

justified to conclude that the repeated whole-body treatment with the DDT-containing Tenutex® emulsion is the cause of the increased DDE-DDT concentrations and, consequently, when locally applied to the skin, DDT can be percutaneously absorbed, yielding measurably increased plasma concentrations. This is especially so in the case of repeated applications in children, who are known to have a lower skin resistance to penetration. As can be seen in Table II, there was no significant percutaneous uptake following a single 24-hour treatment in adult patients. The lack of agreement between the plasma concentrations in treated children shown in Table I can be explained by the varying degrees of excoriation and there are also great interindividual variations as regards the ability to absorb chemicals through the skin (1).

When Tenutex® was first introduced, Flodén (2) pointed out even then that DDT alone had only a moderate effect on scabies. We have performed a double-blind study (5) and shown that in treating a scabies infection, an emulsion of 2% disulfiram and 22.5% benzyl benzoate (i.e. Tenutex® without DDT) is just as effective as ordinary Tenutex®.

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Erythromycin and Lyme cycline Treatment in Chlamydia-positive and Chlamydia-negative Non-gonococcal Urethritis—A Partner-controlled Study

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Abstract. A group of 213 men with non-gonococcal urethritis and their sexual partners were treated either with erythromycin stearate 500 mg×2 for 15 days or with lymecycline 300 mg×2 for 10 or 20 days. *Chlamydia trachomatis* was isolated from 40% of the men, from 26% of their female partners and from 56% of the partners of men with chlamydia-positive urethritis. One hundred and eighty-one men were available for evaluation of therapy. There were no significant differences between the treatment schedules. The cure rate was 86–90% in men with chlamydia-positive and 89–100% in men with chlamydia-negative urethritis. Four of the 17 chlamydia-positive females treated with erythromycin and 2 of the 20 chlamydia-positive females treated with lymecycline for 10 days still had chlamydia at re-examination.

Key words: *Chlamydia trachomatis*; Non-gonococcal urethritis; Treatment of

One of the major reasons why non-gonococcal urethritis (NGU) has gained a reputation as being difficult to treat is obviously that it generally is not treated as a venereal disease. Failure to treat female partners and to carry out essential epidemiological examinations of sexual contacts results in reinfections in a number of cases. Any therapeutic trial of NGU should therefore include treatment of partners of patients in parallel.

Convincing evidence that *Chlamydia trachomatis* is the cause of 30–50% of cases of NGU has been produced by many groups. There is general agreement that up to 70% of sexual consorts of men with chlamydial urethritis have chlamydial infection of the cervix. Unfortunately the treatment of NGU has remained difficult, despite the recent extension of our understanding of its etiology, and the clinical use of many different antimicrobial agents.

Table 1. *Treatment of chlamydia-positive NGU with erythromycin and lymecycline*

Treatment schedule	Number of patients	Number controlled	Treatment failure
Erythromycin 500 mg every 12 hours for 15 days	36	30	3
Lymecycline 300 mg every 12 hours for 10 days	29	24	3
Lymecycline 300 mg every 12 hours for 20 days	21	21	3 ^a

^a One patient chlamydia-negative.

Tetracyclines and erythromycin seem to be the most effective antimicrobials for practical use in the treatment of NGU. This agrees well with the concept that *Chlamydia trachomatis* is the most important etiological agent in NGU, since both of the above-mentioned antibiotics almost always succeed in eradicating this micro-organism *in vitro* (2). Another probable etiological factor of NGU, *Ureaplasma urealyticum*, is also sensitive to both tetracyclines and erythromycin *in vitro* (3).

The purpose of the present investigation was to evaluate the effectiveness of treatment with lymecycline and erythromycin treatment for varying periods, when the sexual partners of the patients were treated simultaneously with the same antimicrobial.

MATERIAL AND METHODS

The male patients were all seen in the Out-patient Department for Venereal Diseases, University Central Hospital, Helsinki, between May 1977 and January 1978. All the patients had a regular partner and all of these were included in the study too. All women were examined by J. P. at the Out-Patient Clinics of 1st and 2nd Departments of Obstetrics and Gynaecology, University Central Hospital, Helsinki.

The diagnosis of NGU was based on evidence of significant urethritis, shown by the presence of ≥ 10 polymorphonuclear leukocytes per high-power field ($\times 100$ objective) in a Gram-stained urethral smear with no evidence of *Neisseria gonorrhoeae* on microscopy or culture.

Urethral specimens for isolation of *Chlamydia trachomatis* were taken from all men and both urethral and cervical specimens from their female partners. The sampling and isolation of *Chlamydia trachomatis* have been described elsewhere (4).

After the diagnosis had been made, men with NGU were treated with either erythromycin stearate (Abbott) 500 mg, every 12 hours for 15 days, or lymecycline (Carlo-Erba) 300 mg, every 12 hours for either 10 or 20 days. The female partners of the patients were started on the same treatment regimen at the same time as their male

patients. Samples for *Chlamydia trachomatis* isolation had been taken from all females before the treatment was initiated.

Patients were advised to abstain from sexual intercourse until the re-examination.

Follow-up examination was performed 2 weeks after the treatment ended. Patients or female partners with an initially positive *Chlamydia trachomatis* isolation as well as patients with signs of urethritis when re-examined were retested for the presence of *Chlamydia trachomatis*, as described above. Significant urethritis at the follow-up examination was assessed as already defined.

RESULTS

A group of 213 men with NGU were admitted to the trial. Of these, 32 were lost to follow-up because of defaulting after their first attendance. Thus 181 men were available for evaluation of therapy, of whom 75 (41%) had yielded *Chlamydia trachomatis* before treatment. Erythromycin was given to 75 of the 181, lymecycline for 10 days to 60 and lymecycline for 20 days to 46.

The results of treatment of the group with chlamydia-positive urethritis are illustrated in Table 1. Two weeks after treatment was completed, 9 patients still had urethritis according to definition. The treatment failures were distributed evenly among the different treatment groups. Eight of the patients still yielded *Chlamydia trachomatis* in their urethra.

The results of treatment of men with chlamydia-negative urethritis are shown in Table II. One of the patients treated with erythromycin stearate and 4 of those treated with lymecycline for 10 days still had urethritis when re-examined. All the 25 re-examined patients treated with lymecycline for 20 days were cured. None of the patients with treatment failures had positive cultures for *Chlamydia trachomatis* at the follow-up examination.

Table III illustrates treatment results of

Table II. Treatment of chlamydia-negative NGU with erythromycin and lymecycline

Treatment schedule	Number of patients	Number controlled	Treatment failure
Erythromycin 500 mg every 12 hours for 15 days	54	45	1
Lymecycline 300 mg every 12 hours for 10 days	43	36	4
Lymecycline 300 mg every 12 hours for 20 days	30	25	0

chlamydia-positive female partners of the men with NGU. A total of 56 females (26%), i.e. 48 (56%) of the partners of men with chlamydia-positive urethritis and 8 (6%) of the partners of men with chlamydia-negative urethritis, gave a positive chlamydia-culture. Fiftyone (91%) of the 56 chlamydia-positive females were re-examined 2 weeks after the treatment was completed. Four of those treated with erythromycin stearate as well as 2 treated with lymecycline for 10 days still had a positive chlamydia culture. Five were partners of men with treatment failures and positive chlamydia cultures at re-examination. All 6 admitted sexual intercourse with their respective regular partners either during or after treatment.

The only side-effect reported was mild stomach discomfort, which did not interfere with the treatment. This was seen only in a few cases and occurred somewhat more often with erythromycin stearate than with lymecycline.

DISCUSSION

The distinction between relapse and reinfection is very difficult after treatment of non-gonococcal urethritis. It is almost impossible if the partner has been left untreated, as this greatly increases the

possibility of reinfection. The risk of reinfection is definitely decreased if the partner has received an identical and simultaneous treatment. However, there is always a risk of reinfection from other sexual partners than the regular one. With this pitfall in mind, it is suggested that the recurrence of urethritis in some of the men in the present series probably implies treatment failure.

About 10% of patients with chlamydia-positive urethritis still had symptoms or signs of urethritis and yielded *Chlamydia trachomatis* after treatment. In more than half of these cases the partner also yielded *Chlamydia trachomatis* after the therapy was concluded. The treatment failures occurred evenly in all three groups. This further stresses the chronic and latent nature of chlamydial infections, which has caused problems in the antimicrobial therapy of chlamydial eye disease (5). Unfortunately, the isolated strains of *Chlamydia trachomatis* were not tested for their sensitivity to erythromycin or lymecycline.

Treatment failure was observed in about 5% of the men with chlamydia-negative urethritis. Most of these had received lymecycline for 10 days. In these cases an infecting organism could have failed to respond to therapy, as all patients who had received lymecycline for 20 days were found to be cured

Table III. Treatment with erythromycin and lymecycline of chlamydia-positive female partners of males with NGU

Treatment schedule	Number of patients	Number controlled	Treatment failure
Erythromycin 500 mg every 12 hours for 15 days	20	17	4
Lymecycline 300 mg every 12 hours for 10 days	20	20	2
Lymecycline 300 mg every 12 hours for 20 days	16	14	0

when re-examined. However, the difference is not statistically significant. Unfortunately, *Ureaplasma urealyticum* cultures were not performed during the study period. The finding of Bowie et al. (6) that chlamydia-positive urethritis responds better to treatment than chlamydia-negative urethritis could not be confirmed in the present study.

Both erythromycin stearate and lymecycline in the dosages used in this study seem to be effective in the treatment of non-gonococcal urethritis regardless of whether the culture for *Chlamydia trachomatis* is positive or negative. Ten to 15 days of treatment seems to be sufficient, providing the partner is treated simultaneously.

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Acridine Orange Staining of Urethral and Cervical Smears for the Diagnosis of Gonorrhea

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Abstract. Smears of urethral and cervical discharge for direct microscopical examination of gonococci were stained with acridine orange and methylene blue and the findings compared with culture of direct inoculated plates. These two staining methods yielded similar results.

Acridine orange staining seems a valuable alternative due to its sharp image contrast.

Key words: Identification of gonococci; Acridine orange staining; Methylene blue staining

Direct microscopical examination of stained urethral and cervical smears allows the trained physician to make a positive diagnosis of gonorrhea immediately at the patient's first visit. Correct treatment can then be given without delay. The risk of false-positive diagnosis is small. About 90% of gonococcal infections in men are detected (3), whereas in women only 50–60% of infections are detected (1, 3). This is partly due to the presence of other microorganisms and mucus that makes the intracellular diplococci less prominent.

Kronvall & Myhre (4) 1977 described a simple staining method for bacteria in clinical specimens using acridine orange at low pH. Cells and bacteria are easily differentiated by their green vs. orange colour when observed by fluorescence microscopy. We were interested to see whether this contrast staining would yield more positive findings, particularly in women, compared with the routine methylene blue staining.

MATERIAL AND METHODS

Patients seen in the venereal diseases clinic in whom gonorrhea might be suspected on clinical and epidemiological grounds (heavy purulent urethral discharge and/or a known contact with gonorrhea) were selected. The final material consisted of 83 patients, 55 women and 28 men. From each patient two sets of smears were prepared, from the urethra in men and from the urethra and the cervix in women. One smear was immediately stained with methylene blue and examined. The other was later stained with acridine orange *ad modum* Kronvall & Myhre (4) and examined in a Zeiss fluorescence microscope with incident light and blue band activation. The finding of monomorphic, intracellular, coffeebean-shaped diplococci was considered the sole criterion for making a diagnosis of gonorrhea. Swabs for culture were taken at the same time as the smears and plated immediately on GC agar plates at room temperature.

The GC agar used had the following composition: GC agar base (BBL) 10 g, aq. dest. to 1 000 ml. In addition to a plate with this mixture, another plate using the same composition but with the addition of VCN-inhibitor (BBL) 10 ml/l was used. After the inoculation, the plates were immediately placed in a candle jar and sent within 4 h to the laboratory, where they were incubated for 48 h at 37°C with 5% CO₂ and 95% humidity and then examined for gonococci. Oxidase-positive colonies with a morphology