Comparative periurethral bacteriology of uncircumcised and circumcised males

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Background: It has been established that lack of circumcision increases the risk of urinary tract infection in infants. During the first six months, the presence of foreskin is associated with a greater quantity and a higher concentration of uropathogens in the periurethral area. Very little is known about this association in older males.

Objective: To compare the periurethral bacteriology of uncircumcised healthy males of more than one year of age.

Methods: The periurethral area of 125 uncircumcised and 46 circumcised healthy males (mean age, 26.5 and 28.3 years, respectively) was swabbed and cultured for facultative and anaerobic bacteria, genital mycoplasmas and Chlamydia trachomatis.

Results: Facultative Gram positive cocci predominated in both groups (62% and 80%, respectively). Pure culture of facultative Gram negative rods was more common in uncircumcised males (17% vs 4% in circumcised males, \( p = 0.01 \)). Streptococci, strict anaerobes and genital mycoplasmas were found almost exclusively in uncircumcised males of more than 15 years of age. No case of C trachomatis was identified.

Conclusions: The higher prevalence of potential uropathogens in the subpreputial space is in accordance with a previous finding of increased risk of urinary tract infection in uncircumcised young men. Our results also support the role of the prepucce as a reservoir for sexually transmitted organisms.

Keywords: circumcision; genital flora; bacteriology

Introduction

The medical interest in circumcision has focused mainly on the association between the prepuce and urinary tract infections in infants. Ginsburg and McCraken first noted that 95% of male infants with urinary tract infection were uncircumcised. Wiswell and Roscelli, in retrospective cohort studies, have documented that uncircumcised infants had a ten-fold to twenty-fold greater risk of urinary tract infection in the first few months of life. Wiswell et al. have also demonstrated that during the first six months of life, the presence of a foreskin was associated with a greater number of periurethral bacteria and a greater likelihood for the presence of, as well as higher concentrations of, potentially uropathogenic organisms. More recently, Spach et al. observed that lack of circumcision increased the risk of urinary tract infection in young men. However, very little is known about the subpreputial bacteriology of healthy males during childhood and adulthood. The purpose of the present study was to address the above question and to examine whether the healthy prepuce can serve as a reservoir for sexually transmitted organisms, such as genital mycoplasmas and Chlamydia trachomatis.

Material and methods

Healthy uncircumcised males, participating in a programme of ritual circumcision among new immigrants, were included in the study. A group of circumcised individuals admitted for minor surgery served as controls. None had received antimicrobial agents in the preceding month, and no external cleansing was done before sampling. In the uncircumcised males, the preputial sac was sampled, while in the circumcised ones, the periurethral area was swabbed. Three swabs were obtained from each subject and immediately transferred to the laboratory. For general bacterial cultures, a plain cotton wool swab was transported in modified Stuart’s transport medium and plated onto four plates: phenylethanol agar (Difco Laboratories, Detroit, USA) for isolation of facultative Gram positive organisms; MacConkey agar (Difco Laboratories, Detroit, USA) for isolation of facultative Gram negative organisms; trptic soy agar supplemented with 5% defibrinated sheep blood (El-Dan Technologies, Jerusalem, Israel) for isolation of fastidious organisms; and Columbia agar supplemented with 5% human blood (Becton-Dickinson Microbiology Systems, Cockeysville, MD, USA) for isolation of anaerobes. Organisms were identified by standard microbiological methods. For isolation of genital mycoplasmas, a swab was placed into modified Stuart’s transport medium. Cultures were performed on A3 or A7 Medium (broth and agar). For isolation of Chlamydia trachomatis, a calcium alginate swab was placed into a vial containing 0.2 M
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sucrose in a 0-02 M phosphate buffer with
10 μg/ml of gentamicin and 1 μg/ml of amphotericin B (Chlamydia Transwab, Medical Wire & Equipment, Co, Corsham, W.ils, UK). The
samples were frozen at -70°C until cultured.
Specimens were inoculated on cycloheximide treated McCoy's cells. Chlamydia inclusion
bodies were detected by iodine staining after
48 and 72 hours of incubation. Statistical
comparisons were made using the χ² test and
Fisher's exact test.

Results
A total of 125 uncircumcised individuals, aged
2 to 54 years (mean 26-5) and 46 circumcised
subjects (mean age 28-3) were included in the
study. Eighteen per cent were 15 years' old
or younger. None had complaints or findings
suggestive of sexually transmitted disease or
urinary tract infection.
At least one isolate was detected in 94-5% of
uncircumcised and all of the circumcised
males. The distribution of different bacteria
that were isolated is shown in the table.
Facultative Gram positive bacteria were iso-
lated in 77-6% of uncircumcised and 95-6% of
circumcised males (p = 0-01). Pure facultative
Gram positive organisms were documented in
48% of uncircumcised and 78% of circumcised
individuals (p = 0-001). Facultative Gram negative
rods were observed in 24% of uncircumcised and
22% of circumcised individuals.
Pure facultative Gram negative bacteria
were isolated in 17-6% of uncircumcised and
4-3% of circumcised males (p = 0-01).
More than two Gram negative organisms were
isolated from 5-6% of uncircumcised and 2%
of circumcised individuals.
Strict anaerobes
were detected in 21% of uncircumcised
and none of circumcised individuals (p = 0-001).
One only of the individuals harbouring anaer-
obes (3-5%) was less than 15 years of age (p
= 0-01). Facultative Gram positive bacteria
dominated in both groups (p < 0-001 versus
facultative Gram negative rods), coagulase-
negative staphylococci being the most com-
mon single species and the only Gram positive
bacterium in circumcised males. Streptococci
were significantly more common in the circum-
cised than in the circumcised group (p = 0-04).
All carriers of these organisms were 20
years of age or older. Most of the streptococcal
isolates (~80%) were non-haemolytic. Among
facultative Gram negative rods Klebsiella and
Escherichia coli predominated in uncircumcised
males, while E coli and Actinobacter were most
common organisms in the circumcised; no dif-
ference was observed between the two groups
of individuals in their isolation rate.
Streptococci and anaerobes were isolated in all
instances in combination with coagulase nega-
tive staphylococci. While coagulase negative
staphylococci were isolated in pure culture as
often as mixed cultures (49 versus 43 cases,
respectively), facultative Gram negative organ-
isms were recovered in pure culture twice as
often as in mixed cultures (19 versus 10 cases,
respectively).
One the streptococci and anaerobes, all other
species were similarly distributed in the
two age groups (up to and above 15 years),
although the proportion of Gram negative
organisms was somewhat higher in the young
age group (37% versus 25% in the adult group).
The four uncircumcised individuals who harboured genital
mycoplasmas (Mycoplasma hominis in one,
Ureaplasma urealyticum in two and both
species in the fourth case) were also colonised
by coagulase negative staphylococci. Their age
 ranged between 20 and 39 years. In no case
was C trachomatis isolated.

Discussion
Facultative Gram positive bacteria (mainly
coaagulase negative staphylococci) predomi-
nated both in circumcised and uncircumcised
individuals. There was no difference between
the two groups in the isolation rate of facul-
tative Gram negative organisms. However, when
pure growth was considered, facultative Gram
negative rods which are potential uro-
pathogens were significantly more common
in uncircumcised males. The findings is not nec-
ecessarily fortuitous and might be related to the
increased prevalence of urinary tract infection
in uncircumcised individuals. One may specu-
late that when Gram negative organisms are the
only colonisers of the preputial space, they
achieve higher concentrations; this quantita-
tive difference may contribute to the
development of urinary tract infection.
Of special interest is the observation that
streptococci and anaerobes were found almost
exclusively in uncircumcised males more than
15 years of age. This finding would suggest
that these organisms, which are common
inhabitants of the female genital tract, might
have been acquired by sexual transmission.
The anal origin of the organisms can be
ecluded, because if that were the case, their
occurrence would not be age related. Indeed,
in a previous study conducted among boys
less than 14 years of age, anaerobes were rarely
detected in both circumcised and uncircum-

Prevalence of various bacteria isolated from the periurethral area of uncircumcised and
circumcised males

<table>
<thead>
<tr>
<th>Organism</th>
<th>Uncircumcised</th>
<th>Circumcised</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of isolates</td>
<td>171 *</td>
<td>55</td>
</tr>
<tr>
<td>Facultative Gram positive bacteria</td>
<td>106 (62%) †</td>
<td>44 (80%)</td>
</tr>
<tr>
<td>Coagulase negative staphylococci</td>
<td>92</td>
<td>40</td>
</tr>
<tr>
<td>Streptococci</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Enterococcus spp</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Corynebacterium spp</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Facultative Gram negative bacteria</td>
<td>37 (22%)</td>
<td>11 (20%)</td>
</tr>
<tr>
<td>Klebsiella spp</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>E coli</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Actinobacter spp</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Enterobacter spp</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Citrobacter spp</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>P aeruginosa</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Anaerobes</td>
<td>28 (16%)</td>
<td>0</td>
</tr>
<tr>
<td>Bacteroides fragilis</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Bacteroides spp</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Mycoplasmas</td>
<td>5</td>
<td>ND</td>
</tr>
</tbody>
</table>

* Mycoplasmas excluded.
† Percentages are of total number of isolates.
‡ Ninety non-haemolytic and two alpha haemolytic.
ND = not done.
Podophyllin—the early days

Records of the medicinal use of podophyllin and its derivatives go back over 200 years, long before they became known for the treatment of genital warts. Podophyllum peltatum is a flowering perennial, widely spread throughout North America. The Indians knew of the medical properties of its rhizome, and this knowledge reached the early colonists and, in due course, their doctors. Podophyllin was regarded as an excellent emetic and cathartic, at a time when purging was an important part of medical treatment, and also as a hepatic stimulant. It was included in the first United States Pharmacopoeia, published in 1820. Podophyllin resin was separated from the crude rhizome in 1835, and was thereafter preferred as a more refined product. Another species, Podophyllum emodi, which grows in the Himalayas, was described in 1839. It had similar properties to P. peltatum, but it was not widely used; most podophyllin preparations, even in India, were imported from the United States.

The drug soon became popular among the “eclectic” sect of practitioners, who made special use of indigenous plant remedies. It was said that podophyllin was not only a cathartic and cholagogue, but of value in respiratory, renal, rheumatic, and menstrual disorders. It was found to be irritating when applied to the skin, and this led to its use as a counterirritant for the treatment of neuralgia and synovitis, although the resulting cutaneous inflammation could be severe. There can be no doubt that in the United States at this time podophyllin was regarded as a valuable drug by both doctors and laymen. It was manufactured on a large scale: in 1860, 2000 kilograms were marketed. As information about the “new American remedy” crossed the Atlantic, review articles appeared in the English medical press in 1861 and 1862, and The Lancet published enthusiastic letters from readers who had prescribed the drug. It soon appeared in the British Pharmacopoeia in the form of a powder and tincture, and non-official preparations in which the podophyllin was mixed with other drugs were developed.

In the mid 19th century, pharmacology was in a chaotic state. Many botanical and chemical substances were available, and polypharmacy, with long winded prescriptions, was the rule. The action of some individual drugs was understood, but podophyllin was not one of these. By the end of the century interest had waned, and its use had diminished to the treatment of constipation (when it was usually combined with other products) and of so-called “functional disorders of the liver”. The latter was a vaguely defined syndrome consisting of headache, depression, anorexia, abdominal discomfort, and constipation. Podophyllin was believed, incorrectly, to increase the flow of bile and had a reputation, particularly among the laity, for the relief of the condition; it was a constituent of several proprietary remedies, of which Carter’s Little Liver Pills (a combination of podophyllin and aloes) were the best known. Some individuals took regular small doses of these products indefinitely.

Eventually, the indications for podophyllin were reduced to its use as a hydrogogue purgative, and even here, in due course, it was replaced by less violent medications. Its escharotic properties had not been completely forgotten, however. For many years urologists in New Orleans had treated genital warts with podophyllin, but the treatment was not generally known until 1942, when Isaac Kaplan, working with the United States Army in New Orleans, reported that condylomata acuminata regressed after applications of 25% podophyllin suspended in mineral oil. At this point “the door opened and let the future in.”

J D ORIEL

References