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Evidence-based commentaries on women's reproductive health

SPECIAL FEATURE

Zika Virus: Effects on the Fetus

By John C. Hobbins, MD

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Dr. Hobbins reports no financial relationships relevant to this field of study.

SYNOPSIS: While the Zika virus has been indolent in many South American, Central American, and Caribbean countries, its recent association with microcephaly (and neurologic impairment) has created an outburst of media alerts, response from the Centers for Disease Control and Prevention, and travel recommendations, particularly as the world moves closer to the 2016 Summer Olympics in Brazil.

Zika is a flavivirus that was first described as causing infection in humans in the Zika Valley in Uganda. It is carried by the mosquito, *Aedes aegypti*, which also carries dengue fever, yellow fever, and chikungunya viruses. Although this virus-transporting mosquito is common in the United States, especially in the South, the few cases diagnosed in North America have been in those individuals returning from countries in South America and the Caribbean, where outbreaks are currently occurring.

Zika-related infection is mostly silent, but in about 20% of cases it can be associated with fever, headache, myalgias, a maculopapular rash, and conjunctivitis.[1] The viremia rarely lasts more than 1 week. However, on a few occasions it has been associated with Guillain-Barré syndrome in adults, resulting in neuromuscular weakness and, occasionally, temporary paralysis. What has elicited the most concern is its association with microcephaly in fetuses and newborns in mothers infected with the virus. The Zika virus has been isolated from maternal blood, amniotic fluid, placenta, and brain tissue. Interestingly enough, it has also been isolated from semen in adult males. What this means for the fertile couple considering pregnancy has yet to be determined. Thus far, there is no evidence that the virus is transferred through saliva.

A 2014 case in French Polynesia raised the possible association of Zika with microcephaly.[2] During the past year, there was a rapid rise of microcephaly in newborns in Brazil, with the provinces of Pernambuco and Bahia particularly hard-hit. According to the Brazil Ministry of Health, less than 150 cases were reported in Brazil in 2014, but this figure rose to more than 4000 cases of microcephaly in 2015 (up until October 2015).[3] Of the 732 cases of microcephaly investigated, 270 were

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truly microcephalic and only possibly linked to Zika. Inconsistent definitions used for microcephaly (2 or 3 standard deviations [SD] below the mean, or head circumferences of 32 cm at term) have hampered attempts to accurately diagnose the condition. In addition, the viral infection can be difficult to characterize. For example, in Bahia, 165 cases of microcephaly were identified, and of the first 35 that were thoroughly scrutinized, 27 were discarded.

Nevertheless, it is clear that there has been a substantial increase in microcephaly in areas of greatest Zika exposure, and the virus has been identified in some mothers of microcephalic infants and, in a few cases, in fetal tissue recovered from demised infants.

DIAGNOSIS OF ZIKA INFECTION

Reverse transcriptase–polymerase chain reaction (RT-PCR) has been used to identify the virus from human tissue, and the presence of Zika IgM in maternal serum signifies a very recent infection. Since the PCR test may cross-react with other viruses (in particular, dengue), patients who test positive should have confirmatory testing. Examining maternal serum for the presence of neutralizing antibodies for dengue and Zika via plaque reduction neutralization testing distinguishes these viruses from one another. If there is a fourfold difference in favor of the Zika, the test is presumed positive. If there is less than a fourfold difference, then the result is inconclusive. More importantly, if the IgM is negative for Zika, then infection is unlikely. The problem with the Zika RT-PCR is that after 5 to 7 days, the virus may not be present in maternal serum (while still being present in amniotic fluid), so a negative test should be backed up with antibody testing for IgM. Maternal serum specimens can be channeled through State Health Departments or the Centers for Disease Control and Prevention (CDC; 800-232-4636).

DIAGNOSIS OF MICROCEPHALY

Discrepancy in the definition of microcephaly is the main reason experts in Brazil have struggled with presenting an accurate incidence of microcephaly. The discrepancy between expected cases of microcephaly and actual cases reported occurred because the head circumference charts applied were not uniform and the thresholds used to define microcephaly were different (as noted above). Also, since most infants/fetuses with small heads are simply genetically predisposed to being small, some investigators will label microcephaly according to whether there is documented pathology. For example, in Brazil, where there have been about 3 million births per year, there were only 143 cases of microcephaly reported in 2014. Even using a head circumference threshold of > 3 SD below the mean, this would suggest a major underreporting of the condition in 2014.

Only very recently has information been available regarding how the Zika virus attacks the brain. In one recent report involving two documented cases of Zika-related microcephaly, the virus seemed to be an equal opportunity attacker of most parts of the fetal brain.[4] On prenatal ultrasound, a combination of findings were noted: ventriculomegaly, periventricular calcifications, agenesis of the corpus callosum, small thalami, hypoplasia of the cerebellar vermis, large cisterna magna, as well as large subarachnoid space (interestingly, many of these also accompany perinatal cytomegalovirus infection). Although the early cases from Brazil suggested the damage is related to first trimester exposure, more recent cases have been in second and third trimester infections, with particular predilection for the frontal potions of the brain in late infections. In vitro investigation[5] has pointed to a direct effect on cortical progenitor cells resulting in cell attenuation, which would explain how the brain shrinks to create the microcephalic infant. Each of the findings noted above potentially is diagnosable with ultrasound and could translate into severe neurological disabilities, as well as hearing loss and blindness.

PREVENTION

Presently, there is no anti-Zika vaccine nor is there an antiviral treatment that will combat this infection. Every effort should be made to avoid or kill the mosquito vector to limit potential exposure to the virus. In Florida, there have been a few cases of perinatal Zika infection, all from travel-related activity. This has triggered increased education and measures to prevent the vector from causing harm. For instance, mosquito spraying and resident alerts (to eliminate or report any locations with even small amounts of standing water, where mosquitoes love to breed) are two such measures. Precautionary measures are particularly stringent for fertile women. Currently women who are pregnant or trying to conceive should avoid traveling to target countries (see the CDC website list at http://wwwnc.cdc.gov/travel/page/zika-travel-information). Partners returning from these countries should either avoid

intercourse completely or use condoms for the rest of the pregnancy. CDC recommends that pregnant women with or without symptoms should be offered serum testing with RT-PCR (according to the timing of possible exposures) and antibody testing on their return.[6] If they show any flu-like symptoms, they should have PCR testing within a week of the symptoms and IgM antibody analysis 2-12 weeks following exposure/symptoms.

If a positive diagnosis of Zika is made, then a trans-abdominal ultrasound in late second trimester or third trimester can diagnose microcephaly using a head circumference of > 2 SDs below the mean. A transvaginal approach can diagnose some of the subtle brain abnormalities if the fetus is in a vertex presentation. Amniocentesis can be considered after 15 weeks, looking for Zika RT-PCR, to help with pregnancy decision-making.

An optimistic note: Although the Zika outbreak is a real threat to women and their children, the threat could run its course with time in some problem areas, as evidenced by a rapid drop in the number of infected cases in French Polynesia. ■

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ABSTRACT & COMMENTARY

Who Seeks an Infertility Evaluation?

By Robert W. Rebar, MD

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Dr. Rebar reports no financial relationships relevant to this field of study.

SYNOPSIS: Demographic and lifestyle factors influence who receives a fertility evaluation.

SOURCE: Farland LV, et al. Who receives a medical evaluation for infertility in the United States? *Fertil Steril* 2016; Doi:/10.1016/j.fertnstert.2015.12.132.

Data from the National Survey for Family Growth have estimated that among women with fertility problems, less than half have ever sought any type of infertility care.[1] Is this true for a population of women who work in healthcare? By exploring the attitudes of such a population, is it possible to better understand who does and who does not seek infertility services despite an inability to become pregnant?

Using data from the Nurses' Health Study II, researchers in Boston identified a number of demographic and lifestyle factors associated with whether a woman having trouble getting pregnant obtains medical assistance. This study began in 1989 when 116,430 female registered nurses between the ages of 25 and 42 years returned a mailed questionnaire on their health and lifestyles. Every 2 years thereafter they answered a follow-up questionnaire, with about 92% of the original group continuing to participate. In each questionnaire from 1989 to 2001, and again in 2005 and 2009, the nurses were asked "if they had tried to become pregnant for more than one year without success." They were also asked the cause of their infertility. The questionnaire permitted them to select from any of several different diagnoses, report multiple diagnoses, state the cause of their infertility was not determined, or report that the infertility was not investigated.

Of the women in the study, 7422 reported experiencing infertility after the first questionnaire cycle. About 65% of the women reporting infertility also reported having an infertility evaluation, significantly higher than the population at large, but still relatively low. The mean age at first report of infertility was 35.1 ± 4.7 (standard deviation) years among those who reported medical evaluation for infertility and 36.2 ± 4.7 years among those who did not.

Several factors appeared to play a role in predicting whether a woman would obtain a medical evaluation of her infertility. Women who lived in states with comprehensive insurance coverage (relative risk [RR], 1.09; 95% confidence interval [CI], 1.00-1.19) or who had a higher household income (P = 0.05 for linear trend) were more likely to report receiving an infertility evaluation. Compared with infertile women who had not

reported a physical examination before their infertility, women who had a general physical examination within 2 years of their infertility (RR, 1.14; 95% CI, 1.06-1.22) or an examination for symptoms of any health condition (RR, 1.15; 95% CI, 1.06-1.24) were more likely to report having a fertility evaluation.

Several demographic factors also were important in determining the likelihood that an infertile woman was evaluated for infertility. Older women ($P < 0.001$ for linear trend) and parous women (RR, 0.81; 95% CI, 0.78-0.84) were less likely to undergo an infertility evaluation. Women whose male partners had graduate level education compared to those who had less than a 4-year college degree were more likely to undergo evaluation ($P < 0.001$ for linear trend). No significant difference was observed by race or marital status. Whereas infertile women who ever had an ultrasound or uterine fibroids were not more or less likely to report a medical evaluation, those with a history of surgically confirmed endometriosis were more likely to report having a medical evaluation than infertile women without documentation of previous endometriosis (RR, 1.27; 95% CI, 1.20-1.35).

Lifestyle choices were also important. Women who exercised frequently ($P = 0.04$ for linear trend) and took multivitamins (RR, 1.03; 95% CI, 1.00-1.07) were more likely to undergo a medical infertility evaluation. Current smokers (RR, 0.89; 95% CI, 0.83-0.96) and those with a higher body mass index ($P = 0.01$ for trend) were less likely to report receiving a medical infertility evaluation. Alcohol intake was unrelated to infertility diagnosis.

■ COMMENTARY

This study confirms the findings from other studies while simultaneously expanding our understanding of what compels couples to seek medical evaluation for infertility. Even among a group of individuals with a high degree of medical knowledge, as well as a professional connection to the medical system, many couples choose not to seek medical assistance for infertility. Although there must be a host of subtle individual factors in play, it is clear that it is possible to identify some factors that make it more likely for a couple to seek assistance.

Even after adjusting for confounding, "demographic" (age at infertility, parity, partner's education) and "access" (income, insurance status, connection with the medical system) characteristics were significant predictors of reporting having received an infertility evaluation. The importance of insurance coverage becomes apparent when we consider that women in most European countries are more than twice as likely as American women to undergo cycles of in vitro fertilization. In the United States, women are much more likely to undergo in vitro fertilization in those states mandating some insurance coverage.

Historically, it is just such "demographic" and "access" characteristics that have been viewed as the major barriers to infertility care. This study suggests that other lifestyle factors play important roles as well. Clearly, individuals more concerned with living what they perceive as a "healthy lifestyle" and those who are more apt to seek medical care sought infertility care more frequently. Given the strong correlation between endometriosis and infertility, it is not surprising that women with a diagnosis of endometriosis were more apt to seek evaluation for infertility.

Failure to detect any racial or marital differences in this study may well be related to the highly educated and homogeneous population studied. Given the obvious socioeconomic disparities among ethnic groups in the United States, it is likely that these factors are more important in considering the United States population in its totality.

The authors suggested that the results of this study can help individual practitioners identify women who might benefit from an infertility investigation. Given that the Centers for Disease Control and Prevention recently stated that the detection of infertility and management of infertility care are national public health priorities,[2] it behooves all first-line healthcare providers to be cognizant of the reticence of many women and couples to seek infertility care. ■

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ABSTRACT & COMMENTARY

Pelvic Floor Changes After Delivery

By Chiara Ghetti, MD

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Dr. Ghetti reports no financial relationships relevant to this field of study.

SYNOPSIS: Significant changes in levator muscles are visible by transperineal ultrasound in early and late postpartum period.

SOURCE: Aydin S, Aydin ÇA. Evaluation of labor-related pelvic floor changes 3 months after delivery: A 3D transperineal ultrasound study. *Int Urogynecol J* 2015;26:1827-1833.

The objective of this study was to document changes in levator ani (LA) morphology and levator and genital hiatus measurements by transperineal ultrasound immediately after vaginal delivery and at 3 months post-delivery. This was a prospective cohort (cross-sectional observational) study of 94 primiparous women. Women were examined within 36 hours of vaginal delivery (early evaluation) and 3 months after delivery (late evaluation). Primary outcomes were transperineal 3D ultrasound measurements, including maximum anteroposterior and transverse diameters of levator hiatus at rest and with Valsalva, puboviscerel muscle thickness to left and right of rectum, difference in the anteroposterior and transverse diameters of the hiatus, and difference in levator hiatus between rest and during Valsalva maneuver. Women were excluded who underwent operative delivery, multifetal pregnancy, cesarean delivery, inability to assume lithotomy position, refusal to provide consent, and inability to generate an effective Valsalva maneuver.

Eighty-four subjects were examined within 36 hours of delivery and at 3 months. The rate of levator defects was 71.4% at early evaluation and 39.6% at late evaluation. Levator thickness and transverse hiatal diameters at rest and Valsalva were greater at late evaluation, while anteroposterior hiatal dimensions and hiatal area at rest and Valsalva were greater at early evaluation. There appeared to be an association between presence of levator defects and several maternal and fetal factors, including head circumference, fetal weight, and length of the first stage of labor.

■ COMMENTARY

The passage of the fetal head at time of vaginal delivery is associated with LA trauma. Prior studies using 3D perineal ultrasonography within 48 and 72 hours of delivery found LA avulsion rates of 19% and 40%, respectively. In MRI studies of the pelvic floor in women 9-12 months from delivery, 20% were found to have visible defects of the LA muscles. In a recent study, Van Delft evaluated primiparous women by endovaginal ultrasonography within 4 days of delivery; a quarter of women were found to have levator hematomas. Hematomas at the site of LA muscle attachment to the pubic bone always were predictive of LA muscle avulsion at 3 months.[1]

This study found a 71% rate of LA defects by ultrasonography within 36 hours of delivery and 40% at 3 months after delivery. Of the women with LA avulsions, 52% of the injuries persisted throughout the 3-month period. This study provides important information; however, direct comparisons between this and past studies is not appropriate because of differences in assessment times and imaging modalities. The use of 3D ultrasonography allows for dynamic assessment in real time. Additionally, one of the strengths of this study is the early assessment of the pelvic floor musculature that allowed for evaluation before remodeling occurs. The longitudinal follow-up employed in this study allowed for a better understanding of the dynamic changes in levator morphology and hiatal measurements in the postpartum period. Although prior data suggested that forceps delivery and prolonged second stage are risk factors for LA injuries, women with operative deliveries were excluded.

[Pelvic floor physical therapy after delivery plays a key part in the recovery from levator ani trauma and should be considered for all women undergoing vaginal delivery.]

What does LA avulsion and trauma mean in the long-term? There is increasing evidence that vaginal birth increases a woman's risk for developing pelvic organ prolapse and stress incontinence. However, the long latency between delivery and pelvic floor symptoms has made it difficult to study the clinical relevance of pelvic floor trauma at time of delivery. Studies looking at the association of levator muscle injury and stress incontinence have had conflicting results.[2] However, there are data suggesting a relationship between levator injury and fecal incontinence.[3] Studies strongly indicate the relationship between levator muscle injury and pelvic organ prolapse. In a case-controlled study comparing LA defects and pelvic floor function in women with and without prolapse, women with prolapse were much more likely to have major LA defects on MRI than controls (55% compared with 16%).[4] In a retrospective, observational study comparing prolapse and levator avulsion imaging data of 781 subjects, prolapse was seen in 150/181 (83%) women with avulsion and in 265/600 (44%) women without avulsion, giving a relative risk of 1.9 (95% confidence interval, 1.7-2.1).[5]

This study further elucidates the effect of vaginal delivery on the pelvic floor. To date, there are few effective methods of preventing levator trauma. The use of forceps is a known risk factor for pelvic floor muscle trauma and use should be considered carefully. Perineal and pelvic floor muscle training during pregnancy may have an increasing role in prevention of pelvic floor disorders. Pelvic floor physical therapy after delivery plays a key part in the recovery from LA trauma and should be considered for all women undergoing vaginal delivery. ■

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SPECIAL FEATURE

2016 USPSTF Update: Harms and Supplemental Screening

By Jeffrey T. Jensen, MD, MPH, Editor

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SYNOPSIS: The decision to undergo screening mammography requires a consideration of benefits and harms. Harms include false-positive exams leading to unnecessary interventions, and true-positive exams that lead to overdiagnosis.

SOURCES: Nelson HD, et al. Harms of breast cancer screening: Systematic review to update the 2009 U.S. Preventive Services Task Force Recommendation. *Ann Intern Med* 2016;164:256-267.

Melnikow J, et al. Supplemental screening for breast cancer in women with dense breasts: A systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med* 2016;164:205-214.

Last month, we reviewed the new breast cancer screening guidelines from the U.S. Preventive Services Task Force (USPSTF). The USPSTF recommends biennial screening mammography for all women aged 50 to 74 years. For women younger than 50 years of age, the recommendation for screening mammography received a "C" grade (moderate certainty that the net benefit of screening, while positive, is small). As we discussed, the decision to undergo screening more frequently than every other year or before age 50 requires an evaluation of potential benefits and harms. This article will focus on the potential harms of mammogram screening and the role of supplemental screening tests, particularly in women with dense breasts.

Nelson et al reviewed the available English literature to evaluate the potential harms of routine breast cancer screening, and how they differ by age, risk factor, screening interval, and screening modality. The authors considered potential harms to include both false-positive and false-negative mammography results, overdiagnosis, anxiety and other psychological responses, pain during procedures, and radiation exposure.

Overdiagnosis was defined as a diagnosis of ductal carcinoma in situ (DCIS) or invasive breast cancer considered unlikely to become clinically important in the woman during her lifetime in the absence of screening. Harms associated with an overdiagnosis of breast cancer include unnecessary surgical procedures and medical treatments as well as the emotional burden of receiving a cancer diagnosis. Unfortunately, there is no consensus definition of overdiagnosis, so studies evaluating this harm are highly heterogeneous. It is also important to keep in mind that it is difficult to determine the significance of a breast cancer diagnosis to an individual woman. In other words, overdiagnosis remains a population medicine construct that offers little guidance to individual women and their doctors. The analysis of the Nelson et al paper can be summarized follows.

FALSE-POSITIVE AND FALSE-NEGATIVE RESULTS

Nelson et al reviewed data from the Breast Cancer Surveillance Consortium database to evaluate rates of false-positive results in 405,191 women aged 40-89 years who had routine screening with digital mammography between 2003 and 2011. They found rates of false-positive results and recommendations for additional imaging were highest among women aged 40-49 years and decreased with increasing age. Annual screening is associated with a greater risk of false-positive mammogram results and unnecessary biopsies. For example, the cumulative probability of receiving at least one false-positive mammography result after 10 years for a woman who begins screening at age 40 is 61% with annual screening and 42% with biennial screening; 7% will receive a biopsy with annual screening compared to 5% screened every 2 years. For women ages 50-59 years, the probability of unnecessary biopsy is reduced by one-third (from 9% to 6%) when screening is moved from annually to every 2 years. Women with extremely dense breasts who undergo annual mammography, and are either aged 40-49 years or using combined hormonal therapy, have the highest rates of false-positive mammograms and unnecessary biopsy. The lowest rates of false-positive results were seen in women aged 50-74

years without dense breasts screened every 2 or 3 years. In contrast, false-negative results and recommendations for biopsy did not differ greatly by age. False-positive rates were higher for women with risk factors, particularly family history of breast cancer; previous benign breast biopsy result; high breast density; and, for younger women, low body mass index.

OVERDIAGNOSIS

The authors analyzed 18 new studies, including three randomized, controlled trials to evaluate the potential harm of overdiagnosis. The randomized studies offer the best estimates, as they provide a direct comparison of breast cancer diagnosis (both invasive cancer and DCIS) and mortality in the presence and absence of screening. Since the 2009 USPSTF publication, extended 25-year follow-up from the Canadian National Breast Screening Study was published.[1] The conclusion of the Canadian study was that 22% of screen-detected invasive breast cancers were overdiagnosed. In absolute numbers, this represented one over-diagnosed breast cancer for every 424 women who received mammography screening in the trial. The risk of overdiagnosis appears higher for women aged 40-49 years than for older women.

ANXIETY, DISTRESS, AND OTHER PSYCHOLOGICAL RESPONSES

No randomized studies have evaluated the psychological effects of breast cancer screening, and most of the observational studies have a variety of methodologic limitations (small enrollment, narrowly selected subjects, or other methodologic flaws). Given these limitations, the conclusion that women who are recalled for additional testing after screening mammography suffer from more anxiety, breast cancer-specific worry, and distress than women with negative screening should be viewed with caution. Of particular concern, however, were studies which suggest that women with false-positive results were less likely to return for their next screening.

PAIN ASSOCIATED WITH SCREENING

Pain related to screening could influence whether a woman presents for future screening. A number of individual studies and systematic reviews were evaluated to address this question. Most studies did not support that pain associated with screening has a major impact on the decision to represent for a future mammogram.

RADIATION EXPOSURE

Although radiation exposure from standard two-view digital mammography is considered low-dose, repeated studies theoretically could result in harmful effects. No studies have directly measured the association between radiation exposure from mammography screening and the incidence of breast cancer and death. Nelson et al evaluated two modeling studies which estimated that the number of deaths due to radiation-induced breast cancer ranged from 2/100,000 in women aged 50-59 years screened biennially to 11/100,000 in women aged 40-59 years screened annually.[2] However, this potential risk should be interpreted with great caution due to the assumptions based in the model, and the absolute risk of death is tiny and is dwarfed by the net benefit of screening (80 deaths averted among 100,000 women aged 50-59 years who were screened).

DIFFERENCES BETWEEN SCREENING MODALITIES AND USE OF SUPPLEMENTAL SCREENING

The task force concluded that the evidence for benefits and harms of digital breast tomosynthesis (DBT) as a primary screening method for breast cancer was insufficient (I statement). The task force also found the current evidence insufficient to assess the benefits and harms of adjunctive screening modalities (breast ultrasonography, magnetic resonance imaging, DBT, or other methods) in women identified to have dense breasts on an otherwise negative screening mammogram (I statement). In a separate paper, Melnikow et al found that in good-quality studies with U.S. radiologists, a sizable number of women (13-19%) were reclassified from "nondense" to "dense" or vice versa with sequential screening examinations. This may result in differences in mandated communications in states with breast density notification laws and introduce confusion. Although limited evidence suggests that supplemental ultrasound and MRI screening of women with dense breasts will lead to the detection of more invasive breast cancer cases, no studies have shown that supplemental screening leads to improved clinical outcomes or reduces overdiagnosis. Supplemental screening of women with dense breasts with ultrasound or MRI is also associated with increased recall rates for diagnostic investigation among women without breast cancer.

SUMMARY

Overall, mammography screening results in early diagnosis of breast cancer and saves lives. Unfortunately, screening also leads to potential harms from both false-positive and true-positive screens. Clinicians should discuss these potential harms along with benefits in a balanced fashion. Supplemental imaging modalities may improve screening results, but the evidence is currently insufficient to determine whether this results in the diagnosis of more serious breast cancers or simply an increase in overdiagnosis. In keeping with the USPSTF, I recommend screening every 2 years beginning at age 50 and ending at age 74 as an evidence-based conservative approach. ■

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CME/CE QUESTIONS

1. **Which of the following is a confirmed finding? The Zika virus is transmitted through:**
   a. breastmilk.
   b. tick bites.
   c. sexual intercourse.
   d. kissing.
   e. droplet spray.

2. **In the United States, obtaining a medical evaluation for infertility was associated with which of the following?**
   a. White race
   b. Age > 40
   c. Marital status
   d. Smoking
   e. Insurance coverage for infertility

3. **Based on the Aydin study, levator muscle injury at the time of delivery:**
   a. cannot easily be assessed near the time of delivery.
   b. is not associated with fetal head circumference.
   c. is short-lived and resolves by 3 months.
   d. persists in 52% of patients.

4. **Which of the following is *not* considered an important potential harm of mammography screening?**
   a. False-positive exams that lead to unnecessary biopsies
   b. True-positive exams that lead to overdiagnosis of breast cancer
   c. Breast pain leading to discontinuation of screening
   d. None of the above

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- Explain the latest data regarding diagnosis and treatment of various diseases affecting women;
- Discuss new data concerning prenatal care, neonatal health, and complications arising in pregnancy and the perinatal period; and
- Discuss the advantages, disadvantages, and cost-effectiveness of new testing procedures in women's health.

[IN FUTURE ISSUES]

Screening for Ovarian Cancer: Helpful or Harmful?