Coagulase-negative staphylococci and micrococci in urinary tract infections

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SYNOPSIS One hundred catalase-positive, coagulase-negative, Gram-positive cocci isolated in significant numbers from the urine of patients with urinary tract infections, provisionally subdivided by their sensitivity to novobiocin, were classified according to a slightly modified version of Baird-Parker’s schemes (1965 and 1972). It appeared that strains of Micrococcus were nearly all of subgroup 3, and that these were important pathogens of young women presenting with urinary infections in general practice. All such strains were resistant to novobiocin. Strains of Staphylococcus were heterogeneous, and were found principally in infections arising in hospital, among older people. Most staphylococci were sensitive to novobiocin.

It is suggested that it is easy and sufficiently accurate to separate staphylococci and micrococci isolated from cases of urinary tract infection on the basis of their sensitivity or resistance to novobiocin. The distinction is useful because of its therapeutic and epidemiological significance.

There is a growing acceptance of the role of some Gram-positive, catalase-positive, coagulase-negative cocci as pathogens of the urinary tract. The division of these organisms into staphylococci or micrococci (as defined by Baird-Parker, 1963) by their differing sensitivity to novobiocin (Mitchell and Baird-Parker, 1967) has led to the production of evidence in support of the view of Mitchell (1968) that each has a distinct distribution according to the sex and age of the patient concerned. It has also helped in the identification of a specific organism, apparently a micrococcus, as the second most common pathogen of young women with uncomplicated urinary tract infections (Meers, 1974; Maskell, 1974). Because identification in the surveys quoted was presumptive, there was a need to use similar methods in the collection of a number of strains of Gram-positive, catalase-positive, coagulase-negative cocci which had been isolated in significant numbers from cases of urinary tract infection, and to compare their classification by Baird-Parker’s criteria with separation on novobiocin sensitivity.

Methods

The collection and examination of urine specimens

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(1965, 1972). Novobiocin sensitivity or resistance was detected using a 5 μg disc of the drug on Wellcotest sensitivity test agar (Wellcome Reagents Ltd). Under these conditions all strains were readily separated into those which were sensitive, with zones of inhibition of growth measured radially from the edge of the disc of 8 mm or more, and those that were resistant, growing right up to, or to within 1 to 2 mm of the disc.

Results

A classification by their types of the 100 organisms isolated according to the age, sex, and whether the specimen concerned came from a patient in hospital or in general practice, is given in the table. The 44 micrococci, nearly all of subgroup 3, fitted well into the Baird-Parker scheme, but the 56 staphylococci did not. Of those we designated Staph. epidermidis biotype 1, three did not ferment lactose and 11 did not produce phosphatase. The latter were considered by Baird-Parker (1965) to belong to a separate group, and we have retained this distinction, calling them type 1/L. The lactose-negative strains were designated type 1/P. We have distinguished Staph. epidermidis biotype 4 by its ability to utilize mannitol and not by the other biochemical properties, as these would have excluded the majority from the Baird-Parker scheme. These biotype 4 strains were further divided by their ability to produce acid anaerobically from mannitol (Dean, Williams, Hall, and Corse, 1973); those with this property we have called biotype 4/A.

All the micrococci of subgroup 3, together with the single unclassified micrococcus, were novobiocin resistant. Two of the three subgroup 2 micrococci were novobiocin sensitive, as were all but three of the staphylococci. The staphylococci were generally more resistant to antimicrobial drugs than were the micrococci. The proportions of strains of staphylococci and micrococci, respectively, found to be resistant to cotrimoxazole (and to sulphamides) was 34 and 0%, to benzylpenicillin (and ampicillin) 73 and 52%, to tetracycline 61 and 7%, to nitrofurantoin 0 and 0%, to kanamycin 25 and 0%, to nalidixic acid 100 and 100%, and to erythromycin 20 and 2%.

Discussion

The acceptance of at least some varieties of Gram-positive, catalase-positive, coagulase-negative cocci as pathogens of the urinary tract has been slow, despite the appearance of publications documenting their importance over the last 20 years. For instance, Gallagher, Montgomery, and North (1965) expressed surprise on finding that ‘coagulase-negative staphylococci’, at 14%, were the second most common pathogen in bacteriologically proven cases of urinary tract infection in general practice. Subsequently Dove, Bailey, Gower, Roberts, and de Wardener (1972) reported that 24% of infections diagnosed by

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Staphylococcus epidermidis Biotype</th>
<th>Micrococcus Subgroup</th>
<th>Totals</th>
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<tr>
<td></td>
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<td>1/L</td>
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<td>2</td>
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<td>2</td>
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<tr>
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<td>1</td>
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<tr>
<td>Totals</td>
<td>5</td>
<td>22</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

Table: The distribution of types of Gram-positive, catalase-positive, coagulase-negative cocci isolated in significant numbers from the urine of patients submitted for examination because they were thought to have urinary tract infections

1 Hospital patients in italics, those from general practice in ordinary type.

Types according to Baird-Parker (1965 and 1972) with the following additions: 1/L lactose-negative type 1 strains; 1/P Phosphatase-negative type 1 strains; 4/A type 4 strains which produce acid anaerobically from mannitol; 7 Strains not conforming to any type.
suprapubic aspiration of urine from women in
general practice were due to ‘coagulase-negative
staphylococci’ (not further identified). It was recog-
nized quite early (Pereira, 1962; Mitchell, 1964)
that there was at least one discrete group of closely
related organisms among the apparent pathogens
covered by the wide definition above, but proof of
this had to await the development of an acceptable
classification. This was provided by Baird-Parker
(1963), who used a number of biochemical criteria
to separate Gram-positive, catalase-positive cocci
into staphylococci and micrococci, and to subdivide
them further into subgroups or biotypes. The applica-
tion of this classification to urinary bacteriology
(Alder, Brown, and Mitchell, 1966; Roberts, 1967)
led Mitchell (1968) to observe that infections with
these organisms which result from instrumentation
of, or abnormalities in, the urinary tract, were
usually due to one of the staphylococcal types,
while cystitis in otherwise healthy women was
often caused by strains of the subgroup 3 micro-
coccus, a finding supported by Kerr (1973). It was
noted (Mitchell and Baird-Parker, 1967) that a pro-
visional separation of staphylococci and micrococci
could be made on the basis of novobiocin sensitivity,
the former being sensitive and the latter resistant.
This simple property has been used by some workers
to distinguish between these organisms when isolated
in significant numbers from the urine of those thought
to have an infection, with results that have supported
Mitchell’s view. A survey (Meers, 1974) of 3271
presumptive urinary pathogens included 155 coagu-
lase-negative staphylococci and 116 micrococci,
separated by their sensitivity to novobiocin. The
staphylococci were found chiefly in the urine of
patients of both sexes at either end of the age span,
who were in hospital, while the micrococci were
confined almost exclusively to women between the
ages of 15 and 34 presenting with urinary infections
in general practice. Another survey (Maskell, 1974)
of 2541 cases of urinary infection gave similar
results. Both these surveys produced evidence which
suggested that the micrococcus was more productive
of inflammatory exudate than any other urinary
pathogen, and showed that for patients in general
practice in the sex and age group quoted above,
the Micrococcus subgroup 3, as provisionally
identified, was the second most common pathogen.
The current survey shows that most infections of the
urinary tract by Gram-positive, catalase-positive,
coagulase-negative cocci in general practice are due
to the Micrococcus subgroup 3. It also confirms
the general validity of the provisional identification
of the Micrococcus subgroup 3 on the basis of
novobiocin resistance. In our series, 7% of organisms
would have been misdiagnosed on this basis, as

three staphylococci would have been labelled micro-
cocci, and two Micrococcus subgroup 2 would
have been called staphylococci. In addition two
micrococi other than of subgroup 3 would have
been incorrectly identified as being of that type.
However, we think this degree of error in a
simple practical procedure is acceptable, because
its main function is to alert those concerned to the
way these organisms, when acting as pathogens, are
distributed in the community. The object of this
education is to influence the choice of antimicrobial
to be used in therapy, either before a sensitivity
result is available, or where a bacteriological
examination is not intended. The sensitivity to
various antimicrobial agents of the staphylococci and
micrococci surveyed, given in the Results section,
shows the need for this. The proportions of resistant
strains found agree closely with the results of tests
on a larger number of similar organisms recently
gathered in the same area (Meers, 1974), and
indicate that nalidixic acid is a poor choice for the
‘blind’ treatment of urinary infection in general
practice, and that ampicillin (or amoxycillin),
though an improvement, is not as good as cotrim-
oxazole, and that sulphonamides on their own
are not to be ignored. In hospital, where staphylo-
cocci predominate over micrococci, the advice
concerning nalidixic acid stands, but ampicillin
is of reduced value, and a significant number of
cases of resistance to cotrimoxazole are found.

Møller, Christiansen, and Mortensen (1973)
have suggested that urinary strains of micrococci
should be reclassified as staphylococci because
their DNA base composition is more like the latter,
and Mitchell (1968) reported that strains of Micro-
coccus subgroup 3 have certain cell-wall constituents
in common with Staph. aureus. There is also a move
to reclassify micrococci of subgroups 1-4 as bio-
types of Staph. saprophyticus (Baird-Parker, 1974).
No matter what the taxonomic outcome, it is clear,
however, that there exists a discrete, homogeneous
group of Gram-positive, catalase-positive, coagulase-
negative, novobiocin-resistant cocci with a special
predilection for the urinary tract of apparently
normal young women, in whom they accompany
a severe, acute inflammatory process second in
frequency only to Escherichia coli.

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