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IN THIS ISSUE

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FDA updates study data information on Ortho Evra contraceptive patch labeling

Earlier data on venous thromboembolism risk supported

The Food and Drug Administration (FDA) has revised labeling on the contraceptive patch (Ortho Evra, Ortho-McNeil-Janssen Pharmaceuticals; Raritan, NJ) to include new epidemiology data on the risks of venous thromboembolism (VTE).

News about the increased risk of VTE is not new. Clinicians have counseled women about such risks since the FDA moved in November 2005 to add an addition to the drug's warning label that the patch exposes women to higher levels of estrogen. In September 2006, the Ortho Evra label reported the results of two epidemiologic studies designed to evaluate the risk of VTE in Ortho Evra users.[1,2] One study found that the risk of nonfatal VTE events associated with use of the patch was similar to the risk associated with the use of oral contraceptives (OCs), while the other study showed an approximate twofold increase in the risk of VTE events in patch users compared to OC users. ***(Contraceptive Technology Update* reported on the revised labeling in the articles "FDA revises Evra safety labeling**

EXECUTIVE SUMMARY

Labeling for the contraceptive patch, Ortho Evra, has just been revised to include new epidemiology data on the risks of venous thromboembolism (VTE).

- In September 2006, the drug's label was revised to include results of two epidemiologic studies. One found the risk of nonfatal VTE events associated with patch use was similar to the risk with oral contraceptives (OCs), while the other study showed an approximate twofold increase in the risk of VTE events in patch users compared to OC users.
- The labeling now includes results of a third epidemiologic study, as well as additional information from one of the original studies. The third study shows an increased risk for VTE among patch users compared to those taking OCs.

due to increased estrogen levels," January 2006, p. 1; and "New methods gain favor with women, but Pill use remains strong," November 2006, p. 121.)

The new labeling now includes results of a third epidemiologic study, as well as additional information on the risk of VTE in Ortho Evra users from one of the original studies, based on 17 months of data on new cases.[3,4] Results from the third study shows an increased risk for VTE among patch users compared to those taking OCs.[3]

"For women that choose to use contraceptives, it is important that they thoroughly discuss with their health care providers the risks and benefits involved," says **Janet Woodcock**, MD, the FDA's deputy commissioner for scientific and medical programs, chief medical officer, and acting director of the Center for Drug Evaluation and Research. "This is an example of FDA working in tandem with the drug manufacturer to keep the public informed of new safety data and epidemiological studies that may impact health decisions about the use of FDA-approved products."

Look at the data

The studies quoted in the Ortho Evra labeling all are epidemiological studies designed to evaluate the risk of developing a serious blood clot in women using the patch compared to women using different commonly prescribed, oral contraceptives containing 30-35 mcg of the estrogen ethinyl estradiol and one of two progestins: norgestimate or levonorgestrel. While the studies were conducted using data from electronic health care claims, they were not structured in exactly the same way, and results of the studies are different, notes the FDA.

The first study, conducted by the Boston Collaborative Drug Surveillance Program, found that the risk of nonfatal VTE events associated with the use of the Ortho Evra contraceptive patch is similar to the risk associated with the use of OCs containing 35 mcg ethinyl estradiol and the progestin norgestimate [OR, 0.9; 95% confidence interval (CI), 0.5-1.6].[1] Analysis of 17 months of data on new cases not included in the original report showed a similar finding (OR, 1.1; 95% CI, 0.6-2.1).[4]

The second study, which included review of patients' charts, was conducted by i3 Ingenix, another group of investigators.[2] Results of this study showed an approximately twofold increase in the risk of medically verified VTE events in users of Ortho Evra compared to users of OCs containing 35 mcg estrogen and the progestin norgestimate (OR, 2.4; 95% CI, 1.1-5.5).

The third study, also conducted by BCDSP, compared the risk of nonfatal VTE events among users of Ortho Evra to the risk among users of OCs containing 30 mcg ethinyl estradiol and the progestin levonorgestrel.[3] The results showed an approximate

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Editorial Questions

Questions or comments?
Call **Joy Daughtery Dickinson** (229) 551-9195.

twofold increase in the risk of VTE among the Ortho Evra users (OR, 2.0; 95% CI, 0.9-4.1).

Patch use falling off?

Use of the contraceptive patch is experiencing a drop, according to results from *CTU*'s annual Contraception Survey. In 2007, about 84% of survey participants said their facility offered the method, compared to about 88% in 2006. About 93% of participants indicated the method was in use in 2005.

What has led to the decrease? While the product's labeling changes may have affected use for some women, price may be a factor as well. Clinics that no longer qualify for nominal pricing under the federal 340B Drug Pricing Program might not be able to stock the patch, due to increased costs. **(See the articles, "Student health centers look for price relief," *CTU*, March 2008, p. 31; and "Student health centers scramble due to prices," April 2007, p. 40.)**

A chief benefit of the contraceptive patch lies in its ease of use, because women are no longer tied to taking a daily pill. To use the method, a woman applies a new patch each week for three weeks, with a fourth week being a patch-free week.

Similar convenience is afforded through use of the contraceptive vaginal ring (NuvaRing, Organon USA; Roseland, NJ). To use the method, a woman inserts the ring into the vagina, where it remains for three weeks. The fourth week is ring-free.

While previous studies have directly compared clinical outcomes with use of the patch and combined OCs, as well as the ring and combined pills, the two methods have never been directly compared. Results of a new study that compares use of the patch vs. the ring indicate that women satisfied with combined oral contraceptives and interested in a nondaily method are more likely to continue using the ring than the patch.[5]

To conduct the study, 500 women who were using OCs were randomized to use the ring or the patch, starting with their next menstrual cycle and continuing for four consecutive menstrual cycles. During the fourth cycle, women returned for a single follow-up visit and evaluation.

For users of the contraceptive ring, rate of completion of three cycles was 94.6% (95% confidence interval [CI], 91-97.1%), compared to 88.2% (95% CI, 83.4-92%) for those assigned to the patch (P = 0.03). Of these women, 71% of ring users (95% CI, 64.8-76.6%) and 26.5% of patch users (95% CI, 21-32.6%) planned to continue their assigned method after study completion (P < 0.001).

Compared with women switching to the ring, those switching to the patch were more likely to experience longer menstrual cycles, increased dysmenorrhea, nausea, mood swings, and skin rash. They were less likely to report frequent vaginal discharge. Ring users required less provider time for telephone consultations compared to patch users.

"These findings do not imply that all women using a combined OC should be counseled to switch to a ring," the study authors conclude. "However, the information from this study can help health care providers counsel women who desire a nondaily combined hormonal contraceptive method."

References

1. Jick SS, Kaye JA, Russmann S, et al. Risk of nonfatal venous thromboembolism in women using a contraceptive transdermal patch and oral contraceptives containing norgestimate and 35 mcg of ethinyl estradiol. *Contraception* 2006; 73:223-228.

2. Cole JA, Norman H, Doherty M, et al. Venous thromboembolism, myocardial infarction, and stroke among transdermal contraceptive system users. *Obstet Gynecol* 2007; 109(2 Pt 1):339-346.

3. Boston Collaborative Drug Surveillance Program. Postmarketing study of ORTHO EVRA and levonorgestrel oral contraceptives containing hormonal contraceptives with 30 mcg of EE in relation to nonfatal venous thromboembolism, ischemic stroke and myocardial infarction. Accessed at www.clinicaltrials.gov/ct2/show/NCT00511784.

4. Jick S, Kaye JA, Li L, et al. Further results on the risk of nonfatal venous thromboembolism in users of the contraceptive transdermal patch compared to users of oral contraceptives containing norgestimate and 35 microg of ethinyl estradiol. *Contraception* 2007; 76:4-7.

5. Creinin MD, Meyn LA, Borgatta L, et al. Multicenter comparison of the contraceptive ring and patch: A randomized controlled trial. *Obstet Gynecol* 2008; 111:267-277. ■

Questions raised about mifepristone manufacturer

Patients seeking medication abortion using mifepristone (Mifeprex, Danco Group) may be asking questions after news agencies reported leukemia drug safety issues at a Chinese drug manufacturing firm that serves as the sole U.S. supplier of mifepristone.

Nearly 200 Chinese cancer patients were paralyzed or otherwise harmed in the summer of 2007

EXECUTIVE SUMMARY

Questions about the abortion drug mifepristone have arisen after reports of leukemia drug safety issues at a Chinese drug manufacturing firm that serves as the sole U.S. supplier of mifepristone.

- Chinese drug regulators have closed the Shanghai Hualian factory that produced the drugs and are conducting an investigation into the matter.
- According to the U.S. distributor, mifepristone is manufactured in a mifepristone-only factory and is not subject to cross-contamination from other drugs. Samples of each lot of the drug are checked by a third-party laboratory, inspected by the Food and Drug Administration (FDA), before the product is released in the United States.
- The plant in which mifepristone is manufactured most recently was inspected by the FDA in May 2007. The plant passed regulatory inspection.

by contaminated leukemia drugs linked to Shanghai Hualian, the Chinese manufacturer. Shanghai Hualian is a division of the Shanghai Pharmaceutical Group, one of China's largest pharmaceutical companies. Chinese drug regulators have closed the factory that produced the drugs and are conducting an investigation into the matter.[1]

Danco Group of New York City serves as the sole U.S. distributor of mifepristone, which is marketed as Mifeprex. According to **Abby Long**, MPH, Danco's director of marketing and public affairs, the plant in which mifepristone is manufactured most recently was inspected by the Food and Drug Administration (FDA) in May 2007. The plant passed inspection, says Long.

Mifepristone is manufactured in a mifepristone-only factory and is not subject to cross-contamination from other drugs, states Long. In addition, Danco submits samples of each lot to a third-party FDA-inspected laboratory before the product is released in the United States, she reports.

Rep. Henry Waxman (D-CA), chairman of the Committee on Oversight and Government Reform, has called for the FDA to share its plans for continuing to ensure the safety of drugs manufactured for the United States by Shanghai Pharmaceutical Group.[2] Planned Parenthood Federation of America (PPFA) has joined Waxman in the request for FDA action.[3]

"We, along with the rest of the public health community, look to the FDA to ensure that all drugs entering the United States are safe and effective," said **Vanessa Cullins**, MD, PPFA vice president of medical affairs, in a statement on the request. "We expect the FDA to fulfill its mission and provide information on and assurances for continued monitoring in the upcoming briefing with Rep. Waxman."

In an open letter to Planned Parenthood clients, Cullins acknowledges that some patients may have questions about mifepristone medication abortion as a result of the news reports.[4] "As a trusted reproductive health care provider, Planned Parenthood closely monitors patient experiences to ensure the highest standard of care," Cullins states in the letter. "Our monitoring shows that mifepristone medication abortion continues to be a safe abortion option."

Method gains ground

Mifepristone gained FDA approval in September 2000 as an alternative to surgical abortion. ***(Contraceptive Technology Update* reported on the approval in the article, "Mifepristone approval won't remedy the abortion restrictions you face," December 2000, p. 141.)** Use of the medication method has grown since its approval: In 2005, 57% of abortion providers, or 1,026 facilities, provided one or more medication abortions, a 70% increase from the first half of 2001.[5] According to a Guttmacher Institute report, medication abortion in 2005 accounted for 13% of all abortions and 22% of abortions before nine weeks' gestation.[5]

Safety information for the Mifeprex label was revised in 2005 after reports of deaths from serious bacterial infection and sepsis following use of the mifepristone/misoprostol medication abortion regimen. Since mifepristone's U.S. approval, the FDA has been informed of six deaths in the United States due to serious infections following medical abortion with mifepristone and misoprostol. Five cases were found to involve infection with the bacteria, *Clostridium sordellii,* and one case involved infection with *Clostridium perfringens*. While sepsis is a known risk related to any type of abortion, the symptoms in all of the cases were not the usual symptoms associated with the disease state. In all but one case, misoprostol was used intravaginally.[6]

Reports of fatal sepsis in women undergoing medical abortion are very rare — about one in 100,000, according to the FDA. **(Review the postmarketing history of Mifeprex in the following *CTU* articles: "Mifepristone ruled out in one of**

two deaths," June 2006, p. 68; "Fatal infection caused death in Mifeprex cases," February 2006, p. 20; "Mifepristone label gets new safety information," October 2005, p. 115; "Update: FDA strengthens mifepristone labeling," March 2005, p. 33; and "Medical abortion update: Death sparks questions on abortion pill," December 2003, p. 133.)

References

1. Hooker J, Bogdanich W. Tainted drugs tied to maker of abortion pill. *The New York Times*. Jan. 31, 2008. Accessed at www.nytimes.com/2008/01/31/world/asia/31pharma.html?ref=health.
2. Waxman H. Letter to Dr. Andrew von Eschenbach. Accessed at oversight.house.gov/documents/20080201162401.pdf.
3. Planned Parenthood Federation of America. Planned Parenthood Calls on FDA to Ensure Continued Patient Safety. Press release. Accessed at www.plannedparenthood.org/planned-parenthood-calls-on-fda-19140.htm.
4. Cullins V. *Open Letter to Planned Parenthood Clients From PPFA Vice President of Medical Affairs Vanessa Cullins.* Accessed at www.plannedparenthood.org/mifepristone-medication-abortion-services-at-planned-parenthood.htm.
5. Jones RK, Zolna MRS, Henshaw SK, et al. Abortion in the United States: Incidence and access to services, 2005. *Perspect Sex Reprod Health* 2008; 40:6-16.
6. Food and Drug Administration. Questions and Answers on Mifeprex (mifepristone). August 2007. Fact sheet. Accessed at www.fda.gov/Cder/Drug/infopage/mifepristone/qa2007.htm. ■

More data emerge on circumcision's impact

EXECUTIVE SUMMARY

Data released at a recent international conference suggest that adult male circumcision, which has been looked upon as a possible means of reducing the risk of HIV transmission in Africa, could raise the risk for women there whose male partners seek the procedure after they are infected.

- In another study presented at the conference, researchers found that women whose male partners were circumcised while HIV-negative had a 25% lower rate of infection with genital herpes.
- That same study found a 50% reduction in trichomoniasis and a 20% reduction in bacterial vaginosis.

Data released at a recent international conference suggest that adult male circumcision, which has been seen as possibly reducing the risk of HIV transmission in Africa, could raise the risk for women there whose male partners seek the procedure after they are infected.[1]

In another study reviewed at the 15th annual Conference on Retroviruses and Opportunistic Infections (CROI) in Boston, researchers found that women whose male partners were circumcised while HIV-negative had a 25% lower rate of infection with genital herpes, a 50% reduction in trichomoniasis, and a 20% reduction in bacterial vaginosis.[2]

Interest in male circumcision as a possible preventive tool against HIV has been heightened after data from three randomized controlled trials undertaken in Kisumu, Kenya; Rakai District, Uganda; and Orange Farm, South Africa indicated that the procedure reduces the risk of heterosexually acquired HIV infection in men by about 60%.[3-5] In light of the evidence, the World Health Organization (WHO) in March 2007 added the procedure to its list of recommended AIDS prevention measures.[6] ***(Contraceptive Technology Update*** **reported on the data in the articles "Adult male circumcision reduces risk for HIV," March 2007, p. 31; and "Male circumcision and HIV prevention: Method can dramatically reduce risk, study says,"** ***STD Quarterly*****, October 2005, supplement, p. 1. Coverage of the WHO recommendation was reported in the article, "New recommendations out on HIV & circumcision," June 2007, p. 67.)**

Wound healing key

If male circumcision reduces HIV acquisition in men, what impact does it have for their female partners? Scientists reporting at the CROI conference reviewed the results of their trial, conducted among HIV-positive men and designed to assess HIV transmission to their partners.[1]

Researchers randomized 1,015 HIV-positive African men to undergo immediate male circumcision or a delayed procedure 24 months later. Married men were asked to invite their spouses; 566 wives enrolled, with 43% of that group reporting HIV-negative status. Participants provided written consent; were given information on HIV prevention, wound care, and abstention from sex postoperatively; and were offered free condoms and couples counseling and testing.[1]

The annual HIV incidence rate in the wives of the men who were circumcised was 14.4% over

two years of follow-up compared with 9.1% in women whose partners remained uncircumcised.

While the difference between these two groups was not statistically significant, scientists did not see a trend toward protection. The take-home message is that the data do suggest, but don't prove, that if couples undertake sexual intercourse before circumcision wound healing is complete, there is risk for transmission, says **Maria Wawer**, MD, MHS, professor in the Bloomberg School of Public Health at Johns Hopkins University (JHU). "In our trial of HIV-negative men, we found that the protective effect of HIV circumcision for men was really not particularly pronounced in the first period after circumcision; we started to see a significant effect six or more months after circumcision," says Wawer. "It suggests whether or not a man is positive or negative, it makes sense not to undertake intercourse before the wound is fully healed."

Plus for vaginal health

What is circumcision's role in prevention of herpes simplex 2 (HSV-2) in men and vaginal infections in women?

To determine the method's efficacy, researchers randomized men to undergo immediate male circumcision or delay circumcision for two years. A total of 2,787 HSV-2-negative men were followed for 24 months to determine HSV-2 acquisition. Married women were linked to enrolled men, with 825 wives of circumcised men and 783 wives of delayed-procedure men were followed at one year to assess genitourinary disease (GUD), bacterial vaginosis (BV), and trichomonas.[2]

Data indicate that male circumcision prevents HSV-2 acquisition in men and reduces rates of GUD, trichomonas, and BV in their female partners. These effects of circumcision may influence the protective effect of circumcision on HIV acquisition, the researchers conclude.[2]

What is the next step in research, given that scientists recorded a positive impact of circumcision in improving the vaginal health of women? "We will assess the effects of circumcision on female HPV infection and continue to monitor all female partners of trial participants to assess long-term HIV effects," says **Aaron Tobian**, MD, PhD, a member of the JHU Rakai research team and lead author of the paper.

References

1. Wawer M, Kigozi G, Serwadda D, et al. Trial of male circumcision in HIV+ men, Rakai, Uganda: Effects in HIV+ men and in women partners. Presented at the 15th Conference on Retroviruses and Opportunistic Infections. Boston; February 2008.

2. Tobian A, Serwadda D, Quinn T, et al. Trial of male circumcision: Prevention of HSV-2 in men and vaginal infections in female partners, Rakai, Uganda. Presented at the 15th Conference on Retroviruses and Opportunistic Infections. Boston; February 2008.

3. Bailey C, Moses S, Parker CB, et al. Male circumcision for HIV prevention in young men in Kisumu, Kenya: A randomized controlled trial. *Lancet* 2007; 369:643-656.

4. Gray H, Kigozi G, Serwadda D, et al. Male circumcision for HIV prevention in young men in Rakai, Uganda: A randomized trial. *Lancet* 2007; 369:657-666.

5. Auvert B, Taljaard D, Lagarde E, et al. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: The ANRS 1265 Trial. *PLoS Med* 2005; 2:e298.

6. World Health Organization/UNAIDS. *New Data on Male Circumcision and HIV Prevention: Policy and Programme Implications. Conclusions and Recommendations*. Montreux, Switzerland; March 2007. Accessed at www.who.int/entity/hiv/mediacentre/MCrecommendations_en.pdf. ■

New analysis confirms OC's protective effects

Good news for your patients who use oral contraceptives (OCs): A new analysis of 45 epidemiological studies shows that use of such pills during a woman's lifetime gives substantial long-term protection against ovarian cancer.[1]

Researchers looked at data from 23,257 women with ovarian cancer, 7,308 (31%) of whom had

EXECUTIVE SUMMARY

A new analysis of 45 epidemiological studies shows that use of oral contraceptives (OCs) during a woman's lifetime gives substantial long-term protection against ovarian cancer.

- Researchers looked at data from 23,257 women with ovarian cancer, 31% of whom had ever used OCs, and 87,303 women without ovarian cancer, of whom 37% had ever used the Pill. In women with ovarian cancer, mean age of diagnosis was 56 years. Those who had used contraceptives had done so for an average of 4.4 years in the ovarian cancer group and 5.0 years in the control group.
- The Pill's protection against ovarian cancer persisted for more than 30 years after oral contraceptive use had ceased, but it became somewhat attenuated over time.

ever used OCs, and 87,303 women without ovarian cancer, of which 32,717 (37%) had ever used the Pill. In women with ovarian cancer, mean age of diagnosis was 56 years. Those who had used contraceptives had done so for an average of 4.4 years in the ovarian cancer group and 5.0 years in the control group.

The researchers found that the Pill's protection against ovarian cancer persisted for more than 30 years after oral contraceptive use had ceased, but became somewhat attenuated over time. The proportional risk reductions per five years of use were 29% [95% confidence interval (CI) 23-34%)] for use that had ceased less than 10 years previously, 19% (14%-24%) for use that had ceased 10-19 years previously, and 15% (9%-21%) for use that had ceased 20-29 years previously. The analysis findings indicate the longer OCs were used, the greater the protection.

What does this mean for women in the United States? According to the researchers' estimates, in high-income countries, using oral contraceptives for 10 years reduces the risk of developing ovarian cancer before age 75 from 12 down to eight per 1,000 women and lowers the risk of death from ovarian cancer before age 75 from seven down to five per 1,000 women.

Worldwide, the Pill already has prevented 200,000 women from developing cancer of the ovary and has prevented 100,000 deaths from the disease, notes **Valerie Beral**, MD, director of the Cancer Research UK Epidemiology Unit at Oxford (England) University and lead author of the analysis. "More than 100 million women are now taking the Pill, so the number of ovarian cancers prevented will rise over the next few decades to about 30,000 per year," states Beral.

Does dose matter?

Check the pill formulations offered in your clinic's formulary: Chances are that there are few, if any, pills with a 50 mcg dose of estrogen.

Estrogen doses in oral contraceptives have decreased significantly over the years. Preparations in the 1960s typically contained more than double the estrogen dose of preparations in the 1980s. Despite the variations in pill formulations, the current analysis found no apparent variation in the relative risk of ovarian cancer between women whose oral contraceptive use was during the 1960s, 1970s, or 1980s.

Researchers also found that risk reduction did not vary substantially by women's ethnicity, education, age of menarche, family history of breast cancer, use of hormone replacement therapy, body mass index, height, or consumption of alcohol or tobacco.

Pill offers protection

In the United States, about one-fifth (19%) of women ages 15-44, and about one-third (32%) of those ages 20-24, use the Pill.[2] What does the analysis's findings mean for your patients? Since oral contraceptives help to prevent ovarian malignancy in high- as well as low-risk women, consider Pill use in women at elevated risk for ovarian cancer, including low-parity women and those with a positive family history, says **Andrew Kaunitz**, MD, professor and associate chair in the Obstetrics and Gynecology Department at the University of Florida College of Medicine — Jacksonville.

An accompanying editorial published with the analysis questions whether OCs should be provided over the counter, given their protective benefits. **Eduardo Franco**, MPH, DrPH, professor of epidemiology and oncology director of the Division of Cancer Epidemiology at McGill University in Montreal, Quebec, says providing OCs is a great opportunity for health care providers to give women other health promotion messages that are crucial for them, such as providing cervical cancer screening and tobacco cessation aids. Allowing women to obtain the Pill over the counter would remove this opportunity, says Franco, who co-authored a comment for the current analysis.[3]

"We now know that OCs are safer than what we painted them to be and as such we should make them available without the hesitations of the past," Franco states. "However, if we consider the underprivileged populations in Latin America and Africa, we must keep in mind the totality of benefits that seeing a provider will bring to these women."

References

1. Collaborative Group on Epidemiologic Studies of Ovarian Cancer. Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23,257 women with ovarian cancer and 87,303 controls. *Lancet* 2008; 371:303-314.

2. Chandra A, Martinez GM, Mosher WD, et al. Fertility, family planning, and reproductive health of U.S. women: Data from the 2002 National Survey of Family Growth. *Vital Health Stat* 2005; 23:1-160.

3. Franco EL, Duarte-Franco E. Ovarian cancer and oral contraceptives. *Lancet* 2008; 371:277-278. ■

Radar is up for new multidrug-resistant MRSA

A multidrug-resistant variant of community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) bacteria is emerging in cities on both coasts of the United States, according to data from a new California-led study.[1]

The research is based on information collected from MRSA cases from nine of 10 medical centers serving San Francisco and medical records from outpatients with MRSA infections who were treated in an HIV clinic in San Francisco and a clinic serving a predominantly lesbian/gay/bisexual/transgender population in Boston.

The research suggests that men who have sex with men were at higher risk for infection with a multidrug-resistant variant of the MRSA USA300 bacteria. In the current study, specific sexual behaviors were not assessed or documented in clinic charts, so researchers cannot comment on the association between multidrug-resistant USA300 infection and specific male-male sexual practices, says **Binh Diep**, PhD, a University of California at San Francisco (UCSF) postdoctoral scientist and lead author of the report.

"We are currently conducting several prospective studies to identify if any specific sexual behaviors may be correlated with multidrug-resistant USA300," says Diep.

EXECUTIVE SUMMARY

A multidrug-resistant variant of community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) bacteria is emerging on both U.S. coasts, according to a new study.

- The research is based on MRSA cases from nine of 10 medical centers serving San Francisco and medical records from patients with MRSA infections who were treated in a San Francisco HIV clinic and a Boston clinic serving a predominantly lesbian/gay/bisexual/transgender population.
- The research suggests that men who have sex with men were at higher risk for infection with a multidrug-resistant variant of the MRSA USA300 bacteria. Specific sexual behaviors were not assessed or documented in clinic charts, so researchers cannot comment on the association between multidrug-resistant USA300 infection and specific male-male sexual practices.

MRSA is a common cause of skin infections throughout the United States, according to the Centers for Disease Control and Prevention (CDC). These infections occur in men, women, adults, children, and persons of all races and sexual orientations, and they are known to be transmitted by close skin-to-skin contact.

Concern has arisen concerning drug-resistant strains of MRSA. While evidence of the USA300 strain was not seen before 2000, it is now widely disseminated in 38 U.S. states, Canada, and nine European Union countries.[1] This strain can cause unusually severe human diseases, including necrotizing fasciitis, sepsis, endocarditis, and pneumonia.[1] The spread of this multidrug-resistant MRSA into communities was first reported by the UCSF team in 2006.[2]

Is it an STD?

Can this strain of MRSA be considered a sexually transmitted disease (STD)? Evidence is not available to determine whether *S. aureus*, including MRSA, is a sexually transmitted infection as judged by the classic criteria of sex as a predominant mode of transmission and transmission through genital, anal, or oral mucosal contact, notes an accompanying commentary to the current paper.[3]

The *Staphylococcus aureus* bacterium is transmitted primarily by direct skin-to-skin contact, which includes skin-to-skin contact during sexual activity. While the buttocks and groin area can be a site for MRSA infection, it does not imply sexual transmission, notes **Kim Workowski**, MD, chief of the guidelines unit in the epidemiology and surveillance branch of the CDC's Division of STD Prevention and a commentary co-author. While contact of these infected areas of skin during sexual activity could result in cutaneous transmission, scientists do not yet know if the mucosal contact that can occur with specific sexual practices imparts an independent risk for transmission, she states.

MRSA is resistant to the antibiotic methicillin and closely related drugs, while the variant studied in the new research is resistant to several other antibiotics, which makes it more difficult to treat. While CDC's monitoring of invasive MRSA indicates that such drug-resistant strains are rare, the agency continues to check resistance patterns and strain characteristics in MRSA isolates submitted to the CDC for a variety of investigations.

How can clinicians help in stemming the

spread of infection? Provide the following educational tips to patients to help prevent spreading staph or MRSA skin infections:

• **Cover your wound.** Keep wounds that are draining or have pus covered with clean, dry bandages.

• **Follow instructions on proper care of the wound.** Pus from infected wounds can contain staph and MRSA, so keeping wounds covered will help prevent the spread to others. Bandages or tape can be discarded with the regular trash.

• **Wash your hands.** You, your family, and others in close contact should wash their hands frequently with soap and warm water or use an alcohol-based hand sanitizer, especially after changing the bandage or touching the infected wounds.

• **Do not share personal items.** Avoid sharing personal items such as towels, washcloths, razors, clothing, or uniforms that may have had contact with infected wounds or bandages. Wash sheets, towels, and clothes that become soiled with water and laundry detergent. Drying clothes in a hot dryer, rather than air-drying, also helps kill bacteria in clothes.

• **Tell any health care providers who treat you that you have or had a staph or MRSA skin infection.**[4]

References

1. Diep BA, Chambers HF, Graber CJ, et al. Emergence of multidrug-resistant, community-associated, methicillin-resistant *Staphylococcus aureus* clone USA300 in men who have sex with men. *Ann Intern Med* 2008; 148:249-257.

2. Diep BA, Gill S, Chang R, et al. Complete genome sequence of USA300, an epidemic clone of community-acquired methicillin-resistant *Staphylococcus aureus*. *Lancet* 2006; 367:731-739.

3. Gorwitz R, Fridkin SK, Workowski KA. More challenges in the prevention and management of community-associated, methicillin-resistant *Staphylococcus aureus* skin disease. *Ann Intern Med* 2008; 148:310-312.

4. Centers for Disease Control and Prevention. CDC Statement on MRSA in Men Who Have Sex with Men. Press release. Jan. 16, 2008. Accessed at: www.cdc.gov/print.do?url=http%3A//www.cdc.gov/od/oc/media/pressrel/2008/t080116.htm. ■

Medicaid expansions drive funding growth

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Federal and state funding for family planning client services reached $1.85 billion in FY 2006, a 63% increase over 12 years, adjusting for inflation.[1] Beneath this national trend, however, lie more disparate ones at the state level. Spending decreased or stagnated in 18 states and the District of Columbia since FY 1994, while it increased dramatically elsewhere. **(See list of 18 states on p. 46.)**

Virtually all of this recent increase in funding has come via the joint federal-state Medicaid program. National Medicaid spending on family planning increased by $775 million, which is nearly 150%, since FY 1994. This continues a decades-long rise in the importance of Medicaid to the provision of family planning services: Medicaid now accounts for 71% of total public funding, up from merely 20% in FY 1980. It also parallels growth in the broader Medicaid program and in U.S. health spending generally.

Although the increasing importance of Medicaid can be seen in states across the country, most of the recent growth in spending reflects a revolution in state policy. Over the past decade, there has been an advent of state programs to expand eligibility for family planning under Medicaid above the income eligibility ceiling for their overall Medicaid program. The 14 states that, by 2006, had initiated one of these income-based Medicaid family planning expansions accounted for two-thirds of the new dollars since the mid-1990s. **(See list of 14 states on p. 46.)**

The funding brought into the family planning system as a result of these expansion programs has translated into more Americans being provided with the contraceptive services they need to help them avoid an unplanned pregnancy. The number of Medicaid family planning clients served in the 14 states with expansions increased by 60% from 2000 to 2005, with more than 1 million new clients and more than three times the rate of increase in the rest of the country. An earlier study found that between 1994 and 2001, the entire family planning clinic system in states with these income-based Medicaid expansions managed to increase their client base by

Family Planning Spending Decreased or Stagnated Since FY 1994

- District of Columbia
- Florida
- Georgia
- Hawaii
- Indiana
- Maine
- Michigan
- Minnesota
- Mississippi
- Missouri
- Montana
- Nevada
- New Hampshire
- New York
- North Dakota
- Ohio
- Texas
- Utah
- Vermont

one-quarter, compared with no increase at all in states without an expansion.[2]

More Medicaid ahead

The importance of Medicaid generally and Medicaid expansions specifically to the public provision of family planning services will no doubt continue to grow. Six additional states (Illinois, Louisiana, Minnesota, Pennsylvania, Texas, and Virginia) have implemented such an expansion since mid-2006, and several others are seeking to do so. Currently, states wishing to initiate an expansion program must go through a cumbersome and uncertain process of applying for and periodically renewing a "waiver" from the standard Medicaid rules.

Legislation pending in Congress, the Unintended Pregnancy Reduction Act, is designed to eliminate the barrier of the waiver process. It would give

Initiated Income-based Medicaid Family Planning Expansions by Mid-2006

- Alabama
- Arkansas
- California
- Iowa
- Michigan
- Mississippi
- New Mexico
- New York
- North Carolina
- Oklahoma
- Oregon
- South Carolina
- Washington
- Wisconsin

states authority to expand their coverage of Medicaid family planning services to individuals up to the same income level used by the state to determine eligibility for pregnancy-related care, on a permanent basis and without the need for a waiver.[3] That legislation was approved by the House in August 2007 as a component of a bill to reauthorize and expand the State Children's Health Insurance Program (SCHIP).[4] The Senate never acted on this issue, and it was stripped from the compromise version of SCHIP (along with virtually everything else the House had wanted) that was ultimately vetoed by President Bush. Significantly, however, the family planning expansion provision did not attract public opposition in Congress or from the president, and its sponsors are seeking another legislative train for it to ride.

It's a patchwork system

Despite the ever-increasing importance of Medicaid to the U.S. family planning effort, other programs remain vital nationwide and in specific states. The Title X national family planning program accounts for 12% of U.S. spending on family

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planning client services, and state appropriations account for 13%. Title X comprises at least 25% of funding for family planning in one-third the states.

Because they are not tied to specific clients or services (as is the case with Medicaid), these federal and state grants are especially flexible and valuable to family planning providers. They can be used for outreach and education activities to draw in hard-to-reach and hard-to-serve clients and to shore up and improve the fragile infrastructure of the nation's clinic system. Even as Medicaid grows, clinics will rely on these other grants to provide services beyond the package paid for by Medicaid and to serve those who are ineligible for Medicaid, including many immigrants.

Beyond those roles, Title X, in particular, will continue to set national standards for providing family planning services that are comprehensive, voluntary, confidential, and affordable and will continue to help knit disparate threads of funding into a flawed but functioning safety net.

References

1. Sonfield A, Alrich C, Gold RB. Public funding for family planning, sterilization, and abortion services, FY 1980-2006. *Occasional Report*. New York City: Guttmacher Institute; 2008, No. 38.

2. Frost JF, Frohwirth L, Purcell A. The availability and use of publicly funded family planning clinics: U.S. trends, 1994-2001. *Perspect Sex Reprod Health* 2004, 36:206-215.

3. Unintended Pregnancy Reduction Act of 2007, S. 1075 and H.R. 2523.

4. Children's Health and Medicare Protection Act of 2007, H.R. 3162. ■

CNE/CME Instructions

Physicians and nurses participate in this continuing medical education/continuing education program by reading the articles, 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 and refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. After completing this activity with the **June** issue, you must complete the evaluation form provided and return it in the reply envelope provided in that issue to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you. ■

CNE/CME Questions

After reading *Contraceptive Technology Upd*ate, the participant will be able to:

- **identify** clinical, legal, or scientific issues related to development and provisions of contraceptive technology or other reproductive services.
- **describe** how those issues affect services and patient care.
- **integrate** practical solutions to problems and information into daily practices, according to advice from nationally recognized family planning experts.

13. What were the findings of the three studies which examined risk for venous thromboembolism (VTE) in users of the contraceptive patch and oral contraceptives?

A. All three studies found women who used oral contraceptives had a higher risk for VTEs.
B. All three studies found women who used the patch had a higher risk for VTEs.
C. Two studies found that women who used oral contraceptives had a higher risk for VTEs, while one study showed similar risks for both groups.
D. Two studies found that women used the patch had a higher risk for VTEs, while one study showed similar risks for both groups.

14. What drug is most commonly used with mifepristone for medication abortion in the United States?

A. Misoprostol
B. Methotrexate
C. Gemeprost
D. Sulprostone

15. What is the chief finding of the following research paper? (Tobian A, Serwadda D, Quinn T, et al.)

A. Male circumcision prevents herpes simplex virus-2 acquisition in men, but it increases the rates of genitourinary disease, trichomonas, and bacterial vaginosis in their female partners.
B. Male circumcision prevents herpes simplex virus-2 acquisition in men and reduces rates of genitourinary disease, trichomonas, and bacterial vaginosis in their female partners.
C. Male circumcision has no impact on herpes simplex virus-2 acquisition in men.
D. Male circumcision prevents herpes simplex virus-2 acquisition in men, but it has no impact on rates of genitourinary disease, trichomonas, and bacterial vaginosis in their female partners.

16. A multidrug-resistant strain of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteria is associated with the following conditions:

A. Necrotizing fasciitis, glomerulonephritis, endocarditis, and pneumonia
B. Necrotizing fasciitis, sepsis, proteinuria, and pneumonia
C. Necrotizing fasciitis, sepsis, endocarditis, and pneumonia
D. Necrotizing fasciitis, sepsis, endocarditis, and vasculitis

Answers: 13. D; 14. A; 15. B; 16. C.

Women in the dark on cervical cancer facts

Results of a new survey released by the National Association of Nurse Practitioners in Women's Health (NPWH) indicate that most of the 1,000 women polled often confused myth with fact when quizzed about cervical cancer prevention.

According to the survey, women older than 30, who are most at risk of developing cervical cancer, are half as likely as their younger counterparts to recall speaking to their providers about human papillomavirus (HPV) and its link to cervical cancer. They also are less knowledgeable about the virus. While 90% of survey participants ages 30 and older considered themselves somewhat or very familiar with the preventive tests they need, 58% had not heard of the test for HPV, and 86% did not recall their providers ever talking to them about the test.

One of the myths the survey revealed was that women think they are out of the woods if they have been in a long-term relationship; in fact, HPV can stay in the body for many years, says **Susan Wysocki**, NP, NPWH's president and CEO. Another myth revealed by the survey is that women do not think they need the HPV test if they have had normal Pap smears all their lives.

"However, the Pap isn't foolproof; it's still possible to suddenly discover you have invasive cancer despite a history of normal Paps," says Wysocki. "Getting the HPV test along with your Pap if you're over 30 — when you are most at risk — provides maximum peace of mind." ■