

## LINCOMYCIN, NON-GONOCOCCAL URETHRITIS, AND MYCOPLASMATA\*

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Lincomycin is an antibiotic produced by *Streptomyces lincolnensis* (Mason, Dietz, and DeBoer, 1963), which acts by inhibiting protein synthesis in Gram-positive bacteria (Josten and Allen, 1964). Its main indications are infections caused by Gram-positive organisms though its spectrum has not yet been fully determined.

In a recent report by Mowat, Chalmers, Alexander, and Duthie (1967), lincomycin was considered to be effective in the treatment of a case of Reiter's syndrome. Shipley, Bowman, and O'Connor (1968) found that mycoplasma T-strains were resistant to 200 µg./ml. lincomycin. Williams, Csonka, and Corse (unpublished) also noted that T-strains were resistant to lincomycin *in vitro* but that *Mycoplasma hominis* was sensitive to 5 µg./ml. of the antibiotic; both T-strains and *M. hominis* were isolated from the urethra in patients with non-gonococcal urethritis (NGU).

These reports and our own experience led us to investigate the clinical response of non-gonococcal urethritis (NGU) and Reiter's syndrome to lincomycin and its effect on genital mycoplasma *in vivo*. The present paper gives the results in NGU.

### Material and Methods

51 male patients with NGU who attended the Special Clinics of the Central Middlesex Hospital and St. Mary's Hospital were studied. The only elements of selection were to exclude those patients least likely to attend for observation and those with minimal urethritis.

*N. gonorrhoeae* and *T. vaginalis* were excluded by microscopical examination; urethral discharge was cultured on special medium for the isolation of mycoplasma (Csonka, Williams, and Corse, 1967). Specimens for mycoplasma were taken before and after treatment and subsequently if the discharge persisted or recurred.

The patients received 500 mg. lincomycin capsules four times daily for 5 days and were examined 7 days after the start of treatment and then at weekly intervals for a month and fortnightly for the next 2 months.

Treatment response was considered satisfactory if there were no symptoms and no urethritis and the urine was clear in the two-glass test. Treatment failures were given erythromycin (250 mg. four times daily for 5 days). During the period of study a further 54 patients with NGU were initially treated with erythromycin (250 mg. four times daily for 5 days) and sixty patients with tetracycline (250 mg. four times daily for 5 days) for comparison with lincomycin.

### Results

Of the 51 patients who received lincomycin, only thirteen (25.5 per cent.) were clear a week after the start of treatment, a result which compares unfavourably with erythromycin and tetracycline therapy which yielded cure rates of 68.5 and 80 per cent. respectively (Table I).

TABLE I  
COMPARISON OF LINCOMYCIN WITH ERYTHROMYCIN  
AND TETRACYCLINE IN THE TREATMENT OF NGU  
(All given four times a day for 5 days)

Drug	Dose (mg.)	No. Treated	Failures 1 week after Start of Treatment	
			No.	Per cent.
Lincomycin	500	51	38	74.5
Erythromycin	250	54	17	31.5
Tetracycline	250	60	12	20.0

Re-treatment with erythromycin of cases which had failed to respond to lincomycin gave a success rate of 68 per cent., similar to that achieved by erythromycin alone (Table II).

TABLE II  
RE-TREATMENT OF LINCOMYCIN FAILURES WITH  
ERYTHROMYCIN  
(250 mg. four times daily for 5 days)

No. Re-treated	No. Observed	No. of Failures of Those Observed
38	28	9 (32 per cent.)

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The isolation rates of T-strain mycoplasma before and after treatment are shown in Table III.

TABLE III

ISOLATION RATE OF MYCOPLASMA T-STRAINS IN PATIENTS TREATED WITH LINCOMYCIN AND RE-TREATED WITH ERYTHROMYCIN

Time of Test	No. Investigated	T-strains Isolated		Total No. of Patients with T-strains	
		No.	Per cent.	No.	Per cent.
Before treatment	51	32	63	41	80
After unsuccessful treatment	34	24	71		
After successful treatment or re-treatment	23	2	9		

The 80 per cent. recovery rate represents findings in 41 cases in which T-strains were isolated both before and after unsuccessful treatment, or in which T-strains were first isolated only after unsuccessful treatment.

*M. hominis* was grown from six cases only; in five the organism was isolated before treatment with lincomycin and was not found subsequently although urethritis persisted, and in one it was first noted 2 weeks after treatment when NGU had recurred.

In six cases not included in the series and initially diagnosed as NGU, gonococci were seen in urethral smears after the course of lincomycin and a diagnosis of gonorrhoea was confirmed by culture.

### Discussion

The clinical effect of lincomycin in NGU one week after the start of treatment appeared to be no better than that of a placebo (Leach, 1959; Csonka, 1959); however, in a few patients improvement was prompt and in these lincomycin may have had an effect.

Erythromycin was reported by Shepard, Lunceford, and Baker (1966) to be active against T-strains *in vitro* but not against *M. hominis*, acting in the opposite way to lincomycin in this respect. As erythromycin has been reported to be effective in the treatment of NGU (Willcox, 1955), it was concluded that these results strengthened the case for T-strains being aetiologically significant whilst weakening the case for *M. hominis*.

In our experience erythromycin, used both as initial treatment and as re-treatment of lincomycin failures, gave an immediate success rate of 68-68.5 per cent., showing it to be quite effective against NGU though less so than tetracycline.

It would be unwise to claim that good correspondence between sensitivity *in vitro* and clinical response to antibiotics can alone establish that an organism is a causal agent in NGU but, if lincomycin had been found to be outstandingly successful in the treatment of this condition, it would have seriously damaged the case for T-strains being of possible aetiological importance.

The high isolation rate of T-strains in untreated NGU persisted after unsuccessful treatment but declined sharply after effective therapy.

As regards *M. hominis*, the lack of correspondence between sensitivity *in vitro* and therapeutic response and the low isolation figures imply that this organism plays little or no part in the causation of NGU.

We do not know whether the *Chlamydia* which have been isolated from patients with NGU and Reiter's syndrome are sensitive to lincomycin, but Shipley and others (1968) mentioned that a bovine strain of *Chlamydia* is sensitive *in vitro* to 1-2 µg./ml. It would be of interest to establish the lincomycin sensitivity pattern of these organisms recovered from NGU and allied conditions.

Unlike other antibiotics which have been found to be ineffective in the treatment of NGU (Csonka and others, 1967), lincomycin does not act on the cell wall of micro-organisms. As mycoplasmata have no cell walls, antibiotics acting solely or mainly on this structure are of no use in the investigation of these organisms. Lincomycin, which differentiates between T-strains and other mycoplasmata, has therefore promising characteristics which might make it suitable for the investigation of basic differences within the mycoplasma group itself.

The later discovery that six (10.5 per cent.) of 57 patients first diagnosed by smear findings as having NGU were in fact suffering from gonorrhoea is disturbing; if we had used tetracycline, which unlike lincomycin is effective against the gonococcus and is our usual treatment for NGU, we should not have seen the extent of this diagnostic problem; clearly there is need to improve our methods.

### Summary

51 patients with non-gonococcal urethritis were treated with lincomycin, 500 mg. by mouth four times daily for 5 days. The cure rate 7 days after the start of therapy was 25.5 per cent., which is similar to that found after giving a placebo. Re-treatment of failures with erythromycin was successful in 68 per cent. A second group of 54 patients received erythromycin initially with an early response in 68.5 per cent. A third group of sixty patients was treated with tetracycline, which

gave the best clinical results with 80 per cent. showing prompt response.

*Mycoplasma hominis* was isolated from only six patients of 51 investigated and is not considered to be aetiologically important. Mycoplasma T-strains which are resistant to lincomycin but not to erythromycin or tetracycline were recovered from 63 per cent. before treatment and from 71 per cent. after unsuccessful therapy, but from only 9 per cent. of apparently cured cases.

The significance of these findings is discussed.

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#### La lincomycine, l'urétrite non-blennorragique et les mycoplasmes

##### RÉSUMÉ

51 malades atteints d'urétrite non-blennorragique ont été traités avec de la lincomycine, 500mg par voie buccale quatre fois par jour pendant cinq jours. Le taux de cures sept jours après le commencement du traitement était de 25,5 pour cent, et est semblable au taux constaté après l'administration d'un placebo. Un second traitement donné aux non-réussites avec l'érythromycine était efficace dans 68 pour cent des cas. Un second groupe de 54 malades qui avaient reçu l'érythromycine au début du traitement avait donné un bon résultat chez 68,5 pour cent. Un troisième groupe de 60 patients avait été traité avec de la tétracycline et avait donné les meilleurs résultats cliniques immédiats chez 80 pour cent.

Le *Mycoplasma hominis* avait été isolé chez six malades seulement des 51 examinés et ce résultat n'est pas considéré comme étant important étiologiquement. Les souches T des mycoplasmes qui sont résistantes à la lincomycine mais pas à l'érythromycine ou à la tétracycline ont été trouvées chez 63 pour cent avant le traitement et chez 71 pour cent des cas non-guériss, mais chez 9 pour cent seulement des cas apparemment guéris. La signification de ces constatations est discutée.