

Male Urethritis in Bahrain: The Increasing Incidence of Resistant Gonorrhea

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ABSTRACT

Bahrain has a relatively low incidence of male urethritis; about one-half of these cases are due to *N.gonorrhoeae*. Despite the overall low frequency of sexually transmitted disease in Bahrain, *N.gonorrhoeae* isolates are often highly resistant. One-fourth of recent strains were resistant to penicillin, and 65% of the remaining isolates showed evidence of a chromosomally mediated diminished sensitivity to penicillin. Resistance to tetracycline is not yet common, but emerging chromosomal resistance and potentially poor compliance make tetracyclines inferior agents for gonorrhea therapy. We recommend ceftriaxone as primary therapy for *N.gonorrhoeae* in Bahrain; spectinomycin would be a reasonable second choice.

Urethritis is a common infection worldwide, but little data are available on the prevalence and etiologic agents of urethritis in the Arab World. Generally, the proportion of urethritis caused by nongonococcal pathogens increases with socioeconomic standards;⁷ whether this correlation holds in the Arabian Gulf area is unknown.

Gonococcal antibiotic resistance has been increasing worldwide. Initially exquisitely sensitive to penicillin, tetracycline, and other inexpensive antimicrobials, gonorrhea treatment is now problematic. Resistance to penicillin may be chromosomal, or mediated by a plasmid-acquired ability to produce penicillinase.⁶ Plasmid mediated resistance to tetracycline is usually high level; chromosomal resistance also occurs and can complicate treatment. The most recent gonorrhea treatment guidelines from the US Centers for Disease Control recommend ceftriaxone as the drug of choice for gonorrhea; doxycycline is added to treat possible coexistent chlamydial disease.²

The relevance of these newest US guidelines in the Arabian Gulf area is unclear, as little information on local

sensitivity patterns is available. We have reviewed the prevalence and aetiology of male urethritis in Bahrain, and evaluated long term trends in *N.gonorrhoeae* susceptibility. Treatment recommendations for the Arabian (Persian) Gulf area are offered based upon these data.

METHODS

Bahrain is a small island nation of 500,000 lying just east of Saudi Arabia in the Arabian (Persian) Gulf. Approximately one-third of the population consists of expatriate workers. With the exception of a very small number of patients who are treated privately, all cases of male urethritis in the country are referred to the Microbiology Department at Salmaniya Medical Centre, the largest medical facility on the island and the principal teaching hospital of the Arabian Gulf University Medical School.

Urethral swabs and gram stains were collected from patients and immediately cultivated on Thayer-Martin and chocolate agar. Sensitivity tests were performed on chocolate, using the Kirby-Bauer technique.

RESULTS

Table 1 shows the number of cases of urethritis, the number and percent due to gonorrhea, and gives the proportions resistant to penicillin and tetracycline. Several trends are evident. The total number of cases of urethritis peaked in 1986, and tailed off precipitously after 1988. A similar trend is evident for gonorrheal isolates. The proportion of urethral isolates due to *N.gonorrhoeae* remained consistently between 38-50%. Penicillin resistance climbed rapidly throughout the period surveyed; fully 26% of 1990 isolates were resistant. Tetracycline resistance was much less frequent (in 1989 and 1990), but still at an unacceptable level for this drug to be chosen as gonorrhea therapy.

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Table 1
Urethral Isolates in Bahrain, Data Summary Male Urethritis

| <i>Year</i> | <i>Male Urethritis</i> | <i>Gonorrheal Isolates</i> | <i>Percent PEN Resistant</i> | <i>Percent TCN Resistant</i> |
|-------------|------------------------|----------------------------|------------------------------|------------------------------|
| 1983 | 817 | 377 (46.0%) | 6.4 | N/A |
| 1984 | 1035 | 478 (46.0%) | 6.3 | N/A |
| 1985 | 1066 | 496 (46.5%) | 12.1 | N/A |
| 1986 | 1098 | 436 (39.7%) | 21.8 | N/A |
| 1987 | 961 | 451 (46.9%) | 25.3 | N/A |
| 1988 | 899 | 454 (50.5%) | 20.0 | N/A |
| 1989 | 616 | 239 (38.7%) | 23.0 | 5.0 |
| 1990 | 541 | 234 (43.2%) | 26.0 | 2.5 |

PEN – Penicillin

TCN – Tetracycline

N/A – Not available

DISCUSSION

About 4 million cases of male urethritis occur per year in the US out of a total population of approximately 250 million,⁷ giving a rough incidence rate of 1,600 per 100,000. Bahrain's crude incidence rate for 1990 is 108 per 100,000 (541 of 500,000). This very low rate is likely secondary to the conservative mores of the Muslim religion; serologically confirmed cases of syphilis are also very infrequent.⁹ The decline in urethritis cases since 1988 may reflect increased awareness of sexually transmitted disease, especially AIDS. The proportion of urethritis due to *N.gonorrhoeae* is remarkably stable at around 45%; this is intermediate between the US situation (one-third of male urethritis is due to gonorrhoeae), and the developing world, where up to 80% is due to *N.gonorrhoeae*.⁷ A recent study in Nigeria found 60% were due to gonorrhea.⁸

Since the mid-1970's, penicillinase producing *N.gonorrhoeae* (PPNG) have steadily spread to new populations. Currently some US metropolitan areas have PPNG rates of 10-40%,⁴ and areas of the developing world have rates exceeding 50%.⁶ Evaluation of the 1988 Bahraini strains of gonorrhea revealed that the 20% resistant to penicillin were all PPNG. Additional evaluation of the non-PPNG strains showed that 65% had chromosomally mediated penicillin resistance as determined by the minimal inhibitor concentration (MIC) technique;¹ chromosomal resistant is defined as an MIC > 1 mg/l. Most of this chromosomal resistance is clustered near the cut-off level for defining resistance, accounting for the

fact these strains appear sensitive by disk techniques. This large reservoir of chromosomal resistance, in addition to the climbing PPNG prevalence, argue strongly against the use of penicillin, ampicillin or amoxicillin in gonorrhea therapy.

Tetracycline resistance in Bahrain ranges between 2.5% - 5% (Table 1), but MIC data from 1988 indicate that 69% had evidence of chromosomally mediated resistance with MIC > 4 mg/l.¹ Though plasmid mediated tetracycline resistance has not yet been found in Bahrain,¹ the large percentage of marginally sensitive strains bodes poorly for additional attempts to treat *N.gonorrhoeae* with tetracycline or doxycycline.

All recent *N.gonorrhoeae* strains isolated in Bahrain were sensitive to both ciprofloxacin and ceftriaxone, but those with chromosomally mediated penicillin resistance had a MIC 90 of 0.15 mg/l for ciprofloxacin,¹ a level associated with clinical failure in some recently reported cases from England.³ Because of these growing problems with resistance to penicillin, the tetracyclines, and apparently ciprofloxacin, we now recommend a single 250 mg intramuscular dose of ceftriaxone as the primary therapy of uncomplicated gonorrhea. This dose, endorsed by the US centers for Disease Control,² has proven effective for urethral, endocervical, rectal and pharyngeal disease. It also offers reasonable therapy for possible undiagnosed incubating syphilis.⁵ Spectinomycin would be a reasonable alternative in the patient with a history of severe B-lactam allergy as all 1988 strains were sensitive to this antibiotic.¹

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