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Staphylococci as urinary pathogens

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SUMMARY During the course of one year all (382) strains of staphylococci isolated in significant culture from urine specimens were typed by the Baird-Parker method. *Staphylococcus aureus* accounted for only 63 (16%) of the infections. Novobiocin-resistant micrococcal infection occurred predominantly in young women but also in children of both sexes; it was not restricted to M3. To try to detect possible sources of micrococcal infection other than faeces the normal flora of the throat, urinary tract, and vagina of young women was studied. Novobiocin-resistant micrococci were rarely found. Previous reports that micrococci are the second commonest urinary pathogens in young women in domiciliary practice were confirmed. The laboratory records of patients with these infections suggested that they respond well to treatment and that recurrences are usually due to a different organism.

Some staphylococci can be pathogenic in the urinary tract. Since Mitchell (1968) reported that staphylococcal infections attributable to abnormalities or instrumentation of the urinary tract were caused predominantly by staphylococcus subgroups II, V, and VI, as defined by Baird-Parker (1963), and infections occurring in otherwise healthy young women by micrococcus subgroup 3 supporting evidence has been accumulating slowly (Mabeck, 1969; Kerr, 1973; Maskell, 1974; Meers, 1974; Meers *et al.*, 1975; Sellin *et al.*, 1975). Mitchell (1968) suggested that micrococcus 3 could be provisionally identified by its resistance to novobiocin *in vitro*. Since there are many bacteriological and clinical implications of the recognition of this organism as a urinary pathogen (use of appropriate culture media, selection of appropriate antibacterial therapy) it seemed important to test in a large study the reliability of novobiocin sensitivity as a means of differentiating this organism from the other biotypes of the Micrococcaceae (*Lancet*, 1974).

During the course of one year (December 1974 to November 1975) all strains of catalase-positive Gram-positive cocci isolated in pure culture and significant numbers from urine specimens were typed by the Baird-Parker method and tested for sensitivity to novobiocin. The incidence of micrococcal infection relative to other organisms in domiciliary practice was recorded, and some data were collected on the previous and subsequent bacteriological history of the patients with micrococcal infection.

In an attempt to detect possible sources other than faeces of the infecting organisms we studied the normal flora of the throat and urinary tract of young women and high vaginal swabs from patients complaining of vaginal discharge and patients admitted for gynaecological surgery.

Methods

(1) Urine specimens were cultured on CLED agar (Mackey and Sandys, 1966) using a 0·01-ml fused platinum loop. A pure culture in excess of 10^7 organisms/litre was regarded as indicative of infection. Sensitivity to novobiocin was determined using 5 μg discs. The organisms were identified by the Baird-Parker (1963) method. The division into staphylococci (S) and micrococci (M) was made on the basis of the glucose utilisation test in accordance with the original classification of Baird-Parker (1963); the medium used was that recommended by the International Subcommittee on Taxonomy of Staphylococci and Micrococci (1965). (Organisms assigned to M 1-4 have recently been reclassified as staphylococci (Buchanan and Gibbons, 1974), and this will be considered in the discussion.) Microscopy was carride out on the deposit after centrifugation at 2000 rpm for 5 minutes. The presence of >10 leucocytes per high power field was recorded as

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gross pyuria; the presence of any red cells was recorded as microscopic haematuria.

(2) A record was kept of the infecting organisms in all urinary tract infections in female patients in domiciliary practice during the year for comparison.

(3) The laboratory records of patients known to have had a novobiocin-resistant staphylococcal infection during the period January 1975 to April 1976 were studied.

(4) Catalase-positive Gram-positive cocci isolated from 47 specimens of mid-stream urine from female patients in mixed culture, and therefore considered to be indicative of contamination, were examined for novobiocin sensitivity. Forestream specimens of urine from 21 female laboratory staff in the age group 16-45 years, high vaginal swabs from 20 patients complaining of vaginal discharge and 100 patients admitted for gynaecological surgery, and throat swabs from 46 volunteer female nurses were cultured on CLED agar. All catalase-positive Gram-positive cocci isolated were tested for novobiocin sensitivity, and the novobiocin-resistant strains were typed by the Baird-Parker method. Forestream specimens of urine were collected from the same 46 nurses and all catalase-positive Gram-positive cocci isolated were typed.

Results

STAPHYLOCOCCAL URINARY INFECTIONS IN PATIENTS

During the 12 months from 1 December 1974 to 30 November 1975, 36 374 specimens of urine from hospital and domiciliary patients were examined: 382 strains of staphylococci were isolated in pure growth and significant numbers.

Staphylococcus aureus (SI)

Sixty-three strains were isolated, 32 from hospital and 31 from domiciliary patients. Twenty-eight strains were from males, of whom more than two-thirds were over 55 years of age; 35 strains were from females, who were distributed over the whole age range.

Coagulase-negative staphylococci

Three hundred and nineteen strains were isolated, 132 from hospital and 187 from domiciliary patients. One hundred and fifty-six were classified as SII-VI and 163 as M 1-7. Table 1 shows the age and sex distribution of the patients with these infections. The greatest incidence of staphylococcal infection is in male hospital patients over the age of 55 years and of micrococcal infection in female domiciliary patients between the ages of 16 and 35 years.

Table 2 shows the age and sex distribution of the patients with SII-VI infections, and Table 3 the distribution of those with M 1-7 infections.

Novobiocin sensitivity

Only two of the 219 strains of SI-VI were resistant to novobiocin, one *Staph. aureus* (SI) and one SII. All 148 strains of M 1, 3, and 5 were resistant, as were two of the four strains of M2. The 11 strains of M7 were all sensitive.

Pyuria and haematuria

There was a high incidence of pyuria and haematuria in association with infection due to M1, 2, 3, and 5. Eighty-six per cent of specimens showed gross pyuria and 40% showed microscopic haematuria. In contrast, none of the 11 specimens yielding M7 showed gross pyuria or microscopic haematuria.

INCIDENCE OF M3 AND 5 RELATIVE TO OTHER ORGANISMS IN INFECTIONS IN FEMALE DOMICILIARY PATIENTS

Clearly micrococcal infection occurs predominantly in young women in domiciliary practice (Table 1). One thousand and eighty-one infections were seen in females in the age group 16-35 years from domiciliary practice during the year. *Escherichia coli* and other coliforms (not identified) accounted for 834 (77%), M3 and 5 for 96 (9%), and *Proteus* spp for 62 (6%). Other organisms accounted for the remaining 8%. If the age group 16-25 years is analysed separately M3 and 5 accounted for an even higher percentage of infections—77 out of a total of 574 (13%).

LABORATORY RECORDS OF PATIENTS WITH NOVOBIOCIN-RESISTANT STAPHYLOCOCCAL INFECTION

The laboratory records over the period January 1975 to April 1976 of 152 patients known to have had an episode of novobiocin-resistant staphylococcal infection during this period were studied. One hundred and forty-four female patients had 155 episodes of infection and eight male patients each had one

Table 1 *Age and sex distribution of hospital and domiciliary patients with coagulase-negative staphylococcal infections*

Age group (yr)	Hospital				Domiciliary			
	SII-VI		M1-7		SII-VI		M1-7	
	M	F	M	F	M	F	M	F
0-15	3	4	1	4	—	7	4	9
16-35	4	21	2	11	2	24	—	106
36-55	6	4	1	4	2	8	—	18
>55	48	15	2	1	3	5	—	—
Total	61	44	6	20	7	44	4	133

Table 2 *Age and sex distribution of patients with staphylococcal subgroup infections*

Age group (yr)	*SII*		*SIV*		*SV*		*SVI*		*S*[1]	
	M	*F*	*M*	*F*	*M*	*F*	*M*	*F*	*M*	*F*
0-15	—	5	—	—	2	5	1	1	—	—
16-35	4	38	—	—	—	4	2	—	—	3
36-55	7	8	—	—	1	2	—	1	—	1
>55	38	11	—	2	8	6	—	—	5	1
Totals	49	62	—	2	11	17	3	2	5	5
	111		2		28		5		10	

[1]Strains which did not conform to any of the Baird-Parker types.

Table 3 *Age and sex distribution of patients with micrococcal subgroup infections*

Age group	*M1*		*M2*		*M3*		*M5*		*M7*	
	M	*F*	*M*	*F*	*M*	*F*	*M*	*F*	*M*	*F*
0-15	—	—	—	2	5	8	—	—	—	3
16-35	—	—	—	1	—	111	—	5	2	—
36-55	—	2	—	1	—	13	—	3	1	3
>55	—	—	—	—	—	—	1	—	1	1
Totals	—	2	—	4	5	132	1	8	4	7
	2		4		137		9		11	

episode. One hundred and twenty-three of the organisms from females and six from males were typed; all were found to be M2, 3, or 5. The remaining 34 organisms were not typed but were presumed to be micrococci.

Specimens after treatment for the micrococcal infection were received from two of the eight males and 43 of the 144 females. Forty-three were sterile; two female patients still showed micrococcal infection.

During the 16-month period none of the male patients had evidence of another episode of infection; 23 female patients had 24 other episodes of infection, six with micrococci and 18 with other organisms. There was no laboratory evidence of any other urinary infection in the remaining 121 female patients.

Table 4 *Micrococcaceae isolated from forestream specimens of urine of 46 nurses*

Staphylococcus biotype	*No. of strains*
I	1
II	19
IV	1
V	10
VI	5
S[1]	4
Micrococcus subgroup	
1	3
2	2
3	3
7	1
8	1
M[1]	1
Total	51

[1]These strains did not conform to any of the Baird-Parker subgroups

POSSIBLE SOURCES OF INFECTING ORGANISMS

Only three novobiocin-resistant strains were isolated from the 47 contaminated specimens of mid-stream urine. Two were identified as SV and one as M3. None was isolated from the forestream specimens of urine of the laboratory staff, the high vaginal swabs, or the throat swabs.

Table 4 shows the strains of Micrococcaceae isolated from the forestream specimens of urine of the nurses. Only two strains were resistant to novobiocin; both were micrococci (M3 and M[1]). The nurse from whom the M3 was isolated had urinary infection symptoms, and examination of a mid-stream specimen confirmed the presence of significant infection with this organism.

Discussion

So far as we know this is the first reported study in which all the staphylococci isolated in significant culture from urine specimens, from both hospital and domiciliary sources, over the course of one year have been typed. Coagulase-positive strains accounted for only 16% of these infections.

Typing of the coagulase-negative strains by the Baird-Parker method confirmed the suggestion of

Mitchell (1968) that infections due to SII-VI occur predominantly in elderly male hospital patients and are usually associated with instrumentation or underlying lesion of the urinary tract. Likewise the well-defined incidence of M3 infection in young women in domiciliary practice was confirmed. However, this organism also caused infection in boys and girls. There were 26 infections with the other subgroups of micrococci. Those due to strains of M1, 2, and 5 had a distribution similar to that of M3, and also showed a similar high incidence of pyuria and microscopic haematuria. Infections due to M7, however, seemed to have a different distribution, although it is difficult to be certain of this with such a small number. Strikingly, in contrast to the other micrococcal infections, none of the M7 infections was accompanied by gross pyuria or microscopic haematuria.

It has been suggested that sensitivity to novobiocin *in vitro* might be used as a single laboratory test for discriminating between M3 and other biotypes of the Micrococcaceae (Mitchell, 1968; Meers *et al.*, 1975). We found that all strains of micrococci isolated except two of the four strains of M2 and the 11 strains of M7 were resistant to novobiocin, and that all strains of staphylococci, with the exception of one strain of *Staph. aureus* and one of SII, were sensitive. This test, therefore, is not absolutely specific for M3, but it would seem to be reasonably satisfactory for differentiating the acutely pathogenic micrococci (those which produce a severe inflammatory response indicated by pyuria and haematuria) from M7 and the staphylococcal subgroups. We now feel confident in using the test in this way in our routine laboratory work.

The ability of M2, 3, and 5 to be acutely pathogenic in the urinary tract is not understood. Possibly the mechanism of resistance to novobiocin is the same as that which accounts for their pathogenicity, and further studies are required in this field. The distribution of infection with M3 and 5 was similar; both organisms produced an acute inflammatory response shown by pyuria and often haematuria, and all strains were novobiocin resistant. In marked contrast, M7 infections had a different distribution, were not accompanied by pyuria, and were all sensitive to novobiocin. M1-4 have recently been reclassified as staphylococci on the basis of their DNA base ratios (Buchanan and Gibbons, 1974) and have been renamed *Staph. saprophyticus*. Clinically it seems a misnomer to apply the term saprophyticus to such obviously pathogenic organisms. Whatever the taxonomic outcome, we emphasise that the syndrome of non-hospital urinary infection due to strains other than *Staph. epidermidis* (SII-VI) is not restricted to M3; neither does it occur only in young women.

M3 multiplies less rapidly in urine than *E. coli* (Anderson *et al.*, 1976), and it has been suggested that bacterial counts of less than the normal criterion of 10^8/l should be accepted as significant. In our study 114 (83%) of the M3 infections were isolated in counts in excess of 10^8/l and 23 (17%) in counts of between 10^7 and 10^8/l. This ratio is about the same as that for the total number of infections by all organisms seen in this laboratory (Crump *et al.*, 1976), and we think that the lower counts in about 20% of infections are probably due to the dilution factor of a high fluid intake and frequent micturition in patients with acute symptoms rather than to the rate of multiplication of the micrococci.

Our findings suggested that M3 and 5 may be the second commonest pathogens to *E. coli* in young women in domiciliary practice, and this was confirmed in 1976 (Crump *et al.*, 1976).

Although laboratory reports do not, of course, provide full information about the clinical progress of the patient, our study of the records of patients known to have had micrococcal infection suggests that these infections respond well to treatment and do not recur often. Most recurrences were with different organisms, suggesting that the micrococci do not persist as a focus for recurrent infection.

The source of the novobiocin-resistant strains which cause acute infections in the urinary tract is unknown. Other studies (Sellin *et al.*, 1975) have shown that these organisms are only rarely found in the normal flora of the genitourinary tract of young women. Our studies confirm this, and we have also failed to isolate them from throat swabs from young women. Since infection with these organisms occasionally occurs in children of both sexes, an observation we have also made previously (Maskell and Pead, 1976), the infection is unlikely to be sexually transmitted. The bowel must be considered the probable source of infection. There is a need for further studies of this aspect, especially in patients known to have had an M3 or 5 infection.

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