

SENSITIVITY TO ANTIBIOTICS OF *N. GONORRHOEAE* ISOLATED IN 1966 AND 1968 FROM PATIENTS IN NORTH SWEDEN

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Abstract. Gonococci were isolated from 311 patients in 1966 and from 335 in 1968. Sensitivity to penicillin was measured with the plate dilution technique. Generally speaking, the strains isolated in 1966 were significantly more sensitive to penicillin than those isolated in 1968. Strains from 15 patients in 1966 had an $IC_{50} > 0.1$ IU/ml compared with 39 in 1968. Strains isolated on different occasions from the same patients were tested. When the interval between collection of the first and second sample was more than 1 month, the second was less sensitive.

The number of strains resistant to streptomycin, as determined with this method, was 7 in 1966 and 20 in 1968. No decreased sensitivity to tetracycline or chloramphenicol was found.

Judging from the literature, during the last 10 to 20 years gonococci have become less sensitive to penicillin (8, 9, 12, 13) but in the last few years an increased proportion of strains susceptible to penicillin *in vitro* (6, 7, 10, 15) has been reported.

It was therefore thought worth while to study the penicillin, streptomycin, tetracycline and chloramphenicol sensitivity of gonococcal strains routinely isolated at the bacteriological laboratory of Umeå in 1966 and 1968. Strains isolated on different occasions from the same patients were also tested for any variation in their sensitivity to penicillin.

MATERIAL AND METHODS

Chocolate ascites agar for culture and sensitivity tests was prepared according to Reyn et al. (11). All samples were cultured on this medium with and without an addition of polymyxin B and ristocetin (14). All suspected colonies were seeded on HAP-plates (4) to check the pattern of fermentation.

The sensitivity to penicillin was estimated with the plate dilution technique, including 12 plates with $\frac{1}{2}$ dilution steps from 4 IU/ml to 0.002 IU/ml of benzyl sodium penicillin (Kabi, Stockholm). The testing technique and the calculation of IC_{50} (50% inhibitory concentration)

were done in accordance with the recommendations of Reyn et al. (11). All determinations were repeated once and the mean of the two results was taken as a measure of the sensitivity. The sensitivity of each strain to streptomycin, tetracycline and chloramphenicol was measured with the disc method (2, 3).

RESULTS AND DISCUSSION

N. gonorrhoeae was isolated from 311 patients in 1966 and 335 patients in 1968. The patients' age ranged from 14 to 40, but mostly between 15 and 24. There were 305 males and 341 females including 15 and 104, respectively, between 14 and 18 years. The age and sex distribution in 1966 and 1968 were essentially equal (Fig. 1).

Fig. 2 shows the distribution frequency of the strains (the first isolated strain from each patient) according to IC_{50} -values. Most of the strains had an IC_{50} of 0.02 IU/ml in 1966 as well as 1968, a value also found by others (5). The mean Kärber-value was 16.03 in 1966 compared with 18.37 in 1968 (which correspond to IC_{50} 0.020 and 0.030 respectively) and the difference was significant ($p < 0.001$ according to *t*-test). The mean value in Fig. 2 was based on a distribution plotted in a logarithmic diagram (i.e. Kärber values), which showed an approximately gaussian appearance. In order to find out whether the significance was merely due to the strains with $IC_{50} > 0.1$ IU/ml, the calculation was repeated after exclusion of this group of strains. The mean Kärber values were now 14.85 in 1966 and 16.52 in 1968 (which correspond to 0.017 and 0.024 IU/ml respectively) and the difference was significant ($p < 0.001$).

In 1966 there were 15 patients, whose strains had an IC_{50} of > 0.1 IU/ml compared with 39

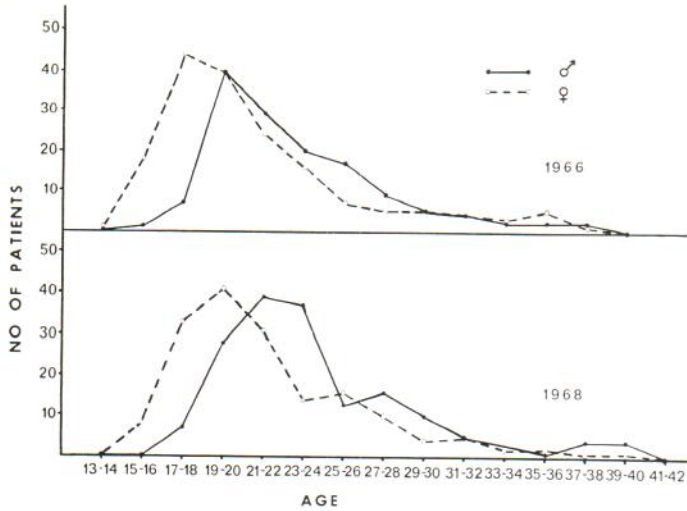


Fig. 1. The age and sex distribution of patients with gonococcal strains isolated in 1966 (311 patients) and 1968 (335 patients) in Umeå.

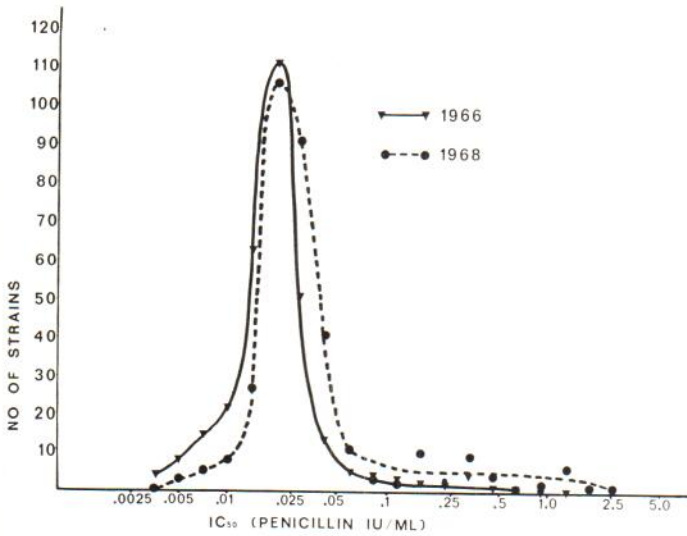


Fig. 2. The distribution of primarily isolated gonococcal strains from 1966 (311 strains) and 1968 (335 strains) in Umeå, according to sensitivity to penicillin. The plate dilution technique was used.

in 1968 (Table I). Strains from 2 patients in 1966 and from 2 in 1968 showed an IC_{50} between 1.5 and 3.0 IU/ml. Of these patients, three were sailors and one was a woman whose partner was living in Stockholm.

Table I. Number of primarily isolated gonococcal strains with decreased sensitivity to penicillin. The plate dilution technique was used

	1966	1968
No. of strains tested ...	311	335
IC_{50} (Penicillin)		
> 0.1 IU/ml		
No. of strains	15	39
Per cent	4.8	11.0

Strains isolated from the same patients on different occasions in 1965, 1966 and 1968 were tested for susceptibility to penicillin with the plate dilution technique (and Kärber-values were recorded). Comparisons between primarily and sec-

Table II. Number of primarily isolated gonococcal strains resistant to streptomycin as determined with the disc method

	1966	1968
No. of strains tested ...	311	335
Strains resistant to streptomycin		
No. of strains	7	20
Per cent	2.25	6.0

Table III. Primary and secondary gonococcal strains isolated and tested for sensitivity to penicillin in 1965, 1966 and 1968 in Umeå. The plate dilution technique was used and differences in Kärber-value were statistically evaluated with the Welch-Aspin method

Δ = secondary minus primary Kärber-value

Interval between primarily and secondarily isolated strains (days)	Mean and 95%—confidence interval of Δ
1-6	0.64 ± 0.64
7-30	0.13 ± 1.46
30	2.37 ± 1.38

ondarily isolated strains were statistically evaluated with a *t*-test adjusted for unequal variances, the Welch-Aspin method (1). The results are given in Table III. When the interval between the isolations was 1-6 days or 7-30 days, there was no significant difference between the pairs of Kärber-values, but when it was more than one month, the second sample proved less sensitive ($0.01 < p < 0.05$).

The repeated isolations of *N. gonorrhoeae* in this group of patients are not included in Fig. 2. This strengthens the evidence of the curve suggesting that in northern Sweden the frequency of strains sensitive to penicillin has decreased during the last few years. In recent investigations in Copenhagen (10), Stockholm (6), and Oslo (15) the frequency of strains sensitive to penicillin decreased until 1962, 1963, and 1964, respectively, after which it increased.

The number of strains resistant to streptomycin when tested with the disc method are given in Table II. The material consists of the first strain from each patient. There were 7 strains in 1966 and 20 in 1968. Twenty-six out of these 27 strains showed decreased sensitivity to penicillin ($IC_{50} > 0.1$ IU/ml).

Decreased sensitivity to tetracycline or chloromycetin was not found.

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