ERYTHROMYCIN IN THE TREATMENT OF GONORRHOEA*

BY

BIRGITTE LYNG

Municipal Hospital, Copenhagen

The standard treatment of gonorrhoea since 1949 in the venereal diseases clinic of the Municipal Hospital of Copenhagen has been and in most cases still is 300,000 units procaine-penicillin, which is given when gonococci are demonstrable either by smears or by culture. To prove the treatment effective we require two negative cultures 1 week and 2 weeks after treatment. This dosage has recently become ineffective in an increasing number of cases, and more and more gonococcal strains have developed reduced sensitivity to penicillin.

The question of recurrence or re-infection is always difficult in a venereal disease, but when a patient denies sexual intercourse a fresh attack is regarded as a recurrence.

Since 1961 the sensitivity of all the gonococcal strains isolated from our patients has been determined at the State Serum Institute. In 1961 we found 10 per cent. with reduced sensitivity to penicillin, but in 1962-63 this had risen to 20 per cent. We have therefore seriously contemplated the use of other drugs in the treatment of gonorrhoea.

The sulphonamides have already had their day on account of the large number of resistant strains which became dominant when they were the common treatment, and many of the strains now isolated still show resistance to sulphonamides.

Several other antibiotics have been tried, usually in recurrences after treatment with penicillin, and we are inclined to associate this with the fact that many strains have developed a reduced sensitivity to the tetracyclines and some also to streptomycin.

We have therefore chosen erythromycin which is not very often used in Denmark, and in the cases studied we have found no strain with reduced resistance to erythromycin *in vitro*, possibly because the drug has been used only very seldom against gonorrhoea, and possibly because we have been warned very strictly against using it without very serious reasons.

Method

From June, 1962, to March, 1963, we have treated all gonorrhoea patients, not cured by the standard treatment 300,000 units procaine-penicillin, with the erythromycin preparation "Ilosone", six doses of 250 mg. 6-hourly. Simultaneously with the first dose of "Ilosone", 300,000 units procaine-penicillin are also given with the intention of preventing the formation of erythromycin-resistant strains. We have used this method in accordance with Prof. K. A. Jensen's investigations of the development of bacterial resistance.

Material

During the study period, 140 patients (97 men and 43 women) with uncomplicated gonorrhoea were treated. 31 of them (24 men and 7 women) still had gonococci in the urethral or cervical secretion one week after penicillin treatment (22 per cent.), and these 31 were thereafter treated with "Ilosone" with the results shown in Table I.

TABLE I
RESULTS IN 31 CASES

Sex	No. of Cases	Result	
		Failure	Cure
Male	24	14	10
Female	7	6	1
Total	31	20	11

Results

Table II (opposite) shows the resistance pattern of the gonococcal strains of the 24 men. The sensitivity to erythromycin, determined by the tablet method, is expressed by the diameter of the inhibition zone given in millimetres, the sensitivity to penicillin, streptomycin, and the tetracyclines is determined by the dilution method, and expressed as 50 per cent. inhibitory concentration.

* Paper read at M.S.S.V.D. meeting in Copenhagen, on June 6, 1963

TABLE II

RESISTANCE PATTERN OF GONOCOCCAL STRAINS IN 24 MALE PATIENTS

Erythro- mycin (mm.)	Penicillin (μ g./ml.)	Strepto- mycin (μ g./ml.)	Tetra- cycline (μ g./ml.)	Effect
46	≤ 0.0047	≤ 1.41	0.31	+
44	≤ 0.0047	≤ 1.41	0.186	+
43	0.0066	≤ 25.0	0.14	+
43	0.21	≤ 1.41	0.31	0
42	0.075	≤ 1.41	0.26	+
42	0.30	> 25.0	0.80	0
42	0.053	> 25.0	0.40	+
42	0.30	> 25.0	0.57	+
41	0.21	≤ 1.41	0.37	0
40	0.075	1.68	0.74	+
40	0.30	2.4	1.25	0
40	0.30	> 2000	0.37	0
40	0.30	> 25.0	1.60	0
39	0.075	≤ 1.41	1.05	0
39	0.106	1.68	0.37	0
39	0.106	> 25.0	0.57	+
39	0.075	≤ 1.41	0.156	+
39	0.075	≤ 25.0	0.28	+
38	0.30	> 2000	0.63	0
37	0.30	≤ 25.0	0.40	0
36	0.30	≤ 25.0	0.40	0
36	0.075	> 25.0	1.60	0
36	0.075	≤ 25.0	0.28	0
35	0.42	> 25.0	1.60	0

TABLE III

ERYTHROMYCIN (mm.) RESISTANCE BEFORE AND AFTER TREATMENT

Before	After
44	40
43	43
43	40
42	40
41	40
40	41
40	41
40	40
40	39
39	41
39	39
39	38
38	40
37	—
36	39
36	37
36	38
36	35
36	41
35	41

first dose taken in the clinic in the presence of the physician.

Summary

It is concluded that erythromycin, in the doses given, is not suitable for the treatment of gonorrhoea, as a drug with a cure rate of only 65 per cent. cannot be recommended for therapy. As the sensitivity of these strains *in vitro* is the same as that seen in most gonorrhoea patients regardless of clinical cure, the drug cannot be recommended for routine treatment.

REFERENCE

Heilman, F. R., Herrell, W. E., Wellman, W. E., and Geraci, J.E. (1952). *Proc. Mayo Clin.*, 27, 285.

La blennorrhagie traitée par l'Érythromycine

RÉSUMÉ

L'auteur constate que l'érythromycine au dosage spécifié n'est pas efficace contre la blennorrhagie, puisque 65% seulement des malades traités ainsi furent guéris, malgré que les organismes en question fussent aussi sensibles *in vitro* que dans la plupart des cas de gonorrhée. On ne peut donc pas recommander l'usage quotidien de ce médicament dans les cliniques antivénéériennes.

The State Serum Institute designated all the strains with an inhibitory zone between 46 and 35 mm. as sensitive to erythromycin. According to the investigations of the State Serum Institute this should correspond to a 50 per cent. inhibitory concentration of 0.1 to 1.0 μ g./ml. as determined by the dilution method. According to the investigations of Heilman, Herrell, Wellman, and Geraci (1952) at the Mayo Clinic, we can assume that the serum level of erythromycin after the dosage given was higher than 1.0 μ g./ml. for several hours.

The three most sensitive strains shown at the top of Table II are also sensitive to penicillin, and as a dose of penicillin was given at the same time one cannot tell whether these patients were cured by the penicillin or by the erythromycin.

There seems to be no relationship between clinical efficacy and sensitivity *in vitro*.

Table III shows that the pattern of resistance to erythromycin seems to be quite uninfluenced by treatment.

The patients have not complained of any side-effects. It is always uncertain whether the patient has in fact taken the tablets, and we have considered changing the standard treatment for a short period, so that all patients will have 1 g. erythromycin as a