*Bulletin of the World Health Organization*, **58** (1): 73-79 (1980)

# *Neisseria gonorrhoeae* isolates from Ethiopia*

## 2. Pair correlations between minimal inhibitory concentration values of five antibiotics and frequency of multiple antibiotic resistance

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*The minimal inhibitory concentration (MIC) values of penicillin, ampicillin, tetracycline, chloramphenicol, and streptomycin for 500 gonococcal strains were studied for product-moment coefficient correlations. The strains were isolated from male patients with acute gonococcal urethritis attending the Venereal Disease Clinic in Addis Ababa.*

*The MICs of all pairs except the ampicillin/streptomycin pair were positively correlated, with* $r = 0.20-0.53$, $P < 0.001$. *The ampicillin/streptomycin pair was not correlated,* $r = 0.06$, $P > 0.05$.

*Despite the significant correlation between the susceptibilities of strains to penicillin and tetracycline, 85% of the penicillin-resistant strains were sensitive to tetracycline. However, 75.6% of tetracycline-resistant strains were also resistant to penicillin. Similar differences in percentages of resistance and susceptibility of strains also occurred between tetracycline and ampicillin as well as between tetracycline and streptomycin pairs, while pair correlations were also noted.*

*No chloramphenicol-resistant strain was isolated. But correlations were found between the MIC values of chloramphenicol and those of the other 4 antibiotics.*

*Forty-seven percent of the 500 strains were resistant to 2 or more antibiotics. One hundred and twenty-six strains (25.2%) were resistant to 2 antibiotics, about half of which were resistant to penicillin and ampicillin. Resistance to 3 antibiotics was shown in 18.6% of strains, the majority being resistant to penicillin, ampicillin, and streptomycin. Eighteen strains (3.6%) were resistant to 4 antibiotics, while no strain was found resistant to all 5 antibiotics.*

Studies on correlations between minimal inhibitory concentration (MIC) values of gonococci and the frequency of multiple antibiotic resistance are relatively few (*1–5*) despite earlier reports indicating correlations between sensitivities of gonococci to various antibiotics (*6–10*).

The *in vitro* antibiotic susceptibility patterns of *Neisseria gonorrhoeae* strains isolated from Ethiopia have been reported earlier (*11*), but correlations between the MIC values of the different antibiotics and the frequency of multiple antibiotic resistance were not analysed in that paper. The purpose of this study was to determine the extent of multiple resistance and to establish correlations in susceptibilities to 5 antibiotics of 500 strains of gonococci isolated in Addis Ababa. This information will assist in the development of better programmes for the control and effective treatment of gonorrhoea in Addis Ababa.

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## MATERIALS AND METHODS

The materials and methods used for isolation, identification, and determination of the MICs of 500 *Neisseria gonorrhoeae* strains were those described in a previous paper (*11*). The gonococci were isolated from male patients with acute gonococcal urethritis at the Venereal Disease Clinic in Addis Ababa and the MIC values of penicillin, ampicillin, tetracycline, chloramphenicol, and streptomycin were determined for each strain. The concentration levels for determining resistance of strains to the respective antibiotics are those used previously (*11*). The extent of cross-resistance of strains for any pair of the 5 antibiotics was studied statistically. Product-moment coefficient correlations of the susceptibilities of all isolates to pairs of the 5 antibiotics were also calculated.

## RESULTS

### *Coefficient correlations*

Comparisons of the MIC values of pairs of the 5 antibiotics for the 500 gonococcal strains are shown in Tables 1–10. The corresponding product-moment

coefficient correlations for the susceptibilities of the strains to the paired antibiotics are also shown in the respective tables.

In Table 1, penicillin MICs are compared with MICs of tetracycline and an $r$ value of 0.53, $P<0.001$ was obtained. The majority of tetracycline-resistant strains (75.6%) were also resistant to penicillin. Eighty-five per cent of the penicillin-resistant strains were, however, sensitive to tetracycline. The MICs of other pairs have been similarly compared (Tables 2-10). The comparison of the penicillin/chloramphenicol MICs showed a similar $r$ value, but none of the 500 strains was resistant to chloramphenicol. The correlation coefficient between penicillin and ampicillin was 0.47, $P<0.001$ (Table 3). Over 75% of the strains resistant to penicillin were also resistant to ampicillin. On the other hand, about 54% of the ampicillin-resistant strains were resistant to penicillin. However, more strains were resistant to ampicillin than to penicillin. The penicillin/streptomycin correlation, with $r = 0.33$, $P<0.001$, is shown in Table 4. Fifty-nine percent of the penicillin-resistant strains were also resistant to streptomycin while the reverse was true for about 55% of strains.

The positive correlations of the paired MIC values for tetracycline/chloramphenicol and tetracycline/streptomycin are shown in Tables 5 and 6, respectively. About 76% of the tetracycline-resistant strains were also resistant to streptomycin. Eighty-six percent of the streptomycin-resistant strains were, however, susceptible to tetracycline. The MIC values of tetracycline and ampicillin are moderately correlated (Table 7), although 89% of the ampicillin-resistant strains were susceptible to tetracycline. The majority of the tetracycline-resistant strains (76%) were, however, also resistant to ampicillin.

As shown in Tables 8 and 9, respectively, correlations were found between chloramphenicol and ampicillin and between chloramphenicol and streptomycin susceptibilities.

Susceptibilities to ampicillin and streptomycin were not positively correlated, the $r$ value being 0.06 and $P>0.05$ (Table 10), although the majority of the strains resistant to one were also resistant to the other antibiotic.

*Frequency of multiple resistance*

The frequency of multiple antibiotic resistance among the 500 isolates of *Neisseria gonorrhoeae* is shown in Table 11. Two hundred and thirty-seven strains (47.4%) were resistant to 2 or more of the 5 antibiotics employed in the study. One hundred and twenty-six strains (25.2%) were resistant to 2 antibiotics. About half of these (11.6%) were resistant to penicillin and ampicillin. Ninety-three strains (18.6%) showed resistance to 3 antibiotics, of which the majority (78 strains) had a pattern of penicillin/ampicillin/streptomycin resistance. Eighteen isolates (3.6%) were resistant to 4 antibiotics. No strain resistant to all 5 antibiotics was isolated, since all 500 strains were susceptible to chloramphenicol.

Table 1. Correlation of penicillin and tetracycline MIC values for 500 strains of *Neisseria gonorrhoeae*

| | No. of strains with the MIC indicated | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Tetracycline MIC (mg/litre) | Penicillin MIC (mg/litre) | | | | | | | | | |
| | ⩽0.005 | 0.01 | 0.02 | 0.04 | 0.08 | 0.16 | 0.32 | 0.64 | 1.28 | 2.56 |
| ⩽0.2 | 64 | 30 | 22 | 24 | 18 | 12 | 0 | 0 | 0 | 0 |
| 0.4 | 35 | 24 | 19 | 39 | 24 | 13 | 4 | 0 | 0 | 0 |
| 0.8 | 6 | 4 | 7 | 11 | 54 | 39 | 9 | 1 | 0 | 0 |
| 1.6 | 0 | 3 | 5 | 2 | 5 | 13 | 9 | 1 | 2 | 0 |
| 3.2 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 6.4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 12.8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 25.6 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| $r = 0.53$ ($P < 0.001$) | | | | | | | | | | |

Table 2. Correlation of penicillin and chloramphenicol MIC values for 500 strains of *Neisseria gonorrhoeae*

| | No. of strains with the MIC indicated | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Chloramphenicol MIC (mg/litre) | Penicillin MIC (mg/litre) | | | | | | | | | |
| | ⩽0.005 | 0.01 | 0.02 | 0.04 | 0.08 | 0.16 | 0.32 | 0.64 | 1.28 | 2.56 |
| ⩽0.125 | 32 | 17 | 14 | 11 | 20 | 4 | 0 | 0 | 0 | 0 |
| 0.25 | 39 | 30 | 17 | 19 | 13 | 9 | 1 | 0 | 0 | 0 |
| 0.50 | 25 | 13 | 16 | 19 | 39 | 17 | 1 | 1 | 0 | 0 |
| 1.0 | 9 | 1 | 4 | 27 | 24 | 31 | 20 | 0 | 0 | 0 |
| 2.0 | 0 | 0 | 2 | 0 | 5 | 6 | 0 | 0 | 0 | 0 |
| 4.0 | 0 | 0 | 0 | 0 | 0 | 10 | 0 | 1 | 0 | 0 |
| 6.0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 8.0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 |
| 10.0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| $r = 0.50$ ($P < 0.001$) | | | | | | | | | | |

Table 3. Correlation of penicillin and ampicillin MIC values for 500 strains of *Neisseria gonorrhoeae*

| Ampicillin MIC (mg/litre) | No. of strains with the MIC indicated: Penicillin MIC (mg/litre) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | ⩽0.005 | 0.01 | 0.02 | 0.04 | 0.08 | 0.16 | 0.32 | 0.64 | 1.28 | 2.56 |
| ⩽0.025 | 5 | 14 | 3 | 3 | 3 | 0 | 0 | 0 | 0 | 0 |
| 0.05 | 28 | 12 | 6 | 7 | 9 | 4 | 0 | 0 | 0 | 0 |
| 0.1 | 28 | 11 | 17 | 26 | 20 | 7 | 5 | 0 | 0 | 0 |
| 0.2 | 32 | 14 | 16 | 19 | 28 | 4 | 4 | 0 | 0 | 0 |
| 0.4 | 10 | 6 | 8 | 12 | 18 | 12 | 6 | 0 | 2 | 0 |
| 0.8 | 2 | 4 | 3 | 9 | 23 | 51 | 7 | 2 | 0 | 0 |
| 1.6 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3.2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 6.4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 12.8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

$r = 0.47$ ($P < 0.001$)

Table 5. Correlation of tetracycline and chloramphenicol MIC values for 500 strains of *Neisseria gonorrhoeae*

| Chloramphenicol MIC (mg/litre) | No. of strains with the MIC indicated: Tetracycline MIC (mg/litre) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | ⩽0.2 | 0.4 | 0.8 | 1.6 | 3.2 | 6.4 | 12.8 | 25.6 |
| ⩽0.125 | 52 | 21 | 14 | 11 | 0 | 0 | 0 | 0 |
| 0.25 | 50 | 42 | 26 | 10 | 0 | 0 | 0 | 0 |
| 0.50 | 35 | 46 | 39 | 11 | 0 | 0 | 0 | 0 |
| 1.0 | 33 | 37 | 46 | 0 | 0 | 0 | 0 | 0 |
| 2.0 | 0 | 2 | 5 | 6 | 0 | 0 | 0 | 0 |
| 4.0 | 0 | 10 | 1 | 0 | 0 | 0 | 0 | 0 |
| 6.0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 8.0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| 10.0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

$r = 0.21$ ($P < 0.001$)

Table 4. Correlation of penicillin and streptomycin MIC values for 500 strains of *Neisseria gonorrhoeae*

| Streptomycin MIC (mg/litre) | No. of strains with the MIC indicated: Penicillin MIC (mg/litre) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | ⩽0.005 | 0.01 | 0.02 | 0.04 | 0.08 | 0.16 | 0.32 | 0.64 | 1.28 | 2.56 |
| ⩽10 | 39 | 17 | 9 | 9 | 13 | 22 | 1 | 0 | 0 | 0 |
| 20 | 23 | 12 | 6 | 10 | 18 | 8 | 5 | 0 | 0 | 0 |
| 40 | 26 | 18 | 10 | 18 | 14 | 3 | 0 | 0 | 0 | 0 |
| 50 | 6 | 1 | 8 | 11 | 14 | 1 | 0 | 0 | 0 | 0 |
| 100 | 0 | 0 | 2 | 1 | 10 | 3 | 7 | 0 | 0 | 0 |
| 200 | 4 | 5 | 5 | 5 | 14 | 12 | 3 | 0 | 0 | 0 |
| >200 | 7 | 8 | 13 | 22 | 18 | 29 | 6 | 2 | 2 | 0 |

$r = 0.33$ ($P < 0.001$)

Table 6. Correlation of tetracycline and streptomycin MIC values for 500 strains of *Neisseria gonorrhoeae*

| Streptomycin MIC (mg/litre) | No. of strains with the MIC indicated: Tetracycline MIC (mg/litre) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | ⩽0.2 | 0.4 | 0.8 | 1.6 | 3.2 | 6.4 | 12.8 | 25.6 |
| ⩽10 | 66 | 35 | 6 | 3 | 0 | 0 | 0 | 0 |
| 20 | 30 | 43 | 4 | 5 | 0 | 0 | 0 | 0 |
| 40 | 22 | 19 | 46 | 2 | 0 | 0 | 0 | 0 |
| 50 | 15 | 19 | 5 | 2 | 0 | 0 | 0 | 0 |
| 100 | 0 | 5 | 10 | 8 | 0 | 0 | 0 | 0 |
| 200 | 5 | 9 | 26 | 8 | 0 | 0 | 0 | 0 |
| >200 | 32 | 28 | 34 | 12 | 1 | 0 | 0 | 0 |

$r = 0.34$ ($P < 0.001$)

## DISCUSSION

The $r$ values of the correlations for the various pairs of antibiotics ranged between 0.06 and 0.53 ($P<0.001$) demonstrating positive correlations except for the ampicillin/streptomycin pair with $r = 0.06$ ($P>0.05$). These results mostly confirm the findings by others (*12–14*) that there are positive correlations between the susceptibilities of the gonococcal strains to pairs of different antibiotics.

The penicillin and tetracycline association ($r = 0.53$, $P<0.001$) was highly significant and is in agreement with the report by several other investigators (*3–5, 10, 13–16*). The positive correlation between penicillin and chloramphenicol was reported by Maness & Sparling (*2*), Maier et al. (*3*), and Amies (*10*). In the present study, however, no chloramphenicol-resistant strains were encountered, taking 10 μg per ml as the MIC level for resistance, while 41% were resistant to penicillin.

Table 7. Correlation of tetracycline and ampicillin MIC values for 500 strains of *Neisseria gonorrhoeae*

| Ampicillin MIC (mg/litre) | No. of strains with the MIC indicated: Tetracycline MIC (mg/litre) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | ⩽0.2 | 0.4 | 0.8 | 1.6 | 3.2 | 6.4 | 12.8 | 25.6 |
| ⩽0.025 | 12 | 10 | 6 | 0 | 0 | 0 | 0 | 0 |
| 0.05 | 40 | 12 | 10 | 4 | 0 | 0 | 0 | 0 |
| 0.10 | 40 | 42 | 26 | 6 | 0 | 0 | 0 | 0 |
| 0.20 | 32 | 40 | 33 | 12 | 0 | 0 | 0 | 0 |
| 0.40 | 16 | 22 | 30 | 6 | 0 | 0 | 0 | 0 |
| 0.80 | 30 | 32 | 26 | 12 | 1 | 0 | 0 | 0 |
| 1.6 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3.2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 6.4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 12.8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

$r = 0.20$ ($P < 0.001$)

Table 8. Correlation of chloramphenicol and ampicillin MIC values for 500 strains of *Neisseria gonorrhoeae*

| Ampicillin MIC (mg/litre) | No. of strains with the MIC indicated: Chloramphenicol MIC (mg/litre) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | ⩽0.125 | 0.25 | 0.50 | 1.0 | 2.0 | 4.0 | 6.0 | 8.0 | 10.0 |
| ⩽0.025 | 12 | 10 | 6 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0.05 | 23 | 12 | 25 | 3 | 3 | 0 | 0 | 0 | 0 |
| 0.10 | 40 | 42 | 26 | 2 | 2 | 2 | 0 | 0 | 0 |
| 0.20 | 12 | 9 | 27 | 66 | 2 | 1 | 0 | 0 | 0 |
| 0.40 | 5 | 22 | 19 | 21 | 3 | 4 | 0 | 0 | 0 |
| 0.80 | 6 | 33 | 28 | 24 | 3 | 4 | 1 | 2 | 0 |
| 1.6 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3.2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 6.4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 12.8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

$r = 0.34$ ($P < 0.001$)

Table 9. Correlation of chloramphenicol and streptomycin MIC values for 500 strains of *Neisseria gonorrhoeae*

| Streptomycin MIC (mg/litre) | No. of strains with the MIC indicated: Chloramphenicol MIC (mg/litre) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | ⩽0.125 | 0.25 | 0.50 | 1.0 | 2.0 | 4.0 | 6.0 | 8.0 | 10.0 |
| ⩽10 | 32 | 39 | 21 | 18 | 0 | 0 | 0 | 0 | 0 |
| 20 | 23 | 12 | 25 | 19 | 3 | 0 | 0 | 0 | 0 |
| 40 | 26 | 18 | 20 | 21 | 2 | 2 | 0 | 0 | 0 |
| 50 | 6 | 1 | 18 | 13 | 2 | 1 | 0 | 0 | 0 |
| 100 | 0 | 5 | 9 | 5 | 1 | 3 | 0 | 0 | 0 |
| 200 | 4 | 15 | 15 | 10 | 2 | 2 | 0 | 0 | 0 |
| >200 | 7 | 38 | 23 | 30 | 3 | 3 | 1 | 2 | 0 |

$r = 0.24$ ($P < 0.001$)

Table 10. Correlation of streptomycin and ampicillin MIC values for 500 strains of *Neisseria gonorrhoeae*

| Ampicillin MIC (mg/litre) | No. of strains with the MIC indicated: Streptomycin MIC (mg/litre) | | | | | | |
|---|---|---|---|---|---|---|---|
| | ⩽10 | 20 | 40 | 50 | 100 | 200 | >200 |
| ⩽0.025 | 5 | 3 | 3 | 3 | 1 | 6 | 7 |
| 0.05 | 28 | 12 | 10 | 4 | 2 | 5 | 5 |
| 0.10 | 28 | 11 | 16 | 6 | 6 | 7 | 40 |
| 0.20 | 32 | 10 | 23 | 12 | 5 | 10 | 25 |
| 0.40 | 10 | 22 | 20 | 6 | 6 | 3 | 7 |
| 0.80 | 7 | 24 | 17 | 10 | 3 | 17 | 23 |
| 1.6 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 3.2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 6.4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 12.8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

$r = 0.06$ ($P < 0.05$)

The positive correlation between penicillin and ampicillin was also shown by Maier et al. (*3*) and Stolz et al. (*15*). Correlations between the susceptibilities to penicillin and streptomycin were reported by Platt (*4*), $r = 0.556$, $P \leqslant 0.05$ and by Maness & Sparling (*2*), $r = 0.51$, $P \leqslant 0.01$. Their findings were also supported by those of Powell & Bond (*5*). In the present study the correlation was moderately positive (Table 4).

Maier et al. (*3*) recorded an $r$ value of 0.72 ($P \leqslant 0.01$) for the susceptibilities of 124 gonococcal strains to tetracycline and chloramphenicol. With 500 strains we also found a positive correlation ($r = 0.21$, $P < 0.001$).

The significant correlation between tetracycline and streptomycin susceptibilities (Table 6) is in agreement with the report of Platt (*4*), who studied 100 strains of *Neisseria gonorrhoeae*.

Table 11. Strains of gonococci with multiple resistance patterns

| Resistance pattern | Resistant strains | |
|---|---|---|
| | No. | % |
| Penicillin/ampicillin | 58 | 11.6 |
| Penicillin/streptomycin | 19 | 3.8 |
| Penicillin/tetracycline | 2 | 0.4 |
| Ampicillin/streptomycin | 44 | 8.8 |
| Tetracycline/streptomycin | 3 | 0.6 |
| Penicillin/ampicillin/streptomycin | 78 | 15.6 |
| Penicillin/tetracycline/streptomycin | 4 | 0.8 |
| Ampicillin/tetracycline/streptomycin | 6 | 1.2 |
| Penicillin/ampicillin/tetracycline | 5 | 1.0 |
| Penicillin/ampicillin/streptomycin/ tetracycline | 18 | 3.6 |
| Total | 237 | 47.4 |

The finding of Stolz et al. (*15*) supports the positive correlation in this study between the susceptibilities of strains to tetracycline and ampicillin.

The correlation between the chloramphenicol/ ampicillin pair (Table 8) was as good as the correlations between streptomycin and penicillin and between streptomycin and tetracycline. The chloramphenicol/streptomycin pair was also moderately correlated (Table 9). These correlations were not apparent when susceptibilities of strains to both drugs were compared. While 58% of the 500 strains were resistant to ampicillin (Table 8) and 44% to streptomycin (Table 9), no chloramphenicol-resistant strains were found.

Despite the lack of correlation between the susceptibilities to ampicillin and streptomycin on the basis of the *r* value (Table 10), 58% of the streptomycin-resistant strains were also resistant to ampicillin, while 71% of those resistant to ampicillin were resistant also to streptomycin.

Resistance of gonococci to multiple drugs has been reported previously (*1–5*). The frequency of multiple drug resistance in this study (47.4%) is quite significant and a cause for serious concern in the control and treatment of gonorrhoea. It is as high as the frequency of resistance to a single drug among previous isolates in Addis Ababa (*17, 18*) and is even higher than the frequency of resistance to penicillin or to other single drugs reported from other countries (*13, 19, 20*).

Various explanations have been advanced for the occurrence of multiple antibiotic resistance in *Neisseria gonorrhoeae*. One explanation considered was selection of several independent mutations to resistance to individual antibiotics, the selection occurring in response to exposure of the strain to the different drugs in different hosts (*1*). There are, however, arguments against this hypothesis, supported by experimental evidence (*1*). A common genetic mechanism through mutation of a single gene has also been suggested as the basis of multiple antibiotic resistance (*2*). The evidence for this was the loss of resistance to a group of 6 drugs following a single-step mutation. Resistance to a variety of antibacterial agents was attributed to a single genetic locus identified from clinical isolates (*21, 22*).

Although antibiotic resistance in gonococci has been transferred experimentally from one cell to another by transformation (*2, 23*), the relevance of this mechanism to clinical problems of multiple antibiotic resistance in any bacteria is questionable. Transduction is equally unlikely to explain the development of multiple drug resistance in *Neisseria gonorrhoeae* strains, since no bacteriophage for this species has been commonly recognized. It has recently been shown (*24, 25*) that β-lactamase-producing gonococci can conjugally transfer the gene for the enzyme to other gonococci and to other bacterial species. Such transfer of *R* plasmid between gonococci and other species may be a possible mechanism for the development of multiple resistance.

## ACKNOWLEDGEMENTS

The authors greatly appreciate the assistance of Ato Desta Shamebo in the statistical analyses of the study. The excellent typing of the manuscript by Woizero Haregewein Zelleke is also gratefully acknowledged.

## RÉSUMÉ

SOUCHES ÉTHIOPIENNES DE *NEISSERIA GONORRHOEAE*

2. CORRÉLATION ENTRE LES CONCENTRATIONS INHIBITRICES MINIMALES DE CINQ ANTIBIOTIQUES CONSIDÉRÉS PAR PAIRES ET FRÉQUENCE DE LA RÉSISTANCE MULTIPLE AUX ANTIBIOTIQUES

La première partie de l'étude, déjà relatée dans un précédent article, avait permis d'isoler et d'identifier selon les méthodes habituelles 500 souches de gonocoques provenant de sujets du sexe masculin traités pour une urétrite gono-

coccique au centre de traitement des maladies vénériennes d'Addis-Abéba. La sensibilité de ces isolats à la pénicilline, à l'ampicilline, à la tétracycline, au chloramphénicol et à la streptomycine avait ensuite été déterminée par la technique de dilution en gel des antibiotiques.

Le présent article concerne l'étude statistique des concentrations inhibitrices minimales (CIM) pour ces antibiotiques considérés par paires. Pour chaque paire d'antibiotiques, un tableau expose la corrélation entre les diverses valeurs CIM ainsi que le coefficient de corrélation général entre les deux antibiotiques. Un dernier tableau présente les divers schémas de multirésistance (à 2 à 4 antibiotiques), avec l'indication du nombre de souches de gonocoques chez qui ce type de résistance a été constaté.

Les valeurs CIM pour le couple pénicilline–tétracycline sont en corrélation positive ($r = 0,53$, $P<0,001$). Soixante-seize pour cent des souches qui s'étaient montrées résistantes à la tétracycline ont aussi opposé une résistance à la pénicilline. Par contre, 85% des souches résistant à la pénicilline se sont révélées sensibles à la tétracycline. Il était apparu dans la première partie de l'étude qu'aucune souche ne résistait au chloramphénicol; le couple pénicilline–chloramphénicol n'en offre pas moins une corrélation positive semblable à celle obtenue pour la paire pénicilline–tétracycline. La sensibilité à la pénicilline et à l'ampicilline a aussi montré une corrélation positive avec un coefficient $r = 0,47$, $P<0,001$. Les 157 souches qui ont opposé une double résistance à la pénicilline et à l'ampicilline représentent 77% des souches qui ont résisté à la pénicilline et quelque 54% seulement des souches qui ont résisté à l'ampicilline—d'ailleurs plus nombreuses (292) que celles résistant à la pénicilline (205). La sensibilité comparée à la pénicilline et à la streptomycine présente également une corrélation positive ($r = 0,33$, $P<0,001$). Une double résistance a été établie pour 59% des souches résistant à la pénicilline et pour environ 55% de celles résistant à la streptomycine.

Les valeurs CIM pour les couples tétracycline–chloramphénicol et tétracycline–streptomycine étaient également en corrélation positive—les souches peu nombreuses résistant à la tétracycline (41 ou 8,2%) étant d'ailleurs toutes inhibées par le chloramphénicol. Quelque 76% des souches résistant à la tétracycline ont résisté à la streptomycine, alors que près de 86% des souches résistant à la streptomycine ont été inhibées par la tétracycline. On a constaté une corrélation modérée entre les valeurs CIM pour le couple tétracycline–ampicilline ($r = 0,20$, $P<0,001$), bien que 89% des souches résistant à l'ampicilline aient aussi été sensibles à la tétracycline et qu'une proportion quelque peu inférieure (76%) de souches résistant à la tétracycline aient résisté également à l'ampicilline.

On a vu précédemment que l'ensemble des 500 souches étaient sensibles au chloramphénicol; la corrélation entre les couples chloramphénicol–ampicilline et chloramphénicol–streptomycine n'en a pas moins été positive ($r = 0,34$ et 0,24 respectivement, $P<0,001$).

Quarante-trois pour cent des souches résistant à l'ampicilline n'ont pas davantage été sensibles à la streptomycine, et 58% de celles résistant à la streptomycine ont aussi résisté à l'ampicilline. Quoi qu'il en soit, les valeurs CIM pour ces deux antibiotiques ont accusé une corrélation négative ($r = 0,06$, $P<0,05$).

Plus de 200 souches (47,4%) se sont montrées résistantes à deux antibiotiques au moins; parmi elles, 126 (25,2%) se sont classées dans la catégorie résistant à deux antibiotiques et la moitié d'entre elles opposaient cette double résistance à la pénicilline et à l'ampicilline. On a trouvé une résistance à trois antibiotiques chez 93 souches (15,6%), la majorité se classant dans le groupe résistant à la pénicilline, à l'ampicilline et à la streptomycine. Dix-huit souches (3,6%) se sont révélées résistantes à quatre antibiotiques, mais aucune n'a manifesté une résistance envers l'ensemble des cinq agents considérés.

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