EDITORIAL

Updated Guidelines for Screening for Asymptomatic Bacteriuria

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In this issue of *JAMA*, the US Preventive Services Task Force (USPSTF) has published updated guidelines for screening for asymptomatic bacteriuria in adults[1] along with an updated evidence report and systematic review.[2] These recommendations are not substantively changed from the previous recommendations, published in 2008.[3] Screening for bacteriuria or antimicrobial treatment for asymptomatic bacteriuria is not recommended for healthy nonpregnant women or healthy men (D recommendation). Screening with a urine culture collected at 12 to 16 weeks of gestation or at the first prenatal visit is recommended for pregnant women, with antimicrobial treatment if asymptomatic bacteriuria is present (B recommendation). These recommendations are consistent with other recent guidelines that have addressed screening and treatment of asymptomatic bacteriuria for these populations.[4,5]

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The USPSTF guidelines have been developed in the context of a changing medical and societal perspective toward antimicrobials, with current approaches favoring the limitation of antimicrobial use, whenever appropriate. This was initially in response to an appreciation that excessive antimicrobial use has contributed to the evolution of antimicrobial resistance, potentially impairing future therapeutic options. More recently, increasing attention to the importance of the human microbiome, and the suggestion that antimicrobial therapy may have deleterious effects on the microbiome influencing both short- and long-term health status for both noninfectious and infectious diseases, has reinforced concerns about antimicrobial use.[6] Inappropriate antimicrobial treatment of asymptomatic bacteriuria is well documented,[4,7] and the implementation of programs to discourage treatment of asymptomatic bacteriuria is an important facet of antimicrobial stewardship initiatives.[8]

For this USPSTF update, there was no new evidence to inform the question of screening or treating asymptomatic bacteriuria for healthy, nonpregnant women. Healthy, young, sexually active women have a prevalence of asymptomatic bacteriuria of 1% to 5%.[4] For most of these women asymptomatic bacteriuria is transient. In a prospective study of 796 women, only 12% had persistent bacteriuria with the same *Escherichia coli* strain 2 months after an initial positive urine culture.[9] The prevalence of asymptomatic bacteriuria in women increases with age and is also increased in women with diabetes. For these women, asymptomatic bacteriuria with the same or different bacterial strains may persist for months or years.[10] Symptomatic urinary tract infection occurs more frequently in women with asymptomatic bacteriuria, but asymptomatic bacteriuria does not cause symptomatic infection, and there is no evidence for other harms with asymptomatic bacteriuria. In fact, there is some suggestion that asymptomatic bacteriuria may protect a woman from symptomatic episodes of urinary tract infection.[4] For men and nonpregnant women living in the community, nontreatment of bacteriuria should be straightforward—it is not necessary to obtain urine specimens for culture unless clinical signs and symptoms are consistent with symptomatic urinary tract infection that warrants antimicrobial treatment.

A recommendation to screen for and treat asymptomatic bacteriuria in pregnant women is reaffirmed in the updated USPSTF guidelines. However, the certainty of evidence has been changed to moderate, from high certainty in the previous guideline. This change acknowledges a substantially lower risk of pyelonephritis for pregnant women with untreated asymptomatic bacteriuria reported in some reports[11,12] and reconsiders the validity of the early clinical trials that were the basis for the previous recommendation. The systematic review, however, concluded that screening and treatment of asymptomatic bacteriuria in pregnant women was associated with substantially reduced risk of pyelonephritis (pooled relative risk [RR], 0.24 [95% CI, 0.14-0.40]) and also with reduced frequency of low birth weight in the infant (RR, 0.64 [95% CI, 0.46-0.90]).[2] These outcomes are compelling but must be considered in context.

Studies of treatment of asymptomatic bacteriuria in pregnant women published more than 30 to 40 years ago have been the basis for recommendations for screening and treatment of asymptomatic bacteriuria in all subsequent guidelines.[5] These foundational studies were undertaken in the first decades of the antimicrobial era. Antimicrobials such as tetracycline, methenamine mandelate, early sulfonamides, cycloserine, and others not used today or now contraindicated in pregnancy were evaluated for treatment of asymptomatic bacteriuria in these previous trials. The use of the quantitative urine culture, which introduced the concept of asymptomatic bacteriuria, was only implemented in

about 1960. The early pregnancy studies were undertaken immediately after the introduction of this diagnostic tool as researchers were struggling to understand the clinical importance of asymptomatic bacteriuria. In addition, the standards of clinical trial design and management were rudimentary compared with current methodology. Thus, the world of urinary tract infection for these studies was very different from current practice.

A strength of the evidence review for this USPSTF update is the approach to evaluation of these older studies. The report acknowledges that "the requirements for clinical trials at that time were substantially different from today."[2] An assessment of these studies using current standards for clinical trial methodology will generally lead to a "poor quality" rating and, sometimes, a dismissal of the observations. However, the USPSTF evidence review applied a "more lenient quality rating" to these older studies, recognizing the limitations but also acknowledging the consistent and large benefits reported for prevention of pyelonephritis and low birth weight. The contributions of early investigators working to improve maternal-child health in a different environment and without current tools are, appropriately, acknowledged.

The morbidity of untreated asymptomatic bacteriuria in pregnant women is largely attributable to acute pyelonephritis occurring in later pregnancy, which may be complicated by severe sepsis or septic shock for some women and which may precipitate preterm labor and delivery.[13] The potential catastrophic outcomes of pyelonephritis complicating a third trimester pregnancy are now relatively uncommon in developed countries. Prevention of pyelonephritis by screening and antimicrobial treatment of asymptomatic bacteriuria in pregnant women for the past 50 years has contributed to this. However, important changes in management of premature labor and care of preterm infants have occurred over the past 30 to 40 years. These advances in obstetric practice also have contributed to a decline in morbidity and mortality should pyelonephritis complicate the third trimester.

The only recent comparative study was reported in 2015 from the Netherlands, a country where universal screening for and treatment of asymptomatic bacteriuria for prenatal care was never introduced. This prospective cohort study with an underpowered nested case-control study screened 4283 women and reported outcomes of pregnant women with treated (n = 40) and untreated (n = 208) asymptomatic bacteriuria.[12] Significantly higher rates of pyelonephritis occurred in pregnant women with untreated asymptomatic bacteriuria, but the incidence of pyelonephritis was lower than in earlier reports and was 2.4% among untreated women and 0.6% among women who were treated. There were no differences in fetal outcomes between women with asymptomatic bacteriuria who were treated or not treated with antimicrobials. This study is more relevant to current clinical practice, and the findings have prompted suggestions that universal screening for all pregnant women and treatment of those with asymptomatic bacteriuria is not beneficial, given the low frequency of pyelonephritis and concerns of potential fetal harms from antimicrobial use in pregnancy, in addition to antimicrobial resistance and potential effects on the microbiome.

However, this study is not generalizable to all pregnant women. Identification of asymptomatic bacteriuria was based on a single urine culture. Recommendations for diagnosis of asymptomatic bacteriuria in healthy women are that an initial positive culture be confirmed by a second positive culture, given the potential for specimen contamination at collection as well as the transiency of asymptomatic bacteriuria in many healthy women.[4] Early pregnancy studies were fastidious in the documentation of bacteriuria—2 or more consecutive urine specimens with the same organism isolated were required before enrolling patients for treatment. In addition, what would now be considered extreme collection methods, such as assiduous vulvar cleaning with antiseptics, collection by nurses with the patient in the lithotomy position, suprapubic aspiration, or in and out catheterization, were used to limit contamination with urine specimen collection. In these studies, a second urine culture was positive in only 50% to 70% of pregnant women after an initial positive culture. Thus, treatment of asymptomatic bacteriuria based on a single positive specimen may promote unnecessary antimicrobial exposure for a substantial proportion of pregnant women. The extent to which treatment of asymptomatic bacteriuria is determined by a single screening specimen in current practice is not clear, but reports describe this practice.[11,12] The updated USPSTF guidelines, in fact, recommend only a single culture, without a second culture to confirm asymptomatic bacteriuria before antimicrobial treatment.

Only women considered "low risk" were enrolled in the Netherlands study. Women with a history of preterm delivery before 34 weeks, imminent preterm delivery, fetal congenital malformation, and risk factors for complicated urinary tract infection were excluded. Early studies did not stratify on the basis of low or high risk, so the differential risk for these patient groups needs to be more fully described. Importantly, the Netherlands has high-quality health care delivery accessible for all citizens, and the small size of the country promotes immediate access to care. The outcomes for pregnant women who develop pyelonephritis and do not have ready access to health care because of socioeconomic issues or geographic remoteness need to be understood if asymptomatic bacteriuria is untreated.

The updated USPSTF guidelines contribute to the evolution of management of asymptomatic bacteriuria in healthy women. However, questions remain about the risks and benefits of universal screening for and treatment of asymptomatic bacteriuria in pregnant women in the context of current clinical practice. The effects of changes in fetal-maternal care, of low- compared with high-risk pregnancies, and of health care access need to be understood. In the short term, application of current diagnostic recommendations for identification of persistent asymptomatic bacteriuria with a second urine culture may provide an immediate opportunity to limit unnecessary antimicrobial use for some pregnant women.

ARTICLE INFORMATION

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