After Bisphosphonate Use, Which Bone-Forming Medication Is Best?

An experimental monoclonal antibody, but not the FDA-approved teriparatide, increased bone-mineral density in former users of bisphosphonates.

Although bisphosphonates, the commonly prescribed antiresorptive agents, represent mainstream therapy for osteoporosis, some patients develop fractures during long-term treatment or cannot tolerate this class of medications. For these patients, clinicians often prescribe the bone-forming agent teriparatide (Forteo). However, teriparatide’s ability to increase bone-mineral density (BMD) appears to be attenuated in former users of antiresorptive agents. In an industry-funded trial, investigators compared teriparatide with romosozumab, a non-FDA-approved monoclonal antibody that binds to and inhibits sclerostin (the negative regulator of bone formation) and thus inhibits bone resorption and stimulates bone formation.

In a 12-month, phase IIIIB, open-label trial, 436 women with postmenopausal osteoporosis and histories of fracture who had used an oral bisphosphonate for ≥3 years before screening were randomized to subcutaneous teriparatide (20 µg daily) or subcutaneous romosozumab (210 mg monthly). At 12 months, both total hip BMD and estimated hip strength significantly increased with romosozumab but declined with teriparatide. Of the serious adverse events reported, none were believed by the investigators to have been caused by the study medications.

COMMENT

In a previous 1-year study, romosozumab increased BMD and bone formation and decreased bone resorption in menopausal women with low bone mass (NEJM JW Women’s Health Feb 2014 and N Engl J Med 2014; 370:412). Editorialists speculate that the disparate effects of romosozumab and teriparatide in former bisphosphonate users might reflect differing mechanisms of action. Serious adverse cardiovascular events associated with romosozumab in another trial have delayed its regulatory approval. The current findings suggest that this monoclonal antibody, if approved, might have advantages over teriparatide in patients with osteoporosis who have used bisphosphonates previously.

— Andrew M. Kaunitz, MD

Langdahl BL et al. Romosozumab (sclerostin monoclonal antibody) versus teriparatide in postmenopausal women with osteoporosis transitioning from oral bisphosphonate therapy: A randomised, open-label, phase 3 trial. Lancet 2017 Jul 26; [e-pub]. (http://dx.doi.org/10.1016/S0140-6736(17)31613-6)


Do Bisphosphonates Prevent Hip Fractures in Glucocorticoid Users?

In an observational study of older patients, those who took alendronate had fewer hip fractures.

Bisphosphonate drugs are recommended to prevent glucocorticoid-related fractures. Because the specific effect of these drugs on hip fracture incidence in steroid-treated patients is unclear, Swedish investigators conducted this retrospective study using a registry of older patients (age, ≥65) called “Senior Alert.” Nearly all of these patients were enrolled during hospitalizations or were nursing home residents. Among patients in this database, 1802 took ≥2 mg of prednisolone daily for at least 3 months.
and started the bisphosphonate alendronate shortly after beginning steroid therapy; these patients were propensity-matched with 1802 patients who took prednisolone but no osteoporosis drug. About half the patients had diagnoses of either polymyalgia rheumatica or rheumatoid arthritis, and about 15% had diagnoses of osteoporosis. Median prednisolone dose was about 8 mg daily.

During average follow-up of 1.3 years, hip fracture incidence was significantly lower in alendronate recipients than in propensity-matched controls (10 vs. 27 fractures per 1000 person-years). Thus, for every 60 steroid-treated patients who took alendronate, roughly 1 fewer hip fractures occurred.

**COMMENT**

With the usual caveat that retrospective observational studies generally do not prove causality, this study suggests that alendronate can prevent hip fractures in older patients who take daily glucocorticoids. However, whether these results apply to average community-dwelling outpatients is unclear, because the database was composed largely of recently hospitalized patients and nursing home residents. An American College of Rheumatology guideline on glucocorticoid-induced osteoporosis bases its recommendations for bisphosphonate therapy on patient age, steroid duration and dose, and presence of other osteoporosis risk factors.**

*Chlorhexidine-alcohol was associated with lower rates of surgical site infection than was povidone-iodine.*

Surgical site infection (SSI) is a major cause of postoperative readmission. To assess the efficacy of topical chlorhexidine-alcohol (CA) compared with povidone-iodine (PI) for preventing SSI after hysterectomy, investigators in Michigan conducted a retrospective study involving 4259 women who underwent abdominal hysterectomy for benign indications. CA was used in 70% of surgeries, and PI was used in 30%.

Rates of SSI were 2.6% with CA and 3.6% with PI (P = 0.09). In analysis adjusted for factors such as estimated blood loss, surgical time, and severity of adhesions, the odds ratio of developing SSI was 0.56 in the CA group versus the PI group (P = 0.01). In a propensity-matched analysis, SSI rates in the CA and PI groups were 1.5% and 4.7%, respectively (P <0.001).

**COMMENT**

CA also provides superior antisepsis in the setting of cesarean delivery (NEJM JW Women’s Health Mar 2016 and N Engl J Med 2016; 374:647). Given that SSI is a major cause of postoperative readmission, it’s likely that CA antisepsis is associated with fewer such readmissions and lower healthcare costs than PI. Because of the high alcohol content of CA (70% isopropyl alcohol), the prep should be allowed to dry for ≥3 minutes following application to allow the alcohol to evaporate (otherwise, use of electrosurgical devices becomes a fire hazard). Accordingly, for emergency surgery where minutes are critical, PI might be best; moreover, about 2% of patients are allergic to CA, necessitating use of PI. Notably, PI — but not CA — is FDA approved for use in the vagina. Preoperative antibiotics remain an important intervention against SSI and should always be administered. — Robert L. Barbieri, MD

*NEJM's Early Job Alert*

Job Postings in Your Specialty


Check it out at NEJMCareerCenter.org.
Hypertensive Disorders of Pregnancy and Weight as Determinants of Chronic Hypertension

As both factors raise risk for hypertension, consistently monitoring blood pressure and maintaining healthy weight are particularly important.

The association between hypertensive disorders of pregnancy (HDP) and subsequent chronic hypertension is well known, but the underlying mechanisms remain unclear. To assess the trajectory of risk for developing hypertension following a pregnancy complicated by HDP, investigators studied the health histories of 1,025,000 Danish women with ≥1 live birth or stillbirth between 1978 and 2012. For women with first pregnancy in their 20s, incidence of developing chronic hypertension within the first 10 years after delivery was 14% (with HDP) and 4% (without HDP). Among women with first pregnancy in their 40s, the corresponding incidences were 32% and 11%, respectively. Twofold higher rates of hypertension among women with HDP persisted more than 20 years later.

In the Nurses’ Health Study (designed to assess lifestyle factors and risk for developing hypertension), 54,600 parous women (age range, 32–59) were studied prospectively. Being overweight or obese raised risk for developing chronic hypertension regardless of history of HDP. Levels of physical activity and sodium intake did not significantly modify the association between body-mass index (BMI) and risk for developing hypertension. After controlling for multiple variables, history of HDP plus elevated BMI increased risk for developing hypertension more than elevated BMI alone.

COMMENT

These studies confirm that a history of HDP, elevated BMI, or both raise risk for developing chronic hypertension. In practice, clinicians might not be aware that a patient has a history of HDP (especially 10 or 20 years after delivery). The electronic medical record system, given its widespread use, could serve as a valuable tool to highlight and permanently record HPD history, helping clinicians to identify women at excess risk for developing hypertension.

— Robert L. Barbieri, MD

Military Servicewomen’s Contraceptive Knowledge and Use

Contraceptive knowledge was low and utilization high among U.S. military women — but probably not as high as in Israeli servicewomen.

Increasingly, women are enlisting in U.S. military services and being deployed. In two U.S. studies, researchers explored military women’s knowledge about and use of contraception. In a third study, investigators examined unintended pregnancy rates among women in the Israeli military service.

The first study assessed contraceptive knowledge in a random sample of women veterans (age range, 18–44) receiving Veterans Administration health services across the U.S. Some 2300 telephone interview respondents (mean age, 35; 91% with education past high school; 52% white, 29% black, 12% Hispanic, 7% other) answered 20 questions about contraceptive principles and methods. Percent correct answers ranged from 48% (knowledge of pregnancy rates without contraception, identification of least effective method) to 88% (methods preventing sexually transmitted infections); knowledge scores by individual method clustered around 50%. Black and Hispanic women generally scored lower than white women.

In the contraceptive utilization study, 376,000 active-duty women (age range, 17–49; 50% white, 25% black, 12% Hispanic, 4% Asian, 9% other) were identified in all five military service branches. Over 6 years, 69% utilized contraception; another 8% received contraceptive counseling only. The youngest (range, 17–19) and oldest (45–49) subsets were least likely to receive contraception. Utilization was similar among racial/ethnic groups. A subset of 131,597 deployed servicewomen had a contraceptive utilization rate of 54%; an additional 3% had received predeployment contraceptive counseling.

The third study showed that, among 130,000 unmarried women in the Israeli military, 3265 reported unintended pregnancies, a rate of 1.8%. Over the 3-year study period, unintended pregnancy rates declined steadily from 1.7% in 2013 to 1.3% in 2015.

COMMENT

U.S. servicewomen have access to healthcare and therefore no financial barriers to contraception. Although neither U.S. study reported unintended pregnancy rates, previous studies have estimated such rates to be 7% in military women and 5% in the general population. The low levels of contraceptive knowledge among military women — especially certain racial/ethnic groups — suggest education as one route to improvement. The contraceptive prescription rate in the second study was relatively high (although receiving a prescription does not necessarily mean using it). Deployed women may or may not need contraception; either way, they will likely benefit from menstrual suppression. Finally, the low unintended pregnancy rates among unmarried Israeli servicewomen give the U.S. military a goal to pursue.

— Diane E. Judge, APN/CNP


An Association Between Vasectomy and Prostate Cancer?

A meta-analysis casts doubt on this enduring belief.

A 30-year debate about the association of vasectomy with excess risk for prostate cancer has been fueled by studies of variable quality and with mixed results. In this meta-analysis, researchers addressed study quality: They evaluated 53 studies (16 cohort, 33 case-control, and 4 cross-sectional) that involved about 15 million patients;
Addressing the Lifetime Healthcare Needs of Lesbian Patients

Creating an inclusive, nonjudgmental healthcare environment can improve patient-centered care for lesbian women.

LESBIAN IDENTITY
The term “lesbian” refers to a sexual identity, a label used to recognize that a woman has physical, emotional, or sexual attractions toward other women.1 This label does not provide information about sexual behaviors or romantic relationships, which are often incongruent with sexual identity. Although 2% of U.S. adult women identify as lesbian,2 >7% report same-sex sexual behaviors.3 If a patient identifies as lesbian, this is merely a starting point for a focused assessment of sexual history and practices.

BEHAVIORAL HEALTH CONSIDERATIONS
Compared with heterosexual women, lesbian women are more likely to live in poverty,4 delay seeking healthcare,5 and be at higher risk for obesity, alcohol use, and tobacco use.1 These factors, in conjunction with nulliparity, place lesbian women at higher risk for breast cancer. Given that lesbian women are less likely to undergo cervical cancer screening, they are also at higher risk for this form of cancer.5 Lesbian women are more likely to report experiencing depression,1 in part due to stigma and discrimination. Further, IPV is as common in same-sex relationships as in heterosexual relationships, but may go unassessed in women in same-sex relationships.

The American Medical Association recommends IPV screening for everyone. Screening questions include:6

- Have you been hit, kicked, punched, or otherwise hurt by someone in the past year? If so, by whom?
- Do you feel safe in your current relationship?
- Is there a partner from a previous relationship who is making you feel unsafe now?

Healthcare screening recommendations for lesbian women are the same as for all women.1 Age, lifestyle behaviors, and health-related practices should guide screening rather than sexual identity. However, given the health disparities unique to lesbian women, it is important to pay special attention to weight and use of alcohol and tobacco, and to conduct regular screening for depression4 and IPV.1,6

SEXUAL HEALTH CONSIDERATIONS
Lesbian women are at risk for STIs. As many as 70% of women who identify as lesbian have engaged in penile-vaginal penetration in their lifetimes.7 Additionally, >86% of women who have sex with women use, or have used, a sexual device.8 Sharing sexual devices can increase risk for bacterial vaginosis and transmission of human papillomavirus (HPV). Like all women, lesbian women should be counseled about using a barrier (condom or dental dam) during sexual activity, not sharing sexual devices between partners or orifices, and washing sexual devices with soap and water after use.4

SEXUAL IDENTITY IN ADOLESCENCE
Adolescents are more likely to identify as queer, no label, or sexually fluid than to identify specifically as lesbian. Sexual identity may also change over time — even between healthcare visits.9 Although sexual minority adolescents have the same healthcare needs as their peers, they are at higher risk for depression, suicide, and substance use or abuse due to stigma and discrimination. Because of the vulnerability associated with the coming-out process, bullying and victimization by peers and other adults, and parental rejection, lesbian adolescents are at higher risk for depression and suicide than their heterosexual counterparts.1,9 Sexual minority adolescents should be screened for mental health concerns, substance use, and sexual risk-taking. Protective factors, including level of parental support and family connectedness, should also be assessed.9 Youth at high risk, including those with inadequate family support, may benefit from referral to a lesbian, gay, bisexual, transgender (LGBT)-affirming therapist or online resources (The Trevor Project) and the Trevor Lifeline (866-488-7386), a 24/7 suicide prevention hotline.

LESBIANISM IN OLDER ADULTHOOD
Older lesbian women are more likely to struggle with obesity, have higher risk for cardiovascular disease, and are 1.3 times more likely to have a physical disability than their heterosexual counterparts. Perhaps more striking than these physical health disparities is that 26% of lesbian adults have reported that their greatest concern about aging is fear of discrimination,10 potentially leading to a delay in seeking assisted living or residential care. Additionally, older lesbian couples are less financially equipped to handle healthcare costs. Services and Advocacy for GLBT Elders (SAGE) has developed a National LGBT Housing Initiative to help older LGBT adults secure LGBT-friendly housing and residential care (information available at www.sageusa.org or 1-888-234-SAGE).

PROVIDING INCLUSIVE CARE
Healthcare providers are in a unique position to reduce the stigma and discrimination experienced by lesbian patients by promoting an inclusive healthcare environment. This includes creating a visually welcoming space and intake questionnaires that do not assume heterosexuality. The American College of Obstetricians
If you are a teen or woman who identifies as lesbian (physically, sexually, or emotionally attracted to women), you have the same healthcare needs as any other woman — with a few added challenges. One can be finding a clinician (physician, nurse practitioner, nurse midwife, physician assistant) with whom you feel comfortable. Lesbians have often felt unwelcome in healthcare settings. That is changing as clinicians learn more about helping you feel at ease.

**The Issues in General** Compared with heterosexual women, lesbians have greater likelihood of some health conditions. They are more likely to live in poverty, delay seeking healthcare, be obese, and use tobacco and excessive amounts of alcohol. Some of these factors (plus the fact that lesbians may be less likely to bear children, which protects against breast cancer) mean breast cancer is more common. Delaying or avoiding healthcare increases the likelihood of cervical cancer, which is mostly preventable with regular Pap smears and the human papillomavirus (HPV) vaccine. Lesbian women are also more likely to report depression, in part because of the stigma and discrimination they face.

Maintaining a healthful diet, exercising regularly, quitting smoking (or not starting), seeking help if you experience symptoms of depression (problems sleeping, losing interest in pleasurable activities, feeling “down” most of or all the time), and avoiding drugs and excessive alcohol are good health practices. For some helpful strategies, see the Resources below. You should also get regular Pap tests — every 3 years from ages 21 to 30 and either a Pap test every 3 years or Pap plus HPV test every 5 years from ages 30 to 65. Screening for breast cancer should be based on your personal risk factors. For women at “average risk,” one recommendation is a mammogram every 2 years starting at age 50, but starting earlier and screening more often are open to discussion with your clinician.

**If You’re an Older Woman** Older lesbian women are especially likely to struggle with obesity and more likely than heterosexual women to have heart disease and physical disabilities. Concern about discrimination may delay seeking the housing help they need, such as assisted living or nursing homes. Because women’s pay is historically lower than men’s, older lesbian couples may be less financially prepared for retirement and healthcare costs than heterosexual couples. Advocacy & Services for LGBT Elders (SAGE) offers assistance in obtaining lesbian, gay, bisexual, and transgender (LGBT)-friendly housing and residential care through the National LGBT Housing Initiative (see Resources below).

**If You’re a Teen or a Friend or Relative of a Teen** If you identify as queer, no identity, sexually fluid, or lesbian, you face the discrimination that comes with being “different,” particularly at this time of life. Bullying and victimization by peers — and even family members — during the coming-out process is difficult and can lead to substance abuse, depression, and thoughts of suicide. The Trevor Project and the Trevor Lifeline (see Resources below) are dedicated to assisting young women in coping with these problems.

**Preventing Sexually Transmitted Infections (STIs)** STIs don’t discriminate. They can and do affect women who have sex with women. Many women and their partners who identify as lesbian have had sex with men and may continue doing so. STIs can spread from man to woman, then from woman to woman. Herpes can be spread between women, including by oral sex if one partner has cold sores (caused by herpes).
Sharing sex toys can spread HPV (the main cause of cervical cancer) between women. This can also transmit bacterial vaginosis — not an STI, but a common vaginal infection causing a fishy-smelling irritating discharge. You can decrease the likelihood of infections, including STIs, with the following measures:

- Use a dental dam or a condom cut halfway through and unrolled to form a barrier between your vulva (the vaginal lips and area outside the vagina) and your partner's during oral sex.
- Wash sex toys with soap and water after every use, and always before sharing them. You can also use latex condoms on sex toys. If a toy has touched your or your partner's anal area, wash it with soap and water before using it on your or her vulva or vagina.
- Use condoms if you have sex with a male partner.
- If you can, get the HPV vaccine to lower the likelihood of getting this infection. The series of 2 or 3 shots is recommended for females between the ages of 9 and 26, ideally starting at age 11 to 12. If you're older than 26, the vaccine may still help protect you; ask your clinician.
- Get tested for chlamydia and gonorrhea every year before age 25, with additional testing at other times depending on your individual situation.

Finding a Clinician  One way to find a clinician is to ask your friends or local lesbian and LGBT social and support groups. You can also check the GLMA: Health Professionals Advancing LGBT Equality directory (see Resources below) for clinicians who welcome lesbian women. If your health insurance or lack of insurance restricts your choice of clinicians, you might want to take someone with you as an “advocate” on your first visit. At some point in your visit your clinician may ask your advocate to step out, for a good reason: partners of abused women often insist on staying in the room to be sure the abuse is not revealed. Your clinician needs a private conversation with you to make sure you are safe.

To assess your health risks, including STIs, your clinician may ask very specific, personal questions about what you do during sex. This is good medical practice for every person who has sexual contact, no matter what their gender identity or sexual preference. If you feel uncomfortable with these questions, it's okay to ask why the information is necessary; your clinician should explain.

In Summary  No matter who you are, your health is important. Take charge of it by getting the information you need and finding a clinician who will help.

— Diane E. Judge, APN/CNP

Resources

General Information  
https://www.womenshealth.gov/a-z-topics/lesbian-and-bisexual-health

Depression  

Smoking Cessation  

Obesity  
https://medlineplus.gov/obesity.html

Drug and Alcohol Abuse  
https://medlineplus.gov/drugabuse.html

Advocacy & Services for LGBT Elders  
National LGBT Housing Initiative  
http://www.sageusa.org  
1-888-234-SAGE

The Trevor Project  
http://www.thetrevorproject.org

The Trevor Lifeline 24/7 Suicide Prevention Hotline  
866-488-7386

GLMA: Health Professionals Advancing LGBT Equality  
http://www.glma.org

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and Gynecologists recommends that relationship and sexual behavior status be assessed with the following questions:\(^1\)

- Are you single, married, widowed, or divorced, or do you have a domestic partner?
- Are you or have you been sexually active with anyone — male, female, or both male and female partners — or are you not sexually active?
- To whom are you sexually attracted — men, women, or both men and women?

Healthcare providers can model inclusivity by asking questions without judgment, minimizing reactions and facial expressions, and using gender-neutral language (e.g., “partner,” “significant other”). Resources for creating an LGBT-inclusive environment can be found online at the American Medical Association. Online education is also available through the National LGBT Health Education Center.

**CONCLUSION**

Although lesbian women are not inherently different from their heterosexual counterparts, they are at greater risk for obesity, certain cancers, substance abuse, and depression, in part because of social stigma and discrimination. Adolescence and older age are particularly vulnerable times for lesbian women. Creating an inclusive healthcare environment with nonjudgmental patient—provider interactions can improve patient-centered care for lesbian women. — **Jordan E. Rullo, PhD, ABPP, Stephanie S. Faubion, MD, FACP, NCMP, IF**

Dr. Rullo is Assistant Professor, Board Certified Clinical Health Psychologist, and American Association of Sex Educators, Counselors and Therapists (AASECT) Certified Sex Therapist, Women’s Health Clinic, Division of General Internal Medicine, Department of Psychiatry and Psychology, Mayo Clinic, Rochester, Minnesota.

Dr. Faubion is Director, Executive and International Medicine and Office of Women’s Health and Associate Professor of Medicine, Women’s Health Clinic, Division of General Internal Medicine, Mayo Clinic, Rochester, Minnesota.  


**FEATURE**

**Oral PrEP Is Effective for Women with Abnormal Vaginal Microbiota**

The efficacy of oral pre-exposure prophylaxis was not decreased in African women with bacterial vaginosis who had high adherence.

Oral tenofovir-based pre-exposure prophylaxis (PrEP) has been shown to be highly effective for HIV prevention when patients are treatment adherent, albeit more so for men than women. Changes in the vaginal microbiota, specifically bacterial vaginosis (BV) with predominance of non-Lactobacillus spp, were recently postulated as a reason for lower protection among women in a trial of 1% tenofovir gel (NEJM JW Infect Dis Jul 2017).

Now, investigators have conducted a post-hoc analysis of the Partners PrEP Study (AIDS 2013; 27:2155) of heterosexual HIV-1 serodiscordant couples from Kenya.
and Uganda to determine if the presence of bacterial vaginosis affects the efficacy of oral PrEP. Vaginal swabs obtained from women at enrollment were assessed by microscopy and classified as healthy microbiota (Nugent score, 0–3), intermediate microbiota (4–6), and BV (7–10). Among 1470 women with baseline Nugent scores, 24% had BV, 12% had an intermediate microbiota, and 63% had healthy microbiota. Co-infection with Neisseria gonorrhoeae, Chlamydia trachomatis, or Trichomonas vaginalis was present in 11% of women with BV, 16% with intermediate microbiota, and 5% with healthy microbiota.

No significant increased risk for acquiring HIV infection while receiving PrEP was seen among women with BV (HIV incidence, 0.9 per 100 person-years) or intermediate microbiota (1.8 per 100 person-years), compared with women with healthy vaginal microbiota (0.6 per 100 person-years). Of note, treatment with metronidazole for BV did not alter the results.

COMMENT
Among these African women, the efficacy of oral PrEP was not decreased by the presence of BV or vaginal dysbiosis. The notion that “bacteria in my vagina ate my Truvada” is not true is certainly reassuring, and, although the studies are somewhat different (BV vs. microbiome), these findings do not support those from a recent analysis of the CAPRISA 004 trial (Science 2010; 329:1168). The results of the current study suggest that oral PrEP is effective in women with BV provided they are adherent.

— Carlos del Rio, MD, NEJM Journal Watch Infectious Diseases

Maraviroc for Preexposure Prophylaxis

Maraviroc-containing PrEP was safe and well tolerated by women at risk for HIV infection in a phase II study.

Preexposure prophylaxis (PrEP) with co-formulated tenofovir and emtricitabine has been established as useful in preventing HIV infection. However, studies of this intervention in women have yielded conflicting results.

Now, investigators in the U.S. and Puerto Rico have conducted a randomized phase II study to test the safety and tolerability among women of PrEP containing maraviroc (MVC), a CCR5 antagonist of viral entry that has been approved for HIV treatment. The study included 188 HIV-negative participants (median age, 35 years; 65% black) who reported condomless vaginal or anal intercourse with at least one man with known HIV infection or unknown serostatus within 90 days before study entry. The women were randomized evenly to one of four interventions for 48 weeks: MVC alone, MVC plus emtricitabine (MVC-FTC), MVC plus tenofovir (MVC-TDF), or tenofovir plus emtricitabine (TDF-FTC).

Through 48 weeks, 85% of participants completed follow-up, 11% had withdrawn, and 4% were lost to follow-up. Approximately a third of participants had discontinued study drugs by week 48; the proportion of discontinuations was similar among treatment groups. Grade 3 or 4 adverse events occurred in 19% of participants: 3% taking MVC, 7% taking MVC-FTC, 5% taking MVC-TDF, and 4% taking TDF-FTC. Among participants with available plasma samples, 65% had detectable drug levels at week 34, and 60% had detectable levels at week 48. No new HIV infections occurred during the study period.

COMMENT
MVC-containing PrEP was safe and well tolerated and may be useful for women at risk for HIV infection. That a third of participants discontinued the study drugs suggests that regimens with easier adherence and better tolerability are needed. No incident HIV infections occurred, but the study was not powered for efficacy, and a relatively low incidence among study participants was expected.

— Carlos del Rio, MD, NEJM Journal Watch Infectious Diseases

Is Your Patient Being Trafficked?

How to tell — how to help.

About 4.5 million women and girls are forced into sexual labor worldwide; in the U.S., about 17% of the 18,500 runaway children in 2016 were probably sex-trafficked. A study of 98 survivors of sex trafficking found most (88%) had seen a physician during their captivity. These authors detail how clinicians can identify and assist exploited women and girls.

Red flags for trafficking include:

- Companion who refuses to leave the room, answers questions for the patient, or does not allow use of a professional interpreter
- Unexpected material possessions
- Excessive familiarity with sex
- Body language indicating fear or distrust
- Injuries suggesting physical abuse or sexual trauma
- Examination inconsistent with history, which may be “scripted”
- Vague or inconsistent answers
- Lack of identification documents
- Inability to provide an address or identify current location, date, or time

The authors suggest strategies for interviewing the patient alone (e.g., accompanying her to the restroom to “instruct her in urine collection”) and for circumventing traffickers’ tracking devices (e.g., providing a hospital gown, putting the patient’s clothing and personal items — including cellphones — elsewhere). Supportive interventions include contacting the National Human Trafficking Resource Center’s 24/7 hotline (1-888-373-7888) as well as local law enforcement and intimate partner violence (IPV) advocates. However, women may refuse assistance, fearing harm to themselves or relatives, deportation, or incarceration. Providing emergency contact information in an easily concealed format (e.g., cards that can be hidden in shoes) may be helpful.

COMMENT
As with IPV, we must be aware that women and girls in forced labor may present in our practices. We still lack evidence-based, successful intervention strategies; for now, more information (including an algorithm

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GUIDELINE WATCH

New ACOG Guidelines on Teen Contraception

**Recommendation:** Subdermal implants and intrauterine contraception should be routinely offered to teens.

**Sponsoring Organization:** American College of Obstetricians and Gynecologists (ACOG)

**Target Audience:** Obstetricians/gynecologists and other clinicians who counsel adolescent patients

**Background**

Three quarters of adolescent pregnancies in the U.S. are unintended. Preventing undesired pregnancy requires effective contraceptive counseling and timely access to contraceptive services. To facilitate this, the ACOG Committee on Adolescent Health Care has identified five clinical best practices.

**Key Points**

- Regardless of a patient’s age or previous sexual activity, contraceptive needs, expectations, and concerns should routinely be assessed.
- Discussions of contraception should begin with information on the safest and most effective methods: intrauterine devices and subdermal implants. As these methods typically provide greater satisfaction, higher efficacy, and higher continuation rates than short-acting contraceptives, they are excellent contraceptives for adolescents.
- Emergency contraception should be routinely included in all discussions of contraceptive options, and clinicians should consider prescribing emergency contraception pills in advance.
- Common misperceptions about contraceptives should be addressed in a way that is age-appropriate and compatible with the patient’s health literacy.
- During initial encounters and all follow-up visits, clinicians should also assess sexual concerns, behavior, relationships, prevention strategies, and testing and treatment for sexually transmitted infections per the Centers for Disease Control and Prevention’s guidelines.

**COMMENT**

Although this committee opinion addresses obstetrician-gynecologists, the guidance is relevant to all clinicians caring for teens, including pediatricians, family physicians, advanced practice nurses, and physician assistants. While great progress has been made in recent years (NEJM JW Womens Health; Oct 2016 and J Adolesc Health 2016; 59:577), continued efforts to provide teens with high-quality contraceptive care are needed, in light of low rates of long-acting contraceptive use among teens who use contraception and shrinking access to safe, legal abortion in the U.S.

— Eleanor Bimla Schwarz, MD, MS


**Breast-Feeding Associated with Reduced Risk for Developing Multiple Sclerosis**

For mothers who breast-fed for a cumulative duration of ≥15 months, risk for MS was half that of those who breast-fed for <15 months.

Having more than one pregnancy has been shown to protect against developing multiple sclerosis (MS). Does prolonged breast-feeding play a similar role? In an analysis utilizing the Kaiser Permanente Southern California system, investigators selected 397 patients with recent MS diagnoses and matched them with 433 disease-free controls. Total cumulative duration of breast-feeding and total ovulatory years were determined through interviews. Sixty percent of women had ≥1 child, and breast-feeding data were available for 239 cases and 262 controls. Socioeconomic factors included household income, race/ethnicity, education, and smoking.

Women who breast-fed for ≥15 months were half as likely to receive diagnoses of MS as those who breast-fed for <15 months. No dose response was found for breast-feeding for 4 to 14 months. MS risk was not associated with age, gravidity, parity, age at first birth, contraceptive use, menstrual years, or ovulatory years.

**COMMENT**

These investigators have previously suggested that prolonged exclusive breast-feeding is associated with reduced risk for disease reactivation in patients with MS (NEJM JW Neurol Nov 2015 and JAMA Neurol 2015; 72:1132). The current study found that cumulative breast-feeding for ≥15 months may be protective (although only 26% of the eligible population reported doing so). Surprisingly, number of pregnancies, children, and ovulatory years were not associated with MS risk. Other studies have suggested numerous benefits of breast-feeding (such as protection against breast and endometrial cancers). Breast-feeding may be a proxy for socioeconomic status and other healthy behaviors, and controlling for all of these is difficult. Although these findings need replication, we should continue to encourage mothers to breast-feed for a variety of known and theoretical benefits.

— Robert T. Naismith, MD, NEJM Journal Watch Neurology

Is Nonobstetric Surgery Harmful During Pregnancy?

Risks are low for miscarriage, preterm birth, and cesarean delivery following non-OB surgery.

Although elective surgery during pregnancy is generally avoided, patients and providers may have concerns when the need for indicated, nonobstetric surgery arises during pregnancy. Counseling regarding the risks for adverse outcomes has been limited by older data, so National Health Service (NHS) investigators in England sought to evaluate such risk in a modern cohort.

Nonobstetric surgeries were performed in 0.7% of 6.4 million pregnancies identified in NHS hospitals from April 2001 through March 2012. The most common surgery types were abdominal (26%), dental (11%), nail/skin (10%), and orthopedic (10%). Surgeries were performed within a week of the end of pregnancy in fewer than 6% of cases. After adjustment for potential confounders, the number needed to harm (NNH) was 143 for miscarriage (i.e., 143 women would need to undergo nonobstetric surgery during pregnancy to cause 1 excess miscarriage), 287 for stillbirth, 31 for preterm birth, and 25 for cesarean delivery. Risks were higher in abdominal surgery in particular (e.g., NNH 20 for miscarriage).

COMMENT

Nonobstetric surgeries performed during pregnancy are generally safe. Of course, comparisons with what outcomes would have been if the underlying conditions remained untreated were not possible; it is likely that the indications for surgery themselves influence the likelihood of adverse outcomes. Although only miscarriages with hospitalization were recorded (and thus likely represent an underestimation of the overall miscarriage rate), I suggest that the message to patients and providers remains that pregnancy is not a contraindication to necessary surgery.

— Allison Bryant, MD, MPH