significant period of time," he says. "A lot of people had felt that in untreated patients if they had gotten infected with drug resistant strains those drug resistant strains would only be detectable for a short period of time and then fade into the background."

If that happened then it wouldn't be much use to do resistance testing in patients who had never been treated before, Henderson explains.

"If patients on medication have drug-resistant strains, and those particular strains are resistant to the drugs they are being given then those strains will be replicating preferentially to other strains that are being suppressed by the drugs," Henderson says.

"If the medication is subsequently changed and the patient starts taking different drugs then those resistant strains may now be suppressed by the new medication," Henderson says. "But there may be other strains present in that person that previously were being suppressed by old medicines, and now in the presence of new medicines those strains can emerge from the backgrounds and become the predominant strains."

All of these factors play into decisions about resistance testing, so any study which shows

durability of drug-resistant virus is notable.

"There is coming to be a recognition that the shifting of viral strains in persons who are on treatments may not occur to the same degree in persons who have never been treated before," Henderson says. "In someone who has never been treated before, if that person is infected with a drug resistant strain then that strain may persist in detectable levels for a long time."

The 10.5 percent detectable drug resistance found in the Jackson clinic's population is significant, Henderson says.

"Most people feel that a level that high would justify routinely doing resistance testing in this setting," Henderson says. "And that is among patients who've never been treated before and who appear for their initial evaluation."

The other implication of the research is that drug resistance is present in smaller cities and rural areas, as well as large urban regions, Henderson says.

Reference

1. Henderson H, Brown B. HIV Drug Resistance Among Untreated Chronically HIV-Infected Person in an Infectious Diseases (ID) Clinic in Jackson, Mississippi. Presented at the 43rd Annual Meeting of the IDSA, Oct. 6-9, 2004, in San Francisco, CA. Abstract: 801.

Updated guidelines issued for occupational PEP use

PEP regimens have changed

The U.S. Public Health Service has changed its treatment guidelines for the use of post-exposure prophylaxis (PEP), following an occupational exposure to HIV infection.

The new guidelines advise clinicians to consider occupational exposures as urgent medical concerns, and to ensure timely postexposure management and administration of HIV PEP.[1]

The list of antiretroviral medications that should be considered for PEP use has been expanded and modified. There now are five classes of HIV antiretrovirals on the PEP list, including the fusion inhibitor enfuvirtide (Fuzeon) and the nucleotide analogue reverse transcriptase inhibitor (NtRTI) tenofovir (Viread, TDF).[1]

Included on the expanded PEP list are five nucleoside reverse transcriptase inhibitors (NRTIs), seven protease inhibitors (PIs), and efavirenz (Sustiva), a non-nucleoside reverse transcriptase inhibitor (NNRTI).[1]

Treatment guidelines state that people receiving PEP should complete a full four-week regimen, although clinicians should select the treatment while considering adverse events and toxicity profiles of the agents. Anecdotal evidence has shown that health care personnel taking HIV PEP have high rates of non-completion of therapy because of an inability to tolerate the drugs.[1]

Data from the National Surveillance System for Health Care Workers show that about 47 percent of 921 health care persons with at least one follow-up visit after starting PEP experienced one or more symptoms, including nausea, malaise and fatigue.[1]

The guidelines note that there is little evidence of what would be the best PEP to recommend, although a combination of drugs with activity at different stages in the viral replication process, such as a nucleoside analogue with a PI, theoretically might offer additive preventive effect.[1]

Also, the guidelines suggest that offering a two-drug regimen might be a viable option because such a combination might decrease the risk of a person stopping the treatment before completion.[1]

From June 1995 to December 2004, there were 28,010 exposures to blood and body fluids reported by 95 U.S. hospitals in a convenience sample, according to 2005 data from the Centers for Disease Control and Prevention (CDC) of Atlanta, GA.[1]

For the 25,510 with known sources, 1,350 or 5.4 percent were to HIV-positive sources, and 8,859 or 34.7 percent were to sources with unknown HIV status.[1]

Of these health care workers, 788 started PEP and 317 took PEP for 21 or more days, with the median duration of HIV PEP after exposure of 27 days.[1]

The guidelines recommend that PEP regimens be PI-based, preferably with lopinavir/ritonavir, and efavirenz might be considered for expanded PEP regimens, especially when resistance to PIs in the source person's virus is known or suspected.1

Reference

1. Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis. *MMWR Morb Mortal Wkly Rep*. 2005;54(RR-9):1-17.

Here's a nutshell look at US Preventive Service Task Force recommendations

All pregnant women and people at risk should be tested

The U.S. Preventive Services Task Force recommends that clinicians screen all pregnant women for HIV infection, as well as continue to screen all adolescents and adults who are at increased risk for infection.

The guidelines, which were updated recently from the 1996 recommendations, made no recommendation for routine screening for HIV among adolescents and adults who are not at increased risk for infection.[1]

In the past nine years new evidence on screening for HIV has caused the task force to update its recommendations. Previously, the task force had recommended HIV testing only for high-risk pregnant women.

The task force considers a person at increased risk for HIV infection if he or she reports one or more individual risk factors or if the person receives health care in a high-prevalence or high-risk clinical setting. This group includes men who have sex with men (MSM), men and women having unprotected sex with multiple partners, past and present injection drug users, people who exchange sex for money or drugs or are partners with people who do, people who have had HIV-infected, IDU, or MSM sex partners, people treated for sexually-transmitted diseases, and people who request an HIV test.1

The task force's recommendations explain how the standard of care for preventing HIV transmission in seropositive pregnant women has evolved from monotherapy with zidovudine to combination therapies that start at 14 to 34 weeks gestation and continue through labor. Treatment is augmented with six weeks of neonatal prophylaxis with zidovudine, and avoidance of breastfeeding is recommended.1

New research also demonstrates the benefit of elective cesarean section to reduce vertical transmission, the task force says.

Without interventions, vertical transmission of HIV is between 14 percent and 25 percent, while with interventions it is 1 percent to 2 percent.[1]

Reference:
1. Screening for HIV. U.S. Preventive Services Task Force. July, 2005. Http:www.ahrq.gov/clinic/uspstf05/hiv/hivrs.htm.

FDA Notifications

Generic lamivudine tentatively approved

The FDA announced on Nov. 4, 2005, the tentative approval of Lamivudine Oral Solution, 10 mg/mL manufactured by Aurobindo Pharma LTD. of Hyderabad, India. Lamivudine Oral Solution is the first generic version of the already approved Epivir Oral Solution, 10 mg/mL, manufactured by GlaxoSmithKline. This child-friendly-product is indicated for use in pediatric patients with HIV from three months to 16 years.

Lamivudine is in the class of drugs called nucleoside reverse transcriptase inhibitors (NRTIs), which help keep the AIDS virus from reproducing. This antiretroviral drug is intended to be used in combination with other antiretroviral agents for the treatment of HIV-1 infection.

FDA's tentative approval of this product means that although existing patents and/or exclusivity prevent marketing of this product in the United States, the product meet all of FDA's safety, efficacy, and manufacturing quality standards required for marketing in the U.S., and it will now be available for consideration for purchase under the President's Emergency Plan for AIDS Relief (PEPFAR).

FDA approves new Kaletra formulation

On Oct. 28, 2005, the Food and Drug Administration approved a new formulation of lopinavir/ritonavir (Kaletra). Lopinavir/ritonavir is now available as a film coated tablet

(200mg/50mg) that provides advantages over the currently marketed capsule formulation for HIV-1 infected patients. Specifically, the tablet formulation:

- does not require refrigeration;
- can be administered without regard to meals;
- does not require dose adjustments for concomitant use with certain NNRTIs and PIs in treatment-naïve patients;
- has a decreased pill burden compared to the capsule formulation (2 tablets twice daily or 4 tablets once daily in treatment-naïve patients only vs 3 capsules twice daily or 6 capsules once daily in treatment-naïve patients only);
- The following additions and revisions were made to the package insert.

1. The clinical pharmacology section contains the following additions:

Pharmacokinetics

Plasma concentrations of lopinavir and ritonavir after administration of two 200/50 mg lopinavir/ritonavir tablets are similar to three 133.3/33.3 mg lopinavir/ritonavir capsules under fed conditions with less pharmacokinetic variability.

The capsule formulation will be phased out over time by the company. Kaletra is a product of Abbott Laboratories. The original formulation was approved on September 15, 2000.

Ritonavir and lopinavir/ritonavir package inserts are updated

The ritonavir (Norvir) and lopinavir/ritonavir (Kaletra) package inserts (product labeling) were recently updated to include information regarding interactions with fluticasone (a synthetic corticosteroid, the active component of Flonase nasal Spray) and trazodone (Desyrel, a non-tricyclic antidepressant). In addition, alfuzosin (an alpha-blocker used to increase the flow of urine in people with benign prostatic hypertrophy (BPH)) was added to the Contraindications section of the

CE/CME *directions*

To complete the post-test for *AIDS Alert*, study the questions and determine the appropriate answers. After you have completed the exam, check the answers **on p. 144**. If any of your answers are incorrect, re-read the article to verify the correct answer. At the end of each six-month semester, you will receive an evaluation form to complete and return to receive your credits.

CE/CME *questions*

1. The 2004 surveillance data for sexually-transmitted diseases (STDs) in the United States show an increase in syphilis rates among which population?
   A. Young women, ages 15 to 24
   B. Men who have sex with men
   C. African American and Hispanic heterosexuals
   D. All of the above

2. A new study of treatment targeting HIV from resting T-cells found that which drug combined with highly active antiretroviral therapy and subcutaneous enfuvirtide accelerates the clearance of HIV from resting T-cells in vivo.
   A. rifabutin
   B. hydroxyurea
   C. cidofovir
   D. valproic acid

3. A protein from a callus culture of which plant, often used in natural remedies, inhibits transcription of the HIV-1 long terminal repeat by affecting the activity of a transcription factor that regulates expression of the HIV-1 genome in macrophages and monocytic cells, C/EBP-beta, and the viral transactivator, Tat, according to new research.
   A. St. John's Wort
   B. Angelica root
   C. Red Clover
   D. Boswellia

4. Revised guidelines from the U.S. Public Health Service for the treatment of postexposure prophylaxis (PEP) following an occupational exposure to HIV infection include an expanded list of antiretroviral medications. Which of the following is not on the new list?
   A. Five nucleoside reverse transcriptase inhibitors (NRTIs)
   B. Fusion inhibitor enfuvirtide and nucleotide analogue reverse transcriptase inhibitor tenofovir
   C. Seven protease inhibitors and one non-nucleoside reverse transcriptase inhibitor, efavirenz
   D. All of the above

ritonavir package insert.

Listed below are labeling revisions for the ritonavir and lopinavir/ritonavir package inserts.

Summary of Label Changes

Ritonavir

Clinical Pharmacology:

Results of the drug interaction studies with ritonavir and fluticasone propionate aqueous nasal spray and trazodone were included:

Ritonavir increased fluticasone AUC and Cmax by approximately 350-fold and 25-fold respectively. This significant increase in plasma fluticasone propionate exposure resulted in a significant decrease (86%) in plasma cortisol AUC.

Ritonavir increased trazodone AUC and Cmax by 2.4 fold and 34%, respectively.

CONTRAINDICATIONS:

The Alpha1-adrenoreceptor antagonist drug, alfuzosin HCL, was added to the contraindicated list.

WARNINGS:

The following warning regarding fluticasone was included:

A drug interaction study in healthy subjects has shown that ritonavir significantly increases plasma fluticasone propionate exposures, resulting in significantly decreased serum cortisol concentrations. Systemic corticosteroid effects including Cushing's syndrome and adrenal suppression have been reported during postmarketing use in patients receiving ritonavir and inhaled or intranasally administered fluticasone propionate. Therefore, coadministration of fluticasone propionate and ritonavir is not recommended unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side effects. (see Precautions: Drug Interactions).

PRECAUTIONS:

In the Precautions section, the following clinical comment was included regarding the fluticasone interaction:

Concomitant use of fluticasone propionate and ritonavir increases plasma concentrations of fluticasone propionate, resulting in significantly reduced serum cortisol concentrations. Coadministration of fluticasone propionate and ritonavir is not recommended unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side effects (see Warnings).

The following clinical comments were included regarding the trazodone interaction:

Concomitant use of trazodone and ritonavir increases plasma concentrations of trazodone. Adverse events of nausea, dizziness, hypotension and syncope have been observed following coadministration of trazodone and ritonavir. If trazodone is used with a CYP3A4 inhibitor such as ritonavir, the combination should be used with caution and a lower dose of trazodone should be considered.

CE/CME 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. ■

CE/CME *answers*

Here are the correct answers to this month's CME/CE questions.

1. B 2. D 3. A 4. D

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