Who Are You—Staphylococcus saprophyticus?

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Staphylococcus saprophyticus is a leading cause of cystitis in young women. S. saprophyticus shares many clinical features of urinary tract infection caused by Escherichia coli, but differs in pathogenesis, seasonal variation, and geographic distribution. This review summarizes what is known and what still needs to be learned about this microorganism.

Staphylococcus saprophyticus is uniquely associated with uncomplicated urinary tract infection (UTI) in humans. It has special urotropic and ecologic features that are distinctly different from other staphylococci and from Escherichia coli. This article will consider the epidemiology, ecology, pathogenesis, and clinical features of infections caused by this microorganism. Much more needs to be learned about the epidemiology and natural history of UTI caused by S. saprophyticus as well as the role of S. saprophyticus in human and animal health and disease. A series of research questions are offered to address these issues.

Coagulase-negative staphylococci were considered to be urinary contaminants prior to the 1960s. In 1962, Torres Pereira [1] reported the isolation of coagulase-negative staphylococci possessing antigen 51 from the urine of women with acute UTI. In subsequent years, additional reports supported this concept [2]. The organism was found to belong to micrococcus sub-group 3. It was later reclassified as S. saprophyticus. Urease production is another important characteristic, and renal and ureteral stones were found to be associated with S. saprophyticus infection [5].

Laboratory diagnosis. Laboratory identification of S. saprophyticus is made on the basis of resistance to novobiocin, the absence of hemolysin and coagulase, and intense pigment production. Approximately 65% of strains are yellow, and 35% are white [3]. Testing of novobiocin susceptibility is reported to be 100% sensitive and 96% specific [4]. This provides a simple and reliable screening method to differentiate the presence of S. saprophyticus from the presence of other coagulase-negative staphylococci, but further tests are recommended for final identification.

Epidemiology. S. saprophyticus is second only to E. coli as the most frequent causative organism of uncomplicated UTI in women. The more severe complications include acute pyelonephritis [6], septicemia [7], nephrolithiasis [5], and endocarditis [8]. The vast majority of infections occur in young sexually active women. Wallmark et al. [9] isolated S. saprophyticus from the urine of 173 of 787 (22%) consecutive female patients found to have bacteriuria. The highest rate of S. saprophyticus infection was 42.3%, among women aged 16–25 years included in the study. Gupta et al. [10] reported a prevalence of 8% among 665 young women with UTI. In a study conducted in Australia, S. saprophyticus was isolated from 15.2% of the women aged 13–40 years with UTI [11]. There are also several case reports of infections in young girls [12].

S. saprophyticus can also cause UTI in males of all ages; the organism has been isolated in young boys [13], male homosexuals, and elderly men with indwelling urinary catheters [14]. It also can cause urethritis, epididimitis, prostatitis, and nephrolithiasis in men, and is relatively rare in hospitalized men [15].

In contrast, S. saprophyticus appears to be unusual in Israel. In a study performed 20 years ago [16], we did not find any cases of S. saprophyticus infection among 198 young women with acute UTI. In addition, only 103 (0.3%) of 35,580 and 88 (0.6%) of 15,206 urine cultures performed at 2 microbiological laboratories in Northern Israel that were positive for a pathogen yielded S. saprophyticus (unpublished data). There is one puzzling report of the recovery of coagulase-negative staphylococci in 15.6% of young Israeli women with UTI who have been recently sexually active [17]. Unfortunately, the bacterial isolates were not further identified. These significant differences in incidence could be attributed to different techniques of sampling, delivery, culture, and interpretation of cultures used by different authors. Although S. saprophyticus mainly infects young women, other coagulase-negative staphylococci are usually isolated from hospitalized elderly patients with urinary indwelling catheters or other manipulations of the urinary tract. The main reason for this difference is the capacity of S. saprophyticus to adhere to the uroepithelial cells, and other co-
agulase-negative staphylococci have the ability to colonize indwelling catheters.

Another factor that should be considered when data from different sources are analyzed is that most laboratories base the identification of *S. saprophyticus* on novobiocin resistance. Other staphylococci can show resistance [18]. In addition, different laboratories use different identification methods (e.g., colony appearance on chromogenic agar and automated phenotypic methods, among others), making data collected from different sources incomparable. In future epidemiological studies, well-defined methods of comparison should be used.

**Pathogenesis.** The gastrointestinal tract is the major reservoir of *S. saprophyticus*. In an early study, Latham et al. [19] noted that rectal, vaginal, and urethral colonization of *S. saprophyticus* was associated with UTI caused by this organism. Rupp et al. [18] determined that the prevalence of colonization of *S. saprophyticus* of the urogenital tract among healthy women was 6.9%; the most common site of colonization was the rectum (40%). The urine sediment of a patient with UTI caused by *S. saprophyticus* has a characteristic microscopic appearance; methods of chemical screening for bacteriuria do not always succeed in diagnosing UTI caused by *S. saprophyticus*. Even when such an infection occurs in the bladder, comparatively low numbers of colony-forming units (≤10^5 cfu/mL) are found in the bladder and voided urine. The American Society of Microbiology’s *Manual of Clinical Microbiology* [20] recommends a cut-off value of between 10^5 and 10^6 cfu/mL for the diagnosis of significant bacteriuria, but there is not a worldwide consensus for these values. Colonization is more frequent during the summer and fall. Hoveli et al. [21] showed that women with *S. saprophyticus* colonization were more likely to have had a symptomatic UTI during the previous 12 months, to have recently had a menstrual period, and to have had sexual intercourse concurrent with vaginal candidiasis than were women without colonization. None of the women developed symptomatic UTI during the next 6 months. Further support for the existence of a rectal reservoir was the isolation of the same plasmid-identified clone from both urine and stool samples [22].

The remarkable selective susceptibility of young women to colonization by *S. saprophyticus* is further emphasized by a study by Schneider and Riley [11]. They isolated the microorganism from the genital tracts of 4.6% of women aged 13–40 years, but not from older women or men.

These observations are in accord with numerous clinical reports [9–17] that UTI caused by *S. saprophyticus* is associated with recent sexual intercourse and occurs more often during late summer and fall [19]. The microorganisms colonize the human gastrointestinal tract, particularly during the gastrointestinal season in the summer and fall, and this is probably the reason for this seasonal variation in the incidence of UTI caused by *S. saprophyticus*. However, there was no seasonal variation in Western Australia and Israel [11, 16]. There is a strong association between the use of condoms coated with nonoxynol 9 and the occurrence of UTI [23], which suggests that vaginal spermicides interfere with the normal vaginal flora and promote colonization by *S. saprophyticus*.

Other associations include outdoor swimming prior to colonization and occupations related to meat processing and meat products [6]. *S. saprophyticus* has been isolated from 7.1% of rectal swab specimens taken from carcasses of cattle and from 7.3% of rectal swab specimens taken from pigs. The seasonal variation in the prevalence of colonization by *S. saprophyticus* in cattle and pigs was similar to that of UTIs in humans. The microorganism was found to contaminate 16.4% of various food samples in Sweden, with a high prevalence of 34% in samples of raw beef and pork [24–25]. Nevertheless, *S. saprophyticus* UTI can occur in women who are vegetarians [6]. *S. saprophyticus* UTI is susceptible to antibiotics usually prescribed for patients with UTI, with the exception of nalidixic acid [26]. However, recurrence of UTI due to *S. saprophyticus* is common. In addition, single-dose therapy with quinolones is less effective than a 3-day course [27].

The virulence factors of *S. saprophyticus* include adherence to urothelial cells by means of a surface-associated protein, lipoteichoic acid; a hemagglutinin that binds to fibronectin, a hemolysin; and production of extracellular slime [28]. The hemagglutinin appears to be more important than adherence factors in enabling colonization of kidney tissue in rats [29]. Hedman et al. [6] described epidemiological and clinical aspects of 270 randomly selected episodes of UTI caused by *S. saprophyticus* matched with 276 episodes of UTI caused by other organisms, according to the sex and age of each subject and the temporal occurrence of each episode.

**Clinical features.** Common symptoms of inflammation of the lower tract, such as hematuria and pyuria, were seen more often among patients with colonization of *S. saprophyticus*. In addition, *S. saprophyticus* was the cause of 13% of upper UTIs, an incidence higher than that reported for other bacteria. In addition, Jellhen et al. [30] observed that significantly more patients infected with *S. saprophyticus* complained of dysuria, urinary frequency, and back pain than did patients infected with *E. coli*.

**Summary.** These observations provide a framework for the sequence of events in the pathogenesis of infections caused by *S. saprophyticus*. Humans acquire the microorganism from direct exposure to animals or inadequately cooked animal food products. Young women are more susceptible to genitourinary colonization than are others, and some people develop infection in association with hormonal influences that occur near or during menstruation. Sexual intercourse promotes colonization and infection. Alterations in the genital flora effected by spermicides or candidal infection favor colonization by *S. sapro-
phyticus. Anal intercourse may play a role in infection in homosexual men.

**Research questions.** The following questions need to be answered: can the microorganism be transmitted by human-to-human contact? If so, is casual contact among family members sufficient, or is more intimate contact needed, such as vaginal or anal intercourse? How long does the carrier state last? How often do carriers develop UTI? What triggers UTI in some carriers? Does long-term colonization protect against infection? Does infection result in immunity? Are some strains more urovirulent than others? Do the same or different clones cause recurrent infections? How many microorganisms need to be ingested to produce gastrointestinal colonization? Can more thorough cooking or irradiation of meat products reduce the incidence of infection? Can genital colonization occur independently of gastrointestinal colonization? What is the role of vaginal pH and commensal microbes? What is the natural history of *S. saprophyticus* UTI in women? How often do such women acquire urolithiasis? Is climate important? The answers to these and other questions should improve our understanding of this fascinating microorganism and hopefully lead to its control.

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**References**