PENICILLIN SENSITIVITY OF NEISSERIA GONORRHOEAE STRAINS FROM CALICUT, KERALA (1969)

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Introduction

A steady decrease in the penicillin sensitivity of Neisseria gonorrhoeae strains has been recognised since 1957 (Thayer et al[11]). Earlier studies had shown that N. gonorrhoeae strains were uniformly susceptible to very low concentrations of penicillin (Del Love and Finland[5], Reyn et al[8]). Strains of N. gonorrhoeae from different countries have since been shown to require increasing concentrations of penicillin for inhibition, both clinically and *in vitro* (Reyn et al[8]; Cradock-Watson et al[4], Leyn[10], Amies[1]). From India, Chacko and Yogeswari[2] and Moses et al[7] have reported that *N. gonorrhoeae* strains isolated from Madras and Bombay respectively, showed a steady decrease in penicillin sensitivity. The increasing incidence of cases of gonorrhoea refractory to routine penicillin treatment noticed recently in the Venereology Clinic, Medical College, Calicut prompted us to undertake investigation of the sensitivity of local strains of *N. gonorrhoeae* to penicillin.

Materials and Methods

This study was carried out in patients with a clinical diagnosis of acute gonorrhoea attending the Department of Venereology, Medical College Hospital, Calicut during 1969. All specimens for laboratory tests were collected in the Department of Microbiology to avoid delay between collection and processing.

Urethral discharge was collected directly on to glass slides for microscopy and on sterile swabs for culture. Where urethral discharge was absent, urine samples were collected, and the centrifuged deposit used for smear and culture. From female patients, urethral and cervical swabs were collected separately.

Gram's stanied smears were examined for the presence of intra and extra cellular Gram negative diplococci. Cultures were done on chocolate agar and Chacko-Nair (Chacko and Nair[3]) media in candle jars at 37°C. Human placenta broth (Reyn 1965) was used instead of beef digest for the preparation of Chacko-Nair medium. Plates were examined after 24 and 48 hours incubation and colonies were identified by Gram's stain, oxidase test and fermentation reactions.

Sensitivity tests were done by the plate dilution technique using Chacko-Nair medium containing penicillin G in concentrations of 0.025, 0.05, 0.1, 0.2, 0.5, 1.0 and 2.0 international units (IU) per ml. The minimum inhibitory concentration (MIC) of penicillin was taken as the lowest concentration that gave complete inhibition of growth.

Organisms grown in association with *N. gonorrhoeae* were studied further for complete identification, and in the case of Staphylococcus, for penicillin sensitivity by the disc diffusion method.

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Received for Publication on 15—2—1972

Results

A total of 233 cases of clinical gonorrhoea were investigated, from which 101 strains of N. gonorrhoeae were isolated. Table 1 shows the results of smear and culture in the diagnosis of these cases.

TABLE 1

		%
Total number of cases studied	233	
Smear positive, Culture negative	38	16.3
Smear positive, Culture positive	94	40.34
Smear negative, Culture positive	7	3.0
Smear negative, Culture negative	94	40.34

Sensitivity to penicillin was estimated in the case of 96 strains. The MIC values of penicillin for these strains are given in Table 2.

TABLE 2

The Minimum Inhibitory Concentration (MIC) of penicillin for 96 strains of Neisseria gonorrhoeae studied.

Penicillin international units (IU) per ml	No. of Strains inhibited	Percentage
0.025	20	20.8
0.05	7	7.3
0.1	19	19.8
0.2	6	6.3
0.5	15	15.6
1.0	26	27.1
2.0	3	3.1

Only 59 cases could be followed up after a course of penicillin treatment (six lacs units Procain Penicillin daily for 5 days intramuscularly). In 39 of these cases clinical cure was obtained. Table 3 shows the correlation between *in vitro* sensitivity of the isolate and clinical response to penicillin.

TABLE 3

Correlation between in vitro sensitivity of the *N. gonorrhoeae* isolate to penicillin and clinical response to the drug.

	Clinically responsive	%	Clinically resistant	%	Total
N. gonorrhoeae sensitive to penicillin *in vitro* (MIC 0.1 IU/ml or less)	30	90.9	3	9.1	33
N. gonorrhoeae of decreased sensitivity to penicillin *in vitro* (MIC more than 0.1 IU/ml)	9	34.6	17	65.4	26

The clinical response to penicillin treatment was analysed in relation to the presence in the urethral discharge, of penicillin resistant Staphylococcus, and the results are shown in Table 4.

A study of other bacterial flora in the urethral discharge did not reveal any but normal commensals of the anterior urethra.

Discussion

There have been two reports of penicillin sensitivity of N. gonorrhoeae strains from India. Chacko and Yogeswari[2] from Madras, testing strains isolated in 1963–65, found 45.6% with decreased sensitivity to penicillin (MIC more than 0.1 IU/ml). Moses et al[7] found decreased sensitivity in 56% of strains isolated from Bombay in 1968–1969. The present series isolated from Calicut (Kerala) in 1969 shows 52.1% with decreased sensitivity to penicillin. The range of MIC values of Indian strains have been reported as from 0.004 – 1.024 (Chacko and Yogeswari[2]) and $\leq$0.025 to $>$1.0 IU/ml. (Moses et al[7]). In this series, the MIC values varied from $\leq$0.025 to 2.0 IU/ml.

TABLE 4

Correlation between clinical response to penicillin therapy and the presence of penicillin resistant Staphylococcus in the urethral discharge.

Number of cases with associated Staphylococcus (irrespective of *in vitro* sensitivity of N. gonorrhoeae isolated)	46	
Number of cases with associated penicillin resistant Staphylococcus	40	
Number of cases clinically responding to penicillin in the presence of penicillin resistant Staphylococcus	26	(65.0%)
Number of cases with associated penicillin sensitive Staphylococcus	6	
Number of cases clinically responding to penicillin in the presence of penicillin sensitive Staphylococcus	3	(50.0%)
Number of cases with associated Staphylococcus, where the N. gonorrhoeae is sensitive *in vitro* (MIC 0.1 IU/ml or less)	26	
Number of cases with associated penicillin resistant Staphylococcus	25	
Number of cases responding to penicillin clinically in the presence of penicillin resistant Staphylococcus	22	(88.0%)
Number of cases with associated penicillin sensitive Staphylococcus	1	
Number of cases clinically responding to penicillin in the presence of penicillin sensitive Staphylococcus	0	

Clinical failure of penicillin in gonorrhoea may be due to several reasons unassociated with the *in vitro* sensitivity of the infecting strain of *N gonorrhoeae* (Kjillander and Finland[6]). But the growing incidence of penicillin failures in parallel with the decrease in penicillin sensitivity or N. gonorrhoeae strains would indicate a direct relationship between the two. In the present series, 90.9% of cases, where the infecting strain was fully sensitive to penicillin responded to treatment; while only 34.6% of cases where the infecting strain had decreased sensitivity to penicillin showed clinical response to the drug. A correlation between clinical response to penicillin and *in vitro* sensitivity has been reported by other workers also (Chacko and Yogeswari 1966; Moses et al[7]).

It has been suggested that treatment failures with penicilin could be due to the presence of penicillinase producing Staphylococcus in the urethra (Kjillander and Finland[6]). Results of this study do not support this view. In the series as a whole, treatment was successful in 50% of cases where penicillin sensitive Staphylococci were present in the urethral discharge, and in 65% of cases with associated penicillin resistant Staphylococci. But considering only cases caused by *N. gonorrhoeae* strains fully sensitive to penicillin, 88% of cases with associated penicillin resistant Staphylococci responded to treatment; while the only case with penicillin sensitive Staphylococcus did not.

Lack of response to penicillin in gonorrhoea has also been attributed to the infecting organism being Mima polymorpha instead of *N. gonorrhoeae.* However, Mima polymorpha urethritis seems to be uncommon here, as no case has been detected though the organism was specially looked for. Mima polymorpha is a not uncommon isolate from several other types of clinical materials in this laboratory.

Summary

The penicillin sensitivity of 101 strains of Neisseria gonorrhoeae isolated in 1969 from cases of acute gonorrhoeae in Calicut, (Kerala) was estimated. A decreased sensitivity to penicillin was seen in 52.1% of these strains. There was good correlation between *in vitro* sensitivity to penicillin and response to

treatment with this antibiotic. The presence of penicillin resistant Staphylococci in urethral discharge did not appear to be responsible for treatment failures with penicillin. No strain of Mima polymorpha could be obtained from any of the 233 cases of acute gonorrhoeae studied.

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False

Cytarabine topically or systemically has been found beneficial in the treatment of Herpes simplex infections like Herpetic Keratitis, Herpetic skin lesions and generalised Herpes simplex infection.

BMJ 2 : 154, 1970