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Asymptomatic Bacteriuria – Important or Not?

The introduction of quantitative urine cultures in the mid-1950s coincided with the introduction and widespread use of antimicrobial drugs. The first studies of quantitative urine bacteriology, in fact, included a diverse group of asymptomatic patients — medical outpatients, patients with diabetes, pregnant women, women with cystoceles, and patients with indwelling catheters.[1] Widespread application of a standardized microbiologic definition of asymptomatic urinary infection ($\geq 10^5$ colony-forming units of an organism per milliliter in two consecutive urine specimens) revealed that positive urine cultures were common in the absence of symptoms. This was at a time when urinary infection was considered to be an important contributor to chronic renal failure, hypertension, and toxemia of pregnancy. A positive urine culture, even without symptoms, was therefore considered potentially harmful.

These initial observations, together with concern about long-term adverse outcomes, generated a series of population-based screening programs for asymptomatic bacteriuria. These studies focused on women and girls because they were identified as having a higher risk of urinary infection and its complications than men and boys. Acute pyelonephritis, especially in pregnancy, was a serious illness during the preantibiotic era. Among those studied were women in Hiroshima, Japan,[2] nuns and working women in the United States,[3] schoolgirls in the United States,[4] and women in Sweden.[5] These and other studies in other parts of the world showed consistently that 1 to 2 percent of schoolgirls and about 5 percent of sexually active young women had positive urine cultures but no symptoms of urinary tract infection. Also, these studies consistently found no short-term or long-term adverse outcomes that could be directly attributed to asymptomatic bacteriuria. Schoolgirls with asymptomatic bacteriuria were no more likely to have progression to renal scarring or renal failure than those without it, for example, and women with asymptomatic bacteriuria were not at increased risk for hypertension or renal failure.

Interest in asymptomatic bacteriuria then shifted from healthy women to well-defined groups with complicated urinary tract infection, such as pregnant women and catheterized or elderly patients. The prevalence of asymptomatic bacteriuria in some of these groups is high — for example, 100 percent in patients with long-term indwelling catheters, 50 percent in patients with intermittent catheterization, and 15 to 50 percent in institutionalized elderly patients.[6] Most studies of such patients also identified no adverse outcomes of asymptomatic bacteriuria. The important exceptions are in pregnant women, men or women undergoing invasive genitourinary procedures, and renal-transplant recipients in the early post-transplantation period. In these groups, asymptomatic bacteriuria is harmful, and adverse outcomes can be prevented with antimicrobial-drug therapy. Asymptomatic bacteriuria is also considered to increase risk in patients with profound neutropenia; its effect in patients with diabetes remains controversial.[7] In other

groups, such as school-age girls[8] or institutionalized elderly persons,[6] treatment of asymptomatic bacteriuria is harmful. Nonetheless, studies in all these diverse groups have consistently confirmed that patients with asymptomatic bacteriuria are also at increased risk for symptomatic urinary infection.

In this issue of the *Journal,* Hooton et al.[9] report observations from a study of two groups of young, sexually active women who were followed at regular intervals for six months. The prevalence of asymptomatic bacteriuria in the two groups was 5 percent and 6 percent, rates consistent with those found in earlier studies.[2,3,5] The most important behavioral risk factors for asymptomatic bacteriuria were the same as those identified for symptomatic urinary tract infection in young, sexually active women — notably, sexual intercourse and use of a spermicide. In addition, most episodes of asymptomatic bacteriuria in these women were transient. Less than 10 percent of episodes of asymptomatic bacteriuria progressed to symptomatic urinary tract infection in which the organism isolated when the woman was asymptomatic was also isolated at the time of the symptomatic infection. In women who did have symptoms, the symptomatic episode developed soon after asymptomatic bacteriuria was detected, usually within one week.

Some methodologic issues in the study by Hooton et al. should be acknowledged so as to place this study in the context of earlier studies. Asymptomatic bacteriuria was identified by only a single urine culture, whereas in most other studies this diagnosis required two or even three consecutive positive urine cultures. Transient bacteriuria is common, especially after intercourse. Basing the diagnosis only on a single urine culture increases the observed prevalence of asymptomatic bacteriuria. On the other hand, the authors defined a limited group of organisms as indicating asymptomatic bacteriuria. Coagulase-negative staphylococci other than *Staphylococcus saprophyticus* accounted for 5 to 10 percent of episodes of asymptomatic bacteriuria in previous reports but were excluded in this study. The bacteriologic definition of asymptomatic bacteriuria, then, was more restrictive in the study by Hooton et al. and may have led to the underestimation of the prevalence relative to previous surveys.

The intriguing question explored in this study is why, in women who are at increased risk for urinary tract infection, some episodes are symptomatic and some are not. A conceptual context for this question could be that host factors, both hereditary and behavioral, determine a woman's risk of having any urinary infection and that whether symptoms develop is determined by the virulence of the organism. However, Hooton et al. report no difference in the genotypes of *Escherichia coli* in isolates from symptomatic and asymptomatic episodes. The absence of a difference in the frequency of genotypes in organisms isolated from women with the two clinical presentations could have been due to the genotypic determinants' not being important for acute cystitis — the clinical presentation of symptomatic infection identified in this study. An exploration of additional virulence factors might identify differences between strains associated with symptomatic and asymptomatic infections; such a difference would be consistent with the hypothesis that variables intrinsic to the organism determine the extent of symptoms. Alternatively, the development of symptomatic infection may not reflect simply the virulence of the organism but may result from a more complex interplay between the phenotypic expression of virulence factors and variation in the host environment.

Asymptomatic bacteriuria in healthy, nonpregnant women is common and is benign. It does, however, identify a group of women who are at risk for symptomatic urinary tract infection. Antimicrobial-drug treatment is highly successful in women with symptomatic, uncomplicated urinary tract infection, but ultimately, the efficacy of specific antimicrobial drugs is limited by increased antimicrobial resistance in community-acquired strains of *E. coli.* This has been the experience with sulfonamides, ampicillin, and now trimethoprim–sulfamethoxazole.[10] Although asymptomatic infection is not a clinical problem in this group of women, understanding the factors that lead to asymptomatic infection may direct investigations toward nonantimicrobial treatments for symptomatic infections — approaches such as vaccination, colonization with avirulent organisms, or selective interference with bacterial adhesion proteins or cell-surface receptors. The importance of asymptomatic bacteriuria may therefore lie in the insights it provides into symptomatic infection.

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