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ROLITETRACYCLINE BY INJECTION AND TETRACYCLINE PHOSPHATE COMPLEX BY MOUTH GIVEN IN A SINGLE SESSION IN THE TREATMENT OF GONORRHOEA IN MALES

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Abstract. Forty-eight male patients with uncomplicated acute gonorrhoea have been treated with single intramuscular injections of 350 mg of rolitetracycline plus 500 mg of tetracycline phosphate complex by mouth at one session. Of 45 patients followed there were 7 failures, as judged by a history of no further sexual exposure, within three post-treatment months (15.6% of those followed). Three patients (6.6% of those followed) developed Reiter's syndrome within two weeks of treatment. While this may not be significant in view of the size of the series its occurrence or non-occurrence is worthy of noting by other workers who use these drugs. The results obtained in this series are contrasted with those of 18 other personally conducted series using single-session methods. Although somewhat less good than those obtained with penicillin by injection they are in line with those obtained with single oral doses of other tetracyclines or of ampicillin.

With signs of increasing resistance of the gonococcus to penicillin in a number of world areas, and a consequent significant narrowing between the minimum effective dose and the maximum injectable dose of procaine penicillin possible at a single session, and with additional problems posed by the not inconsiderable numbers of patients with a history of penicillin allergy for whom other antibiotics are necessary, there is a continuing need for the investigation of alternative drugs capable of use by single session methods.

The present paper concerns the use of injectable and oral tetracyclines in combination. The injectable tetracycline employed was pyrrolidino methyl tetracycline nitrate (Tetrex PMT)—or rolitetracycline—and the oral preparation, the tetracycline phosphate compleh ("Tetrex").

CASE MATERIAL

The average age of the 48 patients was 25.4 years (extremes 19–41): 16 were married and 32 were single. Six of the patients were West Indian Negroes and of the remainder 31 were born in the United Kingdom, 6 in Pakistan and one each in Cyprus, France, Germany, Italy and Spain.

No previous venereal incident had been experienced by 24 patients but the remainder had had 27 previous attacks of gonorrhoea, 8 of non-gonococcal urethritis and one each of balanitis, herpes genitalis and pediculosis pubis—a total of 38 previous incidents. The six West Indian patients accounted for 5 of these, all of gonorrhoea.

The disease had been present before treatment for 1–3 days in 23 cases, for 4–7 days in 19 and for 8–14 days in 6: all but five patients complained of some dysuria. The apparent incubation period was 1–3 days in 15, 4–7 days in 13, 8–14 days in 11, 15–21 days in 2 and longer than this time in 2: in 5 cases it was unknown. The disease was acquired from a stranger in 25 cases, from a friend in 17, from the wife in 4 and from a male in one, while one patient denied having had sexual intercourse during the previous three months.

The routine Wassermann and VDRL reactions were negative in all cases and the gonococcal complement-fixation test was positive in three and negative in 45.

CASE MANAGEMENT

Diagnosis was established by means of Gram-stained urethral smear in all cases prior to treatment when blood for routine serum tests for syphilis was also taken. The patients were given an intramuscular injection of 350 mg of pyrrolidinomethyl tetracycline nitrate (rolitetracycline —"Tetres PMT") in 2 ml of distilled water plus 500 mg of "Tetrex" tetracycline phosphate complex in one or two capsules in one session by mouth. The patients were subsequently seen 2–5 days later when a further post-treatment smear was made after which they were instructed to attend a week later. It was planned that they should be seen subsequently at two, four, eight and

Table I. *Follow-up and results*

Follow-up	Followed	Satis.	Non-gonococcal urethritis	Reiter's syndrome	Reinfection	Failure
0	48	—	—	—	—	—
1–3 days	45	2	—	1	—	1
4–7 days	41	3	2	1	2	3
8–14 days	32	5	—	1	—	2
15–21 days	22	1	1	—	—	—
22–28 days	20	—	1	—	—	—
1–2 months	19	4	2	—	2	—
2–3 months	13	3	—	—	—	1
More than 3 months	7	5	1	—	1	—
Total	45	23	7	3	5	7

twelve weeks from treatment when the urethra was examined for discharge, a smear being taken if present, and the urine inspected for haze and threads. It was intended also that at least one examination of the prostatic secretion be made during surveillance and a final serum test for syphilis be performed at three months.

Sufficient time has elapsed before writing this report to allow all patients to have been watched for three months but by no means all patients, however, attended at the times instructed.

SIDE EFFECTS

Some patients complained of slight pain for some hours after injection; in one case it was very severe during the first hour and subsequently lasted for two days, but by and large the injection was well tolerated and few patients complained of pain unless specifically asked. No other side effects were noted.

FOLLOW-UP AND RESULTS

The follow-up and results obtained are shown in Table I.

Of 48 patients treated 45 were followed. Of these, six were given additional treatment for non-gonococcal urethritis, within three post-treatment months as were three others who developed Reiter's syndrome. There were also four reinfections within this time and seven treatment failures as judged by a history of no further sexual exposure (15.6 % of those followed).

No adequate criteria exist to distinguish relapse from reinfection apart from a history or absence of same of further sexual exposure. However, if all recurrences regardless of history occurring within one week are regarded as failures, as has been recommended by some authors [e.g. Curtis & Wilkinson (2)], the failure rate would be 13.3 % and if two weeks was chosen the figure of 17.8 % would be obtained.

Of possible interest is that three cases of Reiter's syndrome developed within 2–14 days of treatment, all of whom had a non-gonococcal urethral discharge at the time. One patient subsequently admitted having previously received treatment for iritis and spondylitis on the occasion of an earlier infection but the other two had had no earlier rheumatic disorder. Tetracyclines in higher dosages and other drugs were then given to these patients. In two cases the disease ran a protracted course, admission to hospital being required in one, but ultimately a good recovery was obtained in all. That three patients of the 45 followed (6.6 %) should develop Reiter's syndrome may not be significant in regard to the size of the series but, as its anticipated occurrence in patients treated for gonorrhoea would be 1 % or less, its occurrence or otherwise in other series treated in this way should be noted.

COMPARISON WITH OTHER SINGLE-SESSION METHODS

A comparison is made in Table II of the personal results obtained with other antibiotics using single-session methods.

While the findings of the present series are apparently somewhat less good than those ob-

Table II. *Results compared with other single session procedures*

Antibiotic	Dose	How given	Treated	Followed	Fail	% fail
Penicillins						
Procaine penicillin[a]	2.4 mega units	Injected	280	240	14	5.8
Procaine penicillin[a] (1966–1967)	1.2 mega units	Injected	238	200	17	8.5
Procaine penicillin[b] (1964)	1.2 mega units	Injected	279	207	23	11.1
Ampicillin[b]	0.5–1.0 g	By mouth	200	174	26	14.9
Tetracyclines						
Oxytetracycline[c]	500 mg	Injected	15	14	1	7.1
Tetracycline phosphate[c]	500 mg	Injected	31	23	4	17.4
Tetracycline phosphate[c]	250 mg	Injected	8	7	2	28.0
Oxytetracycline[c]	250 mg	Injected	19	17	5	29.4
Pyrrolidine methyl tetracycline[c]	250 mg	Injected	14	11	4	36.4
Demethylchlor-tetracycline[d]	1.2 g	By mouth	52	46	6	13.0
Limecycline[e]	1.22 g	By mouth	50	43	8	18.6
Demethylchlor-tetracycline[d]	0.9 g	By mouth	33	30	6	20.0
Limecycline[e]	0.816 g	By mouth	25	23	5	21.7
Other antibiotics						
Spiramycin[f]	3–4 g	By mouth	30	25	—	—
Spectinomycin[g]	1.6 g	Injected	151	134	23	9.7
Rifampicin[h]	0.9 g	By mouth	103	84	10	11.9
Spiramycin[f]	2.0 g	By mouth	24	22	6	27.2
Streptomycin[i]	1.0 g	Injected	130	104	33	31.7
This series	See text	By mouth and injection	48	45	7	15.6

[a] Morrison et al. (3). [b] Willcox (7). [c] Willcox (10). [d] Willcox (9). [e] Willcox (8). [f] Willcox (5). [g] Willcox (6). [h] Cobbold et al. (1). [i] Spitzer & Willcox (4).

tained with penicillin by injection, and with those of some other antibiotics, they are in line with previous experience of oral tetracyclines given in a single dose and also of ampicillin administered in this way.

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