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Great results from iPrEx study add to trifecta of good news on prevention

Truvada PrEP provided protection in MSM+transgender

Close on the heels of the first positive findings reported in microbicides and vaccine research ventures, the iPrEx study has shown that a pre-exposure prophylaxis (PrEP) combination drug demonstrates 44% additional protection from HIV infection.

"We were really heartened to see these findings," says **Albert Liu,** MD, MPH, director of HIV prevention intervention studies at the HIV research section of the San Francisco Department of Public Health in California. Liu is one of the investigators involved in the study of the antiretroviral combination of tenofovir and emtricitabine (Truvada®) as a PrEP treatment. Liu also is an assistant clinical professor at the University of California at San Francisco (UCSF).

The iPrEx study enrolled 2,499 HIV-sero-negative men or transgender women who have sex with men. They received a combination of emtricitabine and tenofovir or placebo once daily, and they were followed for a median of 1.2 years.[1]

"IPrEx is the first study to show that an oral pill can be used to prevent HIV infection when given as part of a comprehensive prevention package," Liu says. "It's also the first biomedical intervention to show efficacy in men who have sex with men (MSM), so we think this is a really great advance for HIV prevention."

HIV clinicians should view PrEP as part of a comprehensive prevention strategy that might include microbicides and, perhaps, an HIV vaccine, suggests **Kenneth H. Mayer**, MD, infectious disease physician at Miriam Hospital and professor of medicine and community health at Brown University in Providence, RI. Mayer, who also was an investigator on the iPrEx study, is the medical research director at Fenway Health in Boston, MA.

"Ultimately, we still want a vaccine," Mayer says.

Developing an effective HIV vaccine is critically important in HIV prevention, Liu says.

"In the long term, a vaccine likely will be the best strategy at eliminating HIV infections worldwide," he adds. "We need as many prevention strategies as possible to drive down infection rates, so we remain committed to exploring multiple strategies, including vaccines, PrEP, microbicides, and behavioral interventions."

Achilles heel is adherence

Vaccine researchers reported in September, 2009, that a combination of two vaccines that previously had failed in clinical trials was successful over three years with 31.2% of people receiving the vaccination in a phase III Thailand clinical trial. The combination vaccine included Sanofi Pasteur's Alvac and Global Solutions for Infectious Diseases' AIDSVAX. The Thailand trial enrolled 16,000 people. The vaccine provided protection against HIV in about half of the study volunteers during the first year, but lessened over time.

Then, in July, 2010, researchers announced that the CAPRISA 004 microbicide trial using tenofovir gel vaginally resulted in 39% fewer HIV infections among women who used tenofovir gel before and after sex than those who used placebo. The microbicide's effectiveness was higher for women who had 80% or greater adherence.

"What is exciting is that both the microbicides and PrEP approaches were successful," Mayer says.

However, they are not simple interventions, Mayer notes.

"In both studies the Achilles heel is adherence," Mayer says. "Those who were adherent had much higher levels of protection."

The key for clinicians will be to identify people who will most benefit from the strategy and to help them with adherence.

The tenofovir/emtricitabine PrEP intervention has the advantage of being immediately available.

"I think it has more immediate public health implications because these are medications prescribable right now," Mayer says. "Whereas, the gel is not yet available, and to make the gel accessible to women will take a scaling-up effort that will take time."

And, vaccine research will continue as investigators seek an approach with greater protection than the initial success story reported.

The iPrEx study's efficacy findings held up in a variety of ways as investigators looked at study volunteers' ages, level of education, and other demographic data, Liu notes.

The study started in Peru and Ecuador in South America and was expanded to San Francisco, CA, and Boston, MA, Brazil, Thailand, and South Africa, Liu says.

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"We looked at the results in a variety of different ways, and it seems that PrEP appears to be effective for a variety of different groups."

Whether any PrEP or microbicides prevention strategy will prove to be a successful way to reduce new infection rates in a population will depend on how successfully public health officials convince people to adhere to the treatment.

"HIV prevention will succeed or fail based upon the ability of people to adhere to these strategies for the duration of time they're at risk of being infected," says **David Bangsberg**, MD, MPH, director of the Massachusetts General Hospital Center for Global Health and associate professor at Harvard Medical School in Cambridge, MA.

"We have some really promising findings with CAPRISA and the iPrEx study, which show antiretroviral prevention is possible, and that's exciting," he adds. "But we still have more questions than answers, and sustained adherence to these approaches is one of the top questions that we have yet to answer."

Investigators measured adherence in various ways and found that people who had higher rates of pill taking had higher rates of protection, Liu says.

"We did find that by self-report pill-taking was quite high," he says.

But when researchers tested a small amount of blood samples they found that only 9% of people who became HIV infected had detectable drug versus 51% having detectable drug among those who remained HIV negative, he explains.

"So that shows that people who had detectable drug were more likely to be protected from HIV," Liu adds.

Important variables

Side effects, cost, and length of time are two important variables in PrEP adherence.

"Overall, the study found Truvada appeared to be safe and well tolerated," Liu says. "The rates of serious adverse events or side effects were similar between the two arms of the study of Truvada and the placebo group, but we did see that nausea was slightly more common in the group that received Truvada."

The nausea was resolved within one to three months in most participants, he adds.

"We actually have this initial start-up syndrome, often seen in HIV-positive people who are starting to take medications," Liu says. "So providing support to participants and managing these transient side effects will be important in helping people take the pill more consistently."

There are a number of possible scenarios regarding how long people would need to take PrEP in order to achieve personal protection from HIV infection, as well as for the prevention approach to make an impact on HIV prevalence in any particular population.

"I think it's not clear that men will need to take this life-long," Liu says. "People move in and out of periods of risk, and if PrEP is combined with other prevention strategies then it might help people as they are adopting other behavioral change strategies."

It could be that PrEP helps keep a generation of at-risk people healthy as they wait for an HIV vaccine. Also, PrEP is only necessary for people who are engaging in risky behaviors. For some people, their risky behaviors might be limited to a certain period of years. After this period ends, they might be safe in discontinuing PrEP.

"We'll need to do additional studies to see how long people will need to take the drug and how long the protective benefits will last and whether other dosing regimens are safe and effective," Liu says.

Investigators studied daily dosing in the iPrEx study, but it's possible less frequent dosing would prove effective in preventing HIV infection as well.

"The important point is that people who decide to use PrEP should do it under medical supervision, frequent HIV testing, and monitoring for side effects," Liu says. "Intermittent use is not recommended because we don't have data on that."

Cost also is a factor since ARTs are very expensive and it's unclear who would pay for a PrEP approach.

In the United States, daily Truvada treatment can cost $10,000 a year. In low-resource countries where generic drugs have been approved, the treatment can cost $500 to $600 per year, Mayer says.

While it's plausible that some people at risk for HIV infection will try to take Truvada on their own, this would be a mistake since this is a biomedical intervention that requires physician supervision, Mayer notes.

For instance, Truvada use could result in an elevation of creatinine, indicating kidney issues. This was found in 1% of iPrEx study participants on placebo and 2% on Truvada, he says.

"It went away when the medication was stopped, and it didn't come back, so it was a

transient and reversible kidney problem," Mayer adds. "But the important point is that taking a pill is different from using a condom or getting a vaccine, and so people should be monitored by professionals."

From an HIV clinician's perspective, media coverage of the study's findings likely will mean some partners of HIV patients will inquire about using PrEP as a way to prevent HIV infection.

For example, some HIV-discordant couples are intent on conceiving a child, and it would be unfortunate to not make PrEP available to seronegative women who want to have a child with their HIV-positive partner, Mayer says.

"I would handle these on a case-by-case basis," Mayer suggests. "I certainly would consider making PrEP available to someone where I understood their pattern of risk and had a sense they'd be adherent to medication and knew what they were getting themselves into."

However, there's a need for the Centers for Disease Control and Prevention (CDC) to come up with guidance for providers and education on PrEP and HIV treatment for non-HIV physicians.

"Most providers who are going to take care of these clients are not HIV specialists, so a lot of education needs to go on to scale this up for wider public health intervention," Mayer says.

The initial study found that risk behavior declined as part of the trial, which had included a comprehensive prevention package of HIV testing, counseling, free condoms and lubricants, and regular treatment for sexually-transmitted diseases, Liu notes.

IPrEx investigators are continuing study of the PrEP with plans to offer participants a rollover protocol. If enrollment is successful, researchers will monitor participants' behavior to see if they continue to maintain a lower level of risk or if their risky behaviors increase, Mayer says.

"The first step was to demonstrate oral PrEP would prevent HIV, which we've done in this study," Liu says. "Now we'll be talking with community members, health care providers, and regulatory agencies to figure out how this might best be used, and this also will inform how PrEP might be paid for."

REFERENCE

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Legislative barriers hinder progress in opt-out testing

Non-HIV doctors need education on opt-out

Opt-out HIV testing goals by the Centers for Disease Control and Prevention (CDC) of Atlanta, GA, would have greater success if states were to reduce legislative barriers, an expert says.

"We need to reduce legislative barriers so everyone can get an HIV test," says **Ping Du**, PhD, an assistant professor of medicine at Pennsylvania State University College of Medicine in Hershey, PA.

Since the CDC published its recommendations for nearly universal, routine HIV testing, some federal agencies have allocated money to promote HIV testing, Du says.

"So it's important to take into consideration these public health resources," she says. "To better understand HIV testing behavior, we need to understand individual factors and policy factors."

From the policy aspect, some states have requirements of having people sign a consent form and receive pre-test counseling. These can be a barrier to routine, opt-out HIV testing, Du says.

"Physicians might worry it will take too much time, especially if patients have many questions with regard to HIV testing or if they have concerns," she explains.

Many states have modified public health law to promote opt-out testing, but some lag behind with opt-in HIV testing requirements, Du notes.

According to data collected from the Behavioral Risk Factors Surveillance System, HIV testing has decreased since 2000, despite the CDC's 2006 recommendations for routine HIV testing in health care settings for everyone, ages 13 to 64 years.[1]

Of 284,688 adults asked about HIV testing in 2008, 38.7% reported having been tested for HIV. This compares with 40.25% of adults having been tested in 1996, 48.11% in 2000, and 35.38% in 2006.[1]

Blood donors were excluded from the analysis, Du says.

Du's research has found that people living in rural areas are less likely to have HIV testing.

"It could be related to resources," she adds. "They don't have regular access to health care, which may be the reason why rural residents are less likely to be tested for HIV."

Another policy barrier involves payment for

HIV tests. Many insurers will not cover HIV testing unless there is a high risk indicated, she adds.

"In the United States population, only a small proportion of people have a high-risk situation, such as drug use, men having sex with men," Du says. "The majority of people do not perceive any high risk for HIV infection."

Routine HIV screening is available to women when they are pregnant, and this strategy has become accepted and widely implemented. So this serves as an example of how it could work in a general population.

"Physicians should promote HIV testing regardless of the individual's risk," Du says.

The study's findings suggest that non-HIV specialists are unaware of the CDC's recommendations for universal and routine HIV testing.

"It's been four years, and everyone should know it according to the literature, but some physicians may not be aware of it," Du says. "Also, physicians are concerned about some logistic issues like insurance and time allocated for counseling and testing."

The solution is a better public health infrastructure strategy, Du says.

There should be insurance coverage for the physician's time for pre-and-post-test counseling, as well as public health resources for testing, she adds.

"Doctors need to screen for HIV for all their patients at least once a year," Du says. "It should be as routine as cholesterol testing."

REFERENCE

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Q&A on one-minute HIV test approval

[Editor's note: With the recent news that the U.S. Food and Drug Administration (FDA) has approved a new HIV test that obtains results within one minute, domestic HIV testing and prevention strategies have a new tool to employ. AIDS Alert asked Philip Bligh, president of bioLytical Laboratories in Vancouver, British Columbia and Chicago, IL, to answer questions in writing about his company's INSTI™ test. His responses are shown in this Q&A story]:

AIDS Alert: BioLytical Laboratories announced on World AIDS Day, Dec. 1, 2010, that it had received FDA approval to market the INSTI™ rapid HIV antibody test in the United States. The test takes one minute to generate results, which makes it much faster than other approved rapid tests, which might take 15 to 30 minutes. How do you think HIV testing sites might use this faster test, and what are the advantages of that 14-29 minutes saved in time spent waiting for results?

Bligh: By eliminating the wait time between performing the test and receiving the results, INSTI offers many advantages, such as higher throughput, increased counseling flexibility, reduced client anxiety, and decreased costs of testing by reducing overall time and logistics and increasing workflow flexibility. Also, it allows testing in novel settings where time is very limited, such as emergency rooms, department of motor vehicle centers, walk-in pharmacy clinics, mass testing events, places of employment, dental offices, and correctional facilities.

Q: The INSTI test's clinical trial data have shown that it has a minimum sensitivity of 99.8% and specificity of 99.5%. How does this compare with other existing HIV tests? Once test results are obtained, how would the HIV testing site follow-up?

A: All of the rapid HIV tests that are FDA approved are extremely accurate, with very comparable rates of sensitivity and specificity. Once the test results are obtained, HIV testing sites should follow their internal procedures of post-test counseling for non-reactive results and for reactive results. All reactive results should be followed up with a confirmatory test and the patient should be referred to appropriate follow-up medical care.

Q: Would you please explain how the INSTI test's unique antigen construct works. How might this test contribute to a multi-rapid test algorithm, and what are the implications?

A: The INSTI rapid HIV test includes a unique antigen construct comprised of recombinant proteins for HIV-1 (gp-41) and HIV-2 (gp-36). Currently this unique antigen is only used in the INSTI test and is not included in any other rapid test on the market. In addition to the unique antigen, INSTI uses a novel flow-through technology platform rather than the traditional lateral-flow platforms utilized by the other rapid tests on the market. When developing a multi-test rapid algorithm, it is important to deploy tests with different antigens and different technology platforms to

include tests that are as different from one another as possible. Algorithms will reduce costs, speed up time to results, improve linkage to care and reduce patients lost due to lack of follow-up/returning for confirmatory results. The ultimate benefit will be to increase the number of positives identified and improve linkage to care.

Q: How much will the test cost clinics and other testing sites, and how does this cost compared with available HIV testing options? How might this method be feasible in resource-limited settings?

A: We are quite sensitive to the resource constraints faced by our prospective customers. The list price of INSTI is $9 for the individual test, and $8.50 per test in the 24-pack format. Discounted pricing based on volume, and public health pricing, are available. Biolytical's high-volume, automated manufacturing capability makes INSTI one of the most cost-effective solutions available for providers of HIV rapid testing. The competitive costs for INSTI, combined with the enhanced productivity that I described earlier, should help our customers reduce their overall costs for HIV testing.

Q: Some states in the U.S. still require pre-testing counseling, which sites sometimes have conducted during the testing wait period. How might they cost-effectively implement such counseling with a one-minute test?

A: A one-minute test provides clinicians and counselors with increased flexibility to design pre/post test counseling to better suit the client and the setting. Counselors no longer need to build-in a sometimes artificial, and occasionally stressful 15-20 counseling script to fill time while waiting for test results. Counselors can devote more time to clients that need/want more extensive counseling, and less time to clients who may already be familiar with the script and/or simply want a test result. It's all about enhanced counseling flexibility and tailoring the counseling to the client, not the test kit. Sites can reduce their costs by more efficiently allocating limited counselor/clinician time to clients that need it most.

Q: What are the potential public health implications of the one-minute HIV test?

A: Major public health benefits from INSTI include enhanced access to testing by permitting testing in a much wider variety of novel settings (prisons, ERs, pharmacies, departments of motor vehicles, on-site testing at events, worksite testing, etc.). INSTI also decreases overall testing costs by streamlining counseling, eliminating the need to build new clinics, and by reducing professional overhead due to INSTI's ease of use by task-shifting (using non-medical professionals to reliably conduct the tests). Another implication is reduced stigma associated with screening by making HIV testing more mainstream — when rapid HIV testing can be implemented in more settings, including the novel settings that I described earlier, it can become as ubiquitous and routine as taking a patient's vital signs. Finally, INSTI could help enable the adoption of rapid-rapid algorithms to reduce costs, decrease testing time, minimize clients lost to follow up, expand access to confirmed results and improve linkage to care. Ultimately, the health experts with whom we have collaborated believe that INSTI will lead to improved health outcomes and serve as another tool in the effort to slow the growth rate of the HIV positive population. ■

Once daily pill yields higher ART adherence

Study looked at marginalized populations

Even HIV-infected individuals who have the greatest challenges in adhering to their antiretroviral (ART) can achieve high adherence on a regimen of one pill taken daily, research shows.

"When we looked at one pill taken once a day, adherence was just short of 90%," says **David Bangsberg**, MD, MPH, director of the Massachusetts General Hospital Center for Global Health and associate professor at Harvard Medical School in Cambridge, MA. Bangsberg was a lead author on the study, which was presented at the 2010 Conference on Retroviruses and Opportunistic Infections (CROI).[1]

The one pill, once-daily regimen consisted of a combination of efavirenz, emcitrabine, and tenofovir.[1]

The study looked at individuals recruited from single room occupancy (SRO) hotels, free meal food programs, and homeless shelters. They were within six months of treatment initiation, and adherence was determined for six months using unannounced pill counts at their usual places of residence.[1]

"This population had all the risk factors for poor adherence," he says. "Indeed, this is an exceptionally high level of adherence in any population."

A near 90% adherence rate is high by ART historical perspective, particularly for a population that is homeless and has drug use and depression issues, Bangsberg notes.

The high level of adherence on ART was associated with good rates of viral suppression, which would imply this one-pill, once-daily treatment would be a successful treatment strategy for a homeless population, he adds.

"Therapy in 1996 was quite complex with 20 pills a day, and it has become much simpler and more potent now with the availability of once-daily, one pill treatment," he explains. "When we looked at adherence in the population receiving more complicated therapy we historically have seen adherence in the high 60s, low 70s."

HIV-infected individuals in the cohort receiving more complicated therapy had an adherence rate of about 70%, Bangsberg says.

Researchers recruited HIV patients who mostly were receiving routine care at publicly-funded HIV clinics in the Tenderloin mission areas of San Francisco, Bangsberg says.

Most of the study participants picked up their medications at pharmacies.

"With their permission and informed consent, we would go to their usual place of residence, sometimes an SRO or homeless shelter, sometimes on the street, and on a random day we would count their pills to see how many they had in their possession," Bangsberg says. "We did that every month for six months."

The study's results clearly demonstrate that excellent adherence results can be achieved with a single-pill, once-daily ART regimen even among a challenging population that has many risk factors for poor adherence, Bangsberg says.

REFERENCE

1. Bangsberg D, Ragland K, Monk A, et al. A one-pill, once-daily fixed-dose combination of efavirenz, emcitrabine, and tenofovir disoproxil fumarate regimen is associated with higher unannounced pill count adherence than non-one-pill, once-daily regimens. Abstract presented at the 17th Conference on Retroviruses and Opportunistic Infections (CROI), held Feb. 16-19, 2010, in San Francisco, CA. Abstract:1000. ■

A key host response to HIV infection

By **Dean L. Winslow,** MD, FACP, FIDSA, Chief, Division of AIDS Medicine, Santa Clara Valley Medical Center; Clinical Professor, Stanford University School of Medicine. Dr. Winslow is on the speaker's bureau for GSK and Cubist Pharmaceuticals, and is a consultant for Siemens Diagnostics.

Synopsis: A polymorphism in the CXCR6 chemokine receptor gene was found to be associated with long-term non-progression (LTNP) to AIDS in a cohort of French patients in which "elite controllers" were excluded.

Source: Limou S, et al. Multiple-cohort genetic association study reveals CXCR6 as a new chemokine receptor involved in long-term non-progression to AIDS. *J Infect Dis*. 2010;202:908-915.

The genomics of resistance to immunodeficiency virus (GRIV) Cohort was established in France in 1995 to generate a large database for genetic studies to identify host genes associated with rapid progression and long-term non-progression to AIDS. To reduce confounding by excess heterogeneity, the cohort was restricted to white people of European descent living in France. LTNPs were defined as patients with asymptomatic HIV infection who maintained consistent CD4+ lymphocyte counts > 500 in the absence of antiretroviral (ARV) therapy. Of the 248 individuals in the cohort who met the criteria for LTNP and had a viral load available, 186 had HIV RNA > 100 copies/mL. These latter patients were included in the analysis described in this paper.

The GRIV cohort and the control group were genotyped initially using a bead-chip method. A total of 283,637 single nucleotide polymorphisms (SNPs) could be tested for potential association with LTNP. After identification of a SNP in CXCR6 as being associated with LTNP, the coding region for this chemokine receptor was amplified by PCR and underwent complete sequencing by conventional dideoxynucleoside sequencing using dye terminators and an ABI DNA analyzer.

The SNP identified as being associated with LTNP in patients who were not "elite controllers" (rs2234358) lies within the CXCR6 gene on chromosome 3, which is only 422 kb from the CCR5 gene. The rs2234538 signal was replicated in three independent, additional cohort studies of white people of European descent (ACS, MACS, and USA HIV-1 cohorts). This SNP is located in the 3' untranslated region of CXCR6, and could influence gene expression, mRNA stability, mRNA regulation, or mRNA splicing.

Commentary

Large cohorts of HIV patients have provided some important early insights into the host genetic factors associated with immune response to a variety of pathogens. This latest SNP association with LTNP is independent of the well-known CCR2-CCR5 locus, is not linked to virologic control of HIV, and is not linked to HLA type. The finding of this additional association of a chemokine receptor with HIV progression is not surprising due to the now well-known effect of chemokine receptors on host response to a variety of pathogens. While CXCR6 has been shown to be a minor coreceptor for HIV-1, this particular SNP is not located in an exon, so its biological effect is postulated to be related to modulation of CXCR6 expression. This may, in turn, affect trafficking of effector T-cells and inflammation. Further research in this area is certain to continue to improve our understanding of host response to HIV infection. ■

Don't test, don't know: The danger of denial

1 in 5 MSM has HIV — 44% unaware

Results of a new analysis of 21 major U.S. cities from the Centers for Disease Control and Prevention indicate approximately one in five (19%) men who have sex with men (MSM) in a study is infected with HIV, and nearly half (44%) of those men are unaware of their infection.[1]

This research serves as a reminder that HIV remains a serious health threat among gay and bisexual men in America's major cities, says **Amanda Smith**, MPH, an epidemiologist in the CDC's Division of HIV/AIDS Prevention and lead author of the paper. The analysis, a review of data from the 2008 National HIV Behavioral Surveillance System, found a high prevalence of HIV among MSM of all races. However, black men who have sex with men were the most affected; 28% of black MSM were infected, versus 18% of Latinos and 16% of whites, Smith states.

A troubling fact: the CDC research also suggests that a high proportion of MSM who were infected were unaware of their illness. In fact, nearly half (44%) of MSM who were infected in the study were unaware of their infections, says Smith.

HIV exacts a devastating toll on men who have sex with men in America's major cities, and yet far too many of those who are infected don't know it, said **Kevin Fenton**, MD, director of CDC's National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, in a statement accompanying the new research.

"We need to increase access to HIV testing so that more MSM know their status, and we all must bring new energy, new approaches, and new champions to the fight against HIV among men who have sex with men," Fenton says.

The new statistics underscore two important points for clinicians who work with MSM, says **Robert Hatcher**, MD, MPH, professor of gynecology and obstetrics at Emory University in Atlanta. They are: Talk with patients about the importance of learning their HIV status, and counsel on the need for consistent condom use for disease protection.

The study provides additional insight into the populations of MSM most in need of HIV testing and prevention, says Smith. Among racial/ethnic groups, black MSM with HIV were least likely to be aware of their infection (59% unaware, compared to 46% for Hispanic MSM and 26% for white MSM).[1]

While those gay and bisexual men under age 30 had lower HIV prevalence than older men, they were far more likely to be unaware of their HIV infection, states Smith. Among MSM ages 18-29 who had HIV, nearly two-thirds (63%) were unaware of their status, versus 37% for men age 30 and older.

Among young gay and bisexual men, young MSM of color were less likely than whites to know they were HIV-infected. Among HIV-infected black MSM under age 30, 71% were unaware of their infection; among HIV-infected Hispanic MSM under age 30, 63% were unaware. This compares to 40% of HIV-infected white gay and bisexual in the same age group, says Smith.

The study's finding of low awareness of HIV

status among young MSM is not surprising. CDC officials note several factors might lead to low awareness among young men, who might:

- have been infected more recently;
- underestimate their personal risk;
- have had fewer opportunities to get tested; or
- believe that advances in HIV treatment minimize the threat of HIV.

For young gay and bisexual men of color, discrimination and socioeconomic factors such as poverty, homophobia, stigma, and limited health-care access might present obstacles to testing and care, CDC officials say. Jonathan Mermin, MD, director of CDC's Division of HIV/AIDS Prevention, in a statement accompanying the new research, said, "For young men who have sex with men — including young men of color who are least likely to know they may be infected — the future is truly on the line. It is critical that we reach these young men early in their lives with HIV prevention and testing services and continue to make these vital services available as they become older."

Testing is the key

The CDC estimates that the majority of new sexually transmitted infections are transmitted by individuals who are unaware of their infection, and studies show that once people learn they are HIV-infected, most take steps to protect their partners. Because undiagnosed infection likely plays a major role in HIV transmission, reaching younger MSM with regular HIV testing is critical, CDC officials state.

The CDC recommends that gay and bisexual men of all ages get tested for HIV at least annually, or more often (every three to six months) if they are at increased risk, such as those with multiple or anonymous sex partners, or who use drugs during sex.[2] Such stepped-up testing is imperative. In the current CDC study, 45% of HIV-infected MSM who were unaware of their infection had been tested in the past year, says Smith.

In April 2010, the agency announced a new three-year, $31.5 million expansion of its testing initiative. Funding for the new phase of the initiative is expected to total approximately $142.5 million over the next three years and will be provided to state and local health departments across the country to increase access to testing and early diagnosis of HIV. The initiative, originally designed to increase testing and knowledge of HIV status primarily among African-American men and women, will now reach more U.S. jurisdictions and populations at risk. These include gay and bisexual men, as well as male and female Latinos and injection drug users.

Smith says, "Here at CDC, HIV prevention for MSM of all races remains a top priority. Supporting HIV testing has long been a critical part of our testing efforts, and the recent three-year, multi-million dollar expansion of our successful HIV testing initiative will enable us to target our testing efforts to increase access to HIV testing and diagnosis of HIV to even more individuals at highest risk, including gay and bisexual men."

REFERENCES

1. Centers for Disease Control and Prevention. Prevalence and awareness of HIV infection among men who have sex with men — 21 cities, United States, 2008. *MMWR* 2010;59:1201-1207.
2. CDC. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR* 2006;*55*:RR-14. ■

FDA Notifications

Tessamorelin approved for lipodystrophy

On Nov. 10, 2010, the Food and Drug Administration (FDA) approved tessamorelin (Egrifta®) to treat HIV patients with lipodystrophy, a condition in which excess fat develops in different areas of the body, most notably around the liver, stomach, and other abdominal organs (visceral body fat).

The condition is associated with many antiretroviral drugs used to treat HIV. Egrifta was approved to induce and maintain a reduction of excess visceral abdominal fat in HIV-infected patients with lipodystrophy.

Tessamorelin, the first FDA-approved treatment for lipodystrophy, is a synthetic growth hormone releasing factor (GRF) drug that is administered in a once-daily injection.

The presence of excess visceral fat accumulations associated with this condition may contribute to other health problems as well as affect

a patient's quality of life. Whether tessamorelin decreases the risk of cardiovascular disease or improves compliance with antiretroviral drugs has not been studied.

Tessamorelin was evaluated in two clinical trials involving 816 HIV-infected adult men and women with lipodystrophy and excess abdominal fat. Of these, 543 patients received tessamorelin during a 26-week, placebo-controlled period. In both studies, patients treated with tessamorelin experienced greater reductions in abdominal fat (15 - 17%) as measured by CT scan, compared with patients receiving another, non-active injectable solution (placebo). Some patients reported improvements in their self-image.

The most commonly reported side effects in the studies included joint pain (arthralgia), skin redness and rash at the injection site (erythema and pruritus), stomach pain, swelling, and muscle pain (myalgia). Worsening blood sugar control occurred more often in patients treated with Egrifta than with placebo.

Tessamorelin was developed by Montreal-based Theratechnologies Inc. and marketed in the U.S. by Rockland, Massachusetts-based EMD Serono. Product labeling for Egrifta will be made available soon on Drugs@FDA. ■

Pediatric abacavir tablets approved

On Nov. 29, 2010, the Food and Drug Administration granted tentative approval for a formulation of abacavir sulfate tablets, 60 mg, made by Matrix Laboratories Limited of Hyberdad, India, indicated for use in combination with other antiretrovirals for the treatment of HIV-1 infection. The tablet formulation is intended for pediatric use, allowing dosing for patients weighing as little as 5kg, and is unique in that it can be dispersed in liquid for patients unable to swallow tablets.

FDA's tentative approval means that although a product meets all of the safety, efficacy, and manufacturing quality standards required for marketing in the U.S., existing patents and/or proprietary issues currently prevent marketing of the product in the United States. Tentative approval, however, does qualify the product for consideration for purchase under the President's Emergency Plan for AIDS Relief, or PEPFAR program.

As with all applications, FDA conducts an on-site inspection of the manufacturing facilities and of the facilities performing the bioequivalence studies prior to granting approval or tentative approval to evaluate the ability of the manufacturer to produce a quality product and to assess the quality of the bioequivalence data supporting the application. ■

Nominations open for Antiviral drug panel

The Food and Drug Administration (FDA), to assist in its mission to protect and promote the public health, uses 49 committees and panels to obtain independent expert advice on scientific, technical, and policy matters.

The FDA is seeking technically qualified medical/scientific consultants to serve as members of its Antiviral Drugs Advisory Committee for future panels to consider potential direct-acting antivirals (DAAs) for the treatment of hepatitis C — specifically hepatologists or other medical doctors who treat a substantial number of hepatitis C patients. Consultants should have experience interpreting and analyzing detailed scientific data, and understand its public health significance.

Potential candidates will be required to provide detailed information concerning such matters as financial holdings, employment, and research grants and/or contracts to permit evaluation of possible sources of conflict of interest. Potential conflicts include, but may not be limited to: employment with a pharmaceutical sponsor, having financial interests or stock in pharmaceutical companies developing DAAs, participating as an investigator in pivotal studies of DAAs in development, being chair of a department in which colleagues are investigating a DAA, or receiving substantial amounts of reimbursement from DAA sponsors for consulting services or presentations.

Advisory Committee meetings are convened in the Washington D.C. metropolitan area, typically for two days twice a year. Committee members are appointed as Special Government Employees, and receive a salary for each meeting day as well as travel and per diem costs.

General information about FDA Advisory Committees can be found at http://www.fda.gov/AdvisoryCommittees/default.htm and information about membership can be found at http://www.fda.gov/AdvisoryCommittees/AboutAdvisoryCommittees/

CommitteeMembership/default.htm.

If you are a medical doctor meeting the criteria above, or would like to nominate a medical doctor with hepatitis C expertise, You may submit your information by:

E-mail to cv@oc.fda.gov or mail to:

Food and Drug Administration;

Advisory Committee Oversight and Management Staff;

10903 New Hampshire Avenue, Bldg. 32, Rm. 5101;

Silver Spring, Maryland 20993-0002.

Please include full contact information of any person you are nominating. ■

CDC issues STD treatment update

Updated information on HIV, STDs

The Centers for Disease Control and Prevention has released new guidelines for the treatment of persons who have or are at risk for sexually transmitted diseases (STDs).[1]

Published Dec. 17, 2010, the guidelines were updated by CDC after consultation with a group of professionals knowledgeable in the field of STDs who met in Atlanta on April 18–30, 2009. The information in the report updates the 2006 Guidelines for Treatment of Sexually Transmitted Diseases. Included in the updated guidelines is new information regarding:

1) the expanded diagnostic evaluation for cervicitis and trichomoniasis;

2) new treatment recommendations for bacterial vaginosis and genital warts;

3) the clinical efficacy of azithromycin for chlamydial infections in pregnancy;

4) the role of Mycoplasma genitalium and trichomoniasis in urethritis/cervicitis and treatment-related implications;

5) lymphogranuloma venereum proctocolitis among men who have sex with men;

6) the criteria for spinal fluid examination to evaluate for neurosyphilis;

7) the emergence of azithromycin-resistant Treponema pallidum;

8) the increasing prevalence of antimicrobial-resistant Neisseria gonorrhoeae; 9) the sexual transmission of hepatitis C;

10) diagnostic evaluation after sexual assault; and

11) STD prevention approaches.

CNE/CME QUESTIONS

1. The first published study of a pre-exposure prophylaxis combination drug given orally to men and transgender women who have sex with men demonstrated what percentage of additional protection from HIV infection?
A. 28%
B. 34%
C. 44%
D. 59%

2. A recent study reports that the percentage of people who have been tested for HIV was 38.7% in 2008. In 2000, that percentage was which amount?
A. 29%
B. 40%
C. 45%
D. 48%

3. The U.S. Food and Drug Administration recently approved a new HIV test, called the INSTI™ rapid HIV antibody test, that can produce accurate results within how many minutes?
A. 1 minute
B. 5 minutes
C. 8 minutes
D. 10 minutes

Answers: 1. C; 2. D; 3. A

COMING IN FUTURE MONTHS

- HIV domestic funding outlook reviewed
- Fracture rate increasing among HIV patients
- Global HIV update shows stabilized epidemic
- Special focus: Women with HIV

The guidelines reiterate that early diagnosis of HIV infection is essential to ensuring that patients are referred promptly for evaluation, provided treatment (if indicated), and linked into counseling and related support services to help them reduce their risk for transmitting HIV to others. Diagnosing persons during acute infection is particularly important. It is during this phase that HIV-infected persons are most infectious, but test negative for HIV antibodies and therefore unknowingly continue to engage in those high-risk behaviors associated with HIV transmission.

Providers are in a particularly good position to diagnose persons during acute HIV infection because such persons might present for assessment and treatment of a concomitantly acquired STD during this phase of the disease. Knowing that a patient is infected with HIV has important clinical implications because HIV infection alters the immune system and thereby affects the diagnosis, evaluation, treatment, and follow-up of other STDs, the CDC reports.

REFERENCE

1. Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines, 2010. *MMWR* 2010;59(RR12):1-110. ■

CNE/CME OBJECTIVES

The CNE/CME objectives for AIDS Alert, are to help physicians and nurses be able to:
• Identify the particular clinical, legal, or scientific issues related to AIDS patient care;
• Describe how those issues affect nurses, physicians, hospitals, and clinics;
• Cite practical solutions to the problems associated with those issues.

Physicians and nurses participate in this medical education program by reading the issue, using the provided references for further research, and studying the questions at the end of the issue.

Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any question answered incorrectly, please consult the source material.

After competing this activity at the end of each semester, you must complete the evaluation form provided and return it in the reply envelope provided to receive a letter of credit. When your evaluation is received, a letter of credit will be mailed to you.