

Most symptoms in mastocytosis appear to be related to effects of histamine release. It has therefore been natural to try various types of drugs, which could influence histamine release or act as antagonizers. However, neither H1 nor H2 antihistamines have proved very effective (12) and the same appears to be the case with histidine decarboxylase inhibitors (14) and histamine liberators (7).

DSCG is effective in the treatment of allergic asthma, allergic rhinitis and allergic conjunctivitis, in which the drug is believed to act by inhibiting mast cell degranulation locally and thereby histamine release. DSCG is, in our experience (11), of no value in chronic urticaria, probably due to insufficient absorption and therefore lack of effect on cutaneous mast cells. These data have been in general agreement with the results of Denman (2). However, Denman found an effect in a subgroup of patients with dietary hypersensitivity, where urticaria could be related to some extent to histamine release from mast cells in the gastrointestinal tract. Our present data support the idea that oral DSCG acts only on symptoms related to mast cell release from the gastrointestinal tract. This would seem to contradict the data of Soter somewhat (10); they reported a time course effect of DSCG on skin as well as on the central nervous system and gastrointestinal tract in a controlled clinical trial on 8 patients with mastocytosis, but no influence on urinary histamine excretion. Our data tally well with the case reported by Sauder & co-workers regarding the finding of reduced urinary histamine in a 5-month-old boy with systemic mastocytosis treated with oral DSCG.

We feel that our results demonstrate that DSCG is a useful drug in the treatment of gastrointestinal manifestations of mastocytosis, but that in the present dosage it has no effect on cutaneous symptoms.

#### REFERENCES

1. Christophers, E., Hönigsmann, H., Wolff, K. & Langner, A.: PUVA treatment of urticaria pigmentosa. *Br J Dermatol* 98: 701-702, 1980.
2. Denman, A.: Oral sodium cromoglycate in treatment of urticaria. *In The Mast Cell, Its Role in Health and Disease* (ed. J. Pepys & A. Edwards). Pitman, Tunbridge Wells, 1979.
3. Jarnum, S. & Zachariae, H.: Mastocytosis of skin, stomach and gut with malabsorption. *Gut* 8: 64-68, 1967.
4. Lindell, S., Rorsman, H. & Westling, H.: Histamine

formation in urticaria pigmentosa. *Acta Dermatovener (Stockholm)* 41: 277-280, 1961.

5. Mutter, R., Tannenbaum, M. & Ullmann, J.: Systemic mast cell disease. *Ann Int Med* 59: 887-906, 1963.
6. Oates, J., Marsh, E. & Sjoerdsma, A.: Studies on histamine in human urine using a fluorometric method of assay. *Clin Chim Acta* 7: 488-497, 1962.
7. Sagher, F. & Even-Paz, Z.: Mastocytosis and the Mast Cell. S. Karger, Basel, 1967.
8. Sauder, D., Bergfeld, W. & Krakauer, R.: Disodium cromoglycate therapy in mastocytosis. *In The Mast Cell, Its Role in Health and Disease* (ed. J. Pepys & A. Edwards). Pitman, Tunbridge Wells, 1979.
9. Sjoerdsma, A., Waalkes, T. & Weisbach, H.: Serotonin and histamine in mast cells. *Science* 125: 1202-1203, 1957.
10. Soter, N.: The efficacy of the oral administration of disodium cromoglycate in systemic mastocytosis. *In The Mast Cell, Its Role in Health and Disease* (ed. J. Pepys & A. Edwards). Pitman, Tunbridge Wells, 1979.
11. Thormann, J., Laurberg, G. & Zachariae, H.: Oral sodium cromoglycate in chronic urticaria. *Allergy* 35: 139-141, 1980.
12. Yamamoto, S., Francis, D. & Greaves, M.: In vitro anaphylaxis in guinea-pig skin: Amplification by burimamide. *J Invest Dermatol* 67: 696-699, 1976.
13. Zachariae, H.: Skin histamine in urticaria pigmentosa. *Acta Dermatovener (Stockholm)* 43: 125-128, 1963.
14. Zachariae, H., Brodthagen, H. & Søndergaard, J.: Studies on a histidine decarboxylase inhibitor NSD 1055, in chronic urticaria and urticaria pigmentosa. *Proc. 18th Meeting, Scand Dermatol Ass. Turku, 1968*, pp. 138-144.

### One-week Treatment of Chlamydia-positive Urethritis with Doxycycline and Tetracycline Chloride in Males

T. Juvakoski, J. Lauharanta, L. Kanerva and A. Lassus

*Department of Dermatology and Venereology, University Central Hospital, Helsinki, Finland*

Received November 25, 1980

*Abstract.* 65 patients with chlamydia-positive urethritis were treated with doxycycline and 59 with tetracycline chloride 1 g/day for one week. All steady sexual partners of these patients were treated with the same regimen during the same period. At control visits 2 and 3 weeks after the beginning of the treatment, all re-examined doxycycline-treated patients and all except 4 tetracycline-treated

patients showed clinical cure and were free from signs of urethritis in the microscopical examination of Gram-stained smears from the urethra. Isolation of *C. trachomatis* was positive in 7 of the doxycycline-treated and 10 of the tetracycline-treated patients at the first control visit and in one more tetracycline-treated patient at the second control visit. The study stresses the importance of attempts to isolate *C. trachomatis* in cases without clinical or microscopical evidence of nongonococcal urethritis at control visits after short-term treatment with tetracyclines. The present investigation indicates that this is true also in cases in which all steady sexual partners are treated simultaneously.

**Key words:** Chlamydia-positive urethritis; One-week treatment; Doxycycline; Tetracycline

Tetracyclines have long been used to treat nongonococcal urethritis (NGU) and are regarded as first-choice drugs. However, the optimal regimen in terms of type of preparation, dose and duration of treatment are not established. According to Thamber et al. (3) satisfactory results can be achieved with a one-week regimen of tetracycline whether the patient's steady sexual partner is treated at the same time or not. We tried to test this with two different tetracyclines in chlamydia-positive cases with NGU.

## PATIENTS AND METHODS

201 male patients attending the Out-Patient Department for Venereal Diseases, University Central Hospital, Helsinki were selected for the study (Table I). In order to gain as high proportion of cases with chlamydia-positive NGU as possible we included especially men with sexual partners diagnosed as having chlamydia-positive cervicitis. The diagnosis of NGU was established by the presence of urethral discharge, dysuria and  $\geq 10$  leukocytes per high-power field in Gram-stained smears from the urethra and culture-negative for *N. gonorrhoeae* (1). Isolation of *C. trachomatis* from the urethra was carried out as described elsewhere (2). The patients were treated with either doxycycline 200 mg on the first day and 100 mg per day for the next 6 days, or tetracycline chloride 1 g per day for 7 days. The treatment was randomized. The steady partner of each patient received the same treatment as the patient himself, starting on the same day. Clinical data of the patients are presented in Table I.

Table II. *Microbiological findings in chlamydia-positive cases after treatment*

	Therapy	
	Doxycycline	Tetracycline chloride
Total no. treated	65	59
Findings 7 days after treatment		
No. re-examined	62	55
No. culture-negative	55 (89%)	45 (82%)
No. culture-positive (relapse)	5 (8%)	7 (13%)
No. culture-positive (probable reinfection)	2 (3%)	3 (5%)
Findings 14 days after treatment		
No. re-examined	54	42
No. culture-negative	54	41 (98%)
No. culture-positive	0	1 (2%)

Re-examinations were performed 7 and 14 days after the last day of treatment. At each re-examination, Gram-stained urethral smears were examined and isolation of *C. trachomatis* was performed in all cases as before treatment.

## RESULTS

Altogether 65 patients treated with doxycycline and 59 treated with tetracycline chloride had a positive isolation of *C. trachomatis* before treatment (Table II). Three of the doxycycline group and 4 of the tetracycline chloride group did not return for the first re-examination 14 days after the treatment had started. At this first re-examination *C. trachomatis* could not be isolated in 89% of the doxycycline-treated and 82% of the tetracycline chloride-treated patients. True relapses were regarded as probable in 8% of the doxycycline- and 13% of the doxycycline chloride-group. Two patients of the former and 3 of the latter group admitted intercourse with untreated partners after treatment all 54 re-examined patients treated with doxycycline had a negative isolation of *C. trachomatis*, while one of the 42 re-examined patients treated with tetracycline chloride had a positive isolation of *C. trachomatis* at this time, despite a negative result one week earlier.

Table I. *Clinical data of the patients*

	Therapy	
	Doxycycline	Tetracycline chloride
Total no. of patients	100	101
Average age (years)	29	31
Average weight (kg)	74	77
<i>C. trachomatis</i> -positive	65	59

Table III. Microscopical findings after treatment in chlamydia-positive cases

	Therapy	
	Doxy- cycline	Tetra- cycline chloride
No. Chlamydia-positive before treatment	65	59
Total no. re-examined 7 days after treatment	62	55
Microscopical examination		
negative	62	53 (96%)
positive	0	2 (4%)
Total no. re-examined 14 days after treatment	54	42
Microscopical examination		
negative	54	40 (95%)
positive	0	2 (5%)

This patient admitted an intercourse with a new partner and could have had a re-infection.

Results of the microscopical examination at the control visits 2 and 3 weeks after the treatment had started are presented in Table III. All doxycycline-treated re-examined patients had fewer than 10 leukocytes per high-power field at both re-examinations. In the tetracycline chloride treated group, 2 patients had more than 10 leukocytes at the first control visit and 2 others likewise at the second control visit.

One patient reported severe stomach pain during the doxycycline treatment. No other severe adverse reactions were reported.

#### DISCUSSION

According to the microscopical examination at the control visits both tetracyclines used in the present

study were very effective when the patients' steady partners were treated at the same time. Unfortunately this finding did not correlate with the isolation of *C. trachomatis* at the control visits. Although doxycycline seemed to be more effective than tetracycline chloride, about 10% of the doxycycline-treated group had a positive isolation one week after the end of the treatment. This indicated that a one-week treatment is not long enough with either of the tetracyclines used in the present study. It also stresses the importance of attempts to isolate *C. trachomatis* at control visits after tetracycline-treatment despite clinical and microscopical cure in *C. trachomatis*-positive cases of NGU. In our experience there is no practical need to follow up these highly promiscuous patients for more than 2 weeks after the treatment, as the incidence of reinfection rises very rapidly with longer follow-up periods.

#### ACKNOWLEDGEMENT

The authors wish to thank the nursing staff of the Department of Dermatology and Venereology for kind help, and A/S Dumex, Copenhagen, for supplying the doxycycline and tetracycline.

#### REFERENCES

1. Lassus, A. & Renkonen, O.-V.: Short-term treatment of gonorrhoea with intramuscular and oral forms of sulphamethoxazole-trimethoprim. *Br J Vener Dis* 55: 24, 1979.
2. Paavonen, J., Kousa, M., Saikku, P. A., Vartiainen, E., Kanerva, L. & Lassus, A.: Treatment of nongonococcal urethritis with trimethoprim-sulphadiazine and placebo. *Br J Vener Dis* 56: 101, 1980.
3. Thambar, I. V., Simmons, P. D., Thin, R. N., Darrouger, S. & Yearsley, P.: Double-blind comparison of two regimens in the treatment of nongonococcal urethritis. Seven-day vs 21-day courses of triple tetracycline (Deteclo). *Br J Vener Dis* 55: 284, 1979.