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Staphylococcus saprophyticus as a urinary pathogen: a six year prospective survey

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Abstract

Over six years (1978-83, inclusive) weekly laboratory records of organisms causing urinary tract infection in women aged 15-25 not attending hospital were kept prospectively and analysed. The incidence of infection with Staphylococcus saprophyticus defined by age and sex was confirmed. This organism caused an increasing proportion of infections in young women over the six years studied, and these infections showed noticeable seasonality. All but four isolates of S saprophyticus were sensitive to all the commonly used antimicrobial agents that were tested. This might be because the organism is not often present in the body as a commensal and therefore not subject to the selection pressures exerted by such agents.

As infection with S saprophyticus has different clinical connotations from infection with other coagulase negative staphylococci it should be differentiated from them in routine laboratory practice.

Introduction

Although published reports on the role of *Staphylococcus saprophyticus* (formerly known as *Micrococcus* subgroup 3) as a urinary pathogen date back to Pereira,[1] Mabeck,[2] and Mitchell,[3] general recognition that it is a true pathogen has been slow.[4] In 1974 we noted the high incidence of pyuria accompanying these infections and that the incidence was well defined by age and sex, most infections occurring in women between the ages of 15 and 25 not attending hospital.[5] Having confirmed our preliminary observations on this organism and the reliability of resistance to novobiocin as a diagnostic test in more detailed studies using the Baird-Parker typing system,[6] we incorporated a novobiocin disc into our first line sensitivity tests. Thus we have been able to detect the organism reliably and without added workload.

Since 1978 we have kept weekly records of all infections with *S saprophyticus*, relating them to the total number of specimens of urine received and infections with other organisms in the principal age group affected.

Subjects and methods

Records for the six years 1978-83, inclusive, were analysed. Women between the ages of 15 and 25, inclusive, not attending hospital (excluding hospital outpatients as well as inpatients) were designated as the study group. The number of urine specimens received from all other sources and the number received from the study group were recorded. The number of specimens from the study group that were infected was recorded and the distribution of the organisms analysed.

The term coliform was used to include all Gram negative bacilli other than *Proteus* spp and *Pseudomonas* spp. All isolations of *S saprophyticus* from patients who were not in the study group (comparison group) were also recorded and the distribution analysed. Records were kept of the antibacterial sensitivities of all isolates of *S saprophyticus* and the presence or absence of pyuria (defined as 10 or more leucocytes/mm^3 of uncentrifuged urine).

Throughout the study the primary isolation medium for culturing midstream urine samples was cysteine lactose electrolyte deficient agar, and our criterion for interpreting significance (a count of at least 10^7 colony forming units/l) did not change. Sensitivity testing was by a modified Stokes' method.[7]

Results

The total number of urine specimens received increased steadily from 39 450 in 1978 to 61 305 in 1983. In 1978 and 1983, 3909 (10%) and 6234 (10%) specimens, respectively, were from women in the study group; there were, however, small variations in this percentage over the six years, and a linear trend test[8] showed evidence of a significant increase during this period ($\chi^2 = 20{\cdot}3$, 1 df, $p < 0{\cdot}01$). In 1978 and 1983 there were 931 (24%) and 1516 (24%) infected midstream urine samples from women in the study group; there were small variations in the intervening years but no significant overall trend.

Table I shows the distribution of the four main groups of organisms

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TABLE I—*Distributions of the four main groups of organisms isolated from study group*

Year	Total No of infected midstream urine samples	No (%) of midstream urine samples infected with: Coliforms	*S saprophyticus*	*Proteus* spp	*Streptococcus faecalis*
1978	931	674 (72)	159 (17)	51 (5)	24 (3)
1979	1041	794 (76)	140 (13)	59 (6)	28 (3)
1980	1087	781 (72)	178 (16)	59 (5)	40 (4)
1981	1277	917 (72)	230 (18)	65 (5)	26 (2)
1982	1282	915 (71)	261 (20)	56 (4)	28 (2)
1983	1516	1103 (73)	269 (18)	91 (6)	33 (2)

TABLE II—*Number of S saprophyticus infections*

Year	Study group	Women aged 26-50 not attending hospital	Others
1978	159	67	37
1979	140	89	39
1980	178	72	31
1981	230	105	38
1982	261	117	45
1983	269	102	44

Statistical tests for seasonality[9,10] were performed using monthly figures summed over the six years as seasonal effects appeared comparable from year to year. Assuming that a simple harmonic cyclic trend over 12 months is followed, the peak compares to the maximum point on a fitted sine curve and the trough to the minimum point.

The summed monthly figures for both the total number of urine specimens received and the number from the study group showed significant seasonal patterns ($\chi^2=613$, 2 df, $p<0{\cdot}01$, and $\chi^2=257$, 2 df, $p<0{\cdot}01$, respectively), each with a peak in early October.

The figure shows the monthly proportions of infections with different organisms to the number of infected midstream urine samples from the study group. There was a significant seasonal pattern for *S saprophyticus* infections ($\chi^2=44{\cdot}7$, 2 df, $p<0{\cdot}01$), the peak occurring in the middle of September, and a significant seasonal pattern for coliform infections ($\chi^2=7{\cdot}5$, 2 df, $p<0{\cdot}05$), the peak occurring in the middle of March. Proteus infections showed no significant seasonal pattern.

Infections with *S saprophyticus* in relation to all midstream urine samples received from the study group also showed a significant seasonal pattern ($\chi^2=67{\cdot}5$, 2 df, $p<0{\cdot}01$), the peak occurring in early September. Likewise, in the comparison group the number of *S saprophyticus* infections in relation to the number of specimens received showed a significant seasonal pattern ($\chi^2=72{\cdot}6$, 2 df, $p<0{\cdot}01$), this peak occurring in early October.

TABLE III—*Distribution of S saprophyticus in comparison group. Values are numbers of isolates*

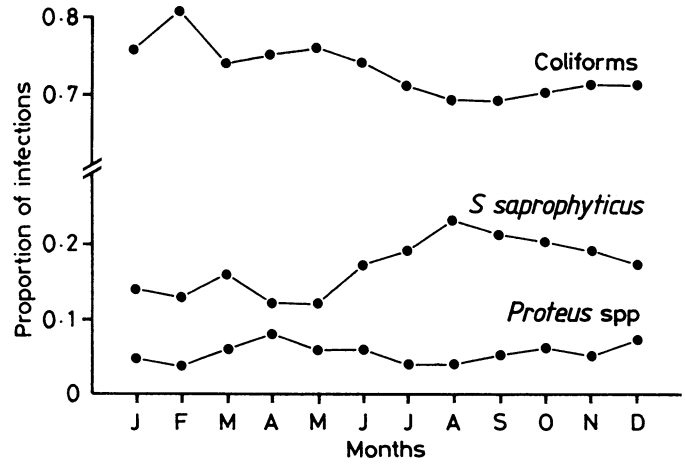
Group	Year 1978	1979	1980	1981	1982	1983	Total
Aged <15:							
Boys		1	6	1	2	4	14
Girls	9	3	3	6	8	7	36
Aged 15-25:							
Men	1	3	2	1	2	4	13
Women, hospital patients	8	10	7	10	19	12	66
Aged 26-50:							
Men		2	1	1	2	3	9
Women, hospital patients	4	9	3	1	6	4	27
Women, general practice patients	67	89	72	105	117	102	552
Aged > 50:							
Men	3	1	2	2			8
Women, hospital patients	2	1	1	1	1		6
Women, general practice patients	10	9	6	15	5	10	55
Total	104	128	103	143	162	146	786

isolated from midstream urine samples from the study group during the six years. In addition to the four main groups of organisms, there were 82 isolates of *Staphylococcus epidermidis*, 43 group B haemolytic streptococci, 17 *Staphylococcus aureus*, and 10 *Pseudomonas* spp. These organisms accounted for less than 4% of the total number of infections. With the exception of the year 1979, when infections with *S saprophyticus* fell to 13%, this organism accounted for between 16% and 20% of all infections in the study group. The decrease in 1979 was significant ($p<0{\cdot}05$), but a linear trend test showed an increase over the six years ($\chi^2=7{\cdot}6$, 1 df, $p<0{\cdot}01$). This increase did not correspond to a significant steady decrease in the proportion of any one particular group of organisms over the same period.

Table II shows the yearly numbers of infections with *S saprophyticus* in women in the study group and in the comparison group. The proportion of *S saprophyticus* infections to the number of midstream urine samples received from the study group showed a significant linear trend upwards: ($\chi^2=6{\cdot}8$, 1 df, $p<0{\cdot}01$). In the comparison group the proportion of *S saprophyticus* infections to the total number of specimens received did not differ significantly over the six years.

Table III shows the distribution of *S saprophyticus* infections in the comparison group. There were no significant changes in the distribution of infections, the greatest number occurring every year in women between the ages of 26 and 50 not attending hospital. A small number of infections occurred in men each year; these were distributed over all the age groups, including children, and showed no significant differences over the period studied.

Pyuria was associated with 1902 of 2023 *S saprophyticus* infections. All except four of 2023 isolates were sensitive in vitro to all agents tested; nitrofurantoin, sulphonamide, amoxycillin, and co-trimoxazole. Four strains, isolated after 1979 when trimethoprim alone became available for clinical use, were sensitive to sulphonamide but resistant to trimethoprim and co-trimoxazole. *S saprophyticus* was isolated repeatedly from the urine of two patients who had renal stones.



Monthly proportions of infections in women in the study group due to each group of organisms.

Discussion

Our methods for diagnosing significant urinary tract infections with aerobic pathogens did not change over the six year study period, and therefore our results from 1983 are comparable to those from 1978. Although there was an increase in the number of midstream urine samples received from the study group during

the six years, there was no significant increase in the proportion that were infected.

Each year *S saprophyticus* was the second commonest pathogen isolated from the study group, and the proportion of infections with this organism increased. In all except one year it accounted for at least 16% of infections. Possible reasons for its absence, or much lower percentage, in results from many other laboratories are the use of inappropriate culture media, unwillingness to accept coagulase negative staphylococci as pathogens, studies undertaken on a wider age group, and studies undertaken at times of the year when the incidence of *S saprophyticus* infection is at its lowest.

We confirmed the results of several previous reports that most of these infections occur in young women not attending hospital, the second largest incidence being in women aged 26-50, also not attending hospital.[5 6 11-13] These infections rarely occur in patients in hospital; in our experience isolates of *S saprophyticus* from hospital inpatients are invariably from those, including some young boys, admitted as emergencies because of the very severe symptoms caused by infection with this organism. We have never encountered a hospital acquired infection.

The high incidence of pyuria (94%) suggests that *S saprophyticus*, despite its inappropriate name, is an acute pathogen causing a severe inflammatory response; we have never knowingly isolated it from a symptom free patient (in contrast with experience with *Escherichia coli* or *Proteus* spp), and it seldom features in screening studies of asymptomatic women.

One of us (RM) has followed patients with recurrent urinary tract infections in a urinary infection clinic over the past 16 years; the only radiological abnormalities found in association with this organism were renal stones in two patients. *S saprophyticus* was isolated repeatedly over several years from both patients, suggesting that the calculi were "infection stones" caused by the presence of organisms that split urea in the renal pelvis.

Hovelius *et al* showed evidence of renal disorder during attacks of infection with *S saprophyticus* (renal tenderness and evidence of reduced concentrating capacity) and reported three patients with renal calculi; from one the organism was isolated from urine collected from the renal pelvis.[14] Fowler also reported the isolation of this organism from a renal stone.[15] *S saprophyticus* may, therefore, reach the renal pelvis, accounting for the severe symptoms, but is not associated with renal scarring. This may be because the renal scarring process begins in childhood when infections with this organism are rare. We have not isolated *S saprophyticus* from children of either sex under 5 years of age.

In contrast with all other urinary pathogens, a proportion of which have become resistant to many commonly used antibiotics, our isolates of *S saprophyticus* remained sensitive to all the agents tested throughout the six year period, the only resistant isolates being four strains that were resistant to trimethoprim. (We were unable to compare our results with those from other reports because all the large published reports include *S saprophyticus* with other coagulase negative staphylococci or with "micrococci," which have developed resistance to many antibacterial agents.) As *S saprophyticus* has remained sensitive to many antibiotics it may not, unlike other pathogens of the urinary tract and other staphylococci, be present normally in the body as a commensal and therefore not subject to the selection pressure exerted on commensals by antibiotics.

Sellin *et al* looked for the organism in the urethral flora of young women but found it rarely.[16] Hovelius *et al* reported isolations from specimens from indwelling catheters from men[17] and urethral swabs from men attending a venereal disease clinic.[18] Perhaps the reservoir of infection is in the male, not female, urethra, and the continuing sensitivity might be due to young men receiving much less antibacterial treatment than young women who are prone to cystitis.

Although *S saprophyticus* infections occur throughout the year, the large number of specimens studied in this series enables us to confirm conclusively that they have a noticeable seasonal incidence, both in the study group and in other age and sex groups. In contrast with coliform infections, which show a significant peak in March, *S saprophyticus* infections occur most often in late summer and early autumn. In this laboratory we serve an area that is a holiday resort and has a large population of students. Thus the number of young women presenting with urinary tract infections will probably rise during the summer and early autumn. This would account for the significant increase in the number of midstream urine samples received from the study group at this time. It does not, however, explain the significant increase in the proportion of infections due to *S saprophyticus*. This organism may be present more often as a commensal during late summer and early autumn; or *S saprophyticus* infection may occur early in a woman's sexual life (holiday encounters or students arriving at college). Why then should infections occur in quite a large number of women over 25 years? Only longitudinal studies of individual patients, their commensal flora, and that of their sexual partners will answer this question. Such studies, in the age group affected, are notoriously difficult to carry out.

The mode of pathogenicity of an organism with such a circumscribed incidence could be relevant. O'Garra *et al* showed that some strains can adhere to human epithelial cells whereas others cannot, and electron microscopy showed that both the adherent strains and the epithelial cells had a surface coat composed of a type of acidic polysaccharide.[19] Pead found that non-specific agglutination occurred between heated suspensions of *S saprophyticus* and IgM fractions of human sera but was not detectable when the suspensions contained a high proportion of cocci bearing an electron lucid halo.[20] Recently, Gunnarsson *et al* reported the presence of oligosaccharide structures mediating agglutination of sheep erythrocytes by *S saprophyticus*.[21]

Many problems relating to infection with this organism remain. It is now clear, however, that it has different clinical connotations from infection with other species of coagulase negative staphylococci and should be differentiated from them in routine laboratory practice.

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