

# Doxycycline HCl (Vibramycin) as a single dose oral treatment of gonorrhoea in women

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While penicillin remains the drug of choice in the treatment of gonorrhoea, the increasing incidence of strains of gonococci less sensitive to penicillin makes the continued search for other effective antibiotics of the greatest importance. Ideally, all treatments should be able to be given at one attendance, whether by injection or orally. Doxycycline hydrochloride (Vibramycin) in a single oral dose was shown to be effective in the treatment of uncomplicated gonorrhoea in the male (Sylvestre and Gallai, 1968; Domescik, McLone, Scotti, and Mackey, 1969). We report here on our experiences with the same drug using a single oral dose regime in the treatment of acute gonorrhoea in the female.

### Material and methods

After diagnosis by means of Gram-stained smears taken from the urethra and cervix, 115 women suffering from uncomplicated gonococcal urethritis and/or cervicitis were treated with a single oral dose of 300 mg. (3 capsules) of doxycycline taken with a glass of milk. Excluded from the investigation were pregnant women, those with complicated infections, and those in transit.

23 per cent. of our patients were teenagers, 34 per cent. between 20 and 24 years of age, 36 per cent. in the 25 to 34 age group, and 7 per cent. aged 35 years or over. 45 per cent. were married, 44 per cent. single, and 11 per cent. separated or divorced. The nominated sources of infection were marital, 32 per cent.; regular consort, 20 per cent.; casual, 48 per cent.

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After treatment on Day 1, the patients reattended for post-treatment assessment, including urethral and cervical smears and cultures, on Days 2, 4 or 5, 8, 15, 22, and 29.

The diagnosis was confirmed by culture, and a full antibiogram was obtained for each strain. Sensitivity to penicillin G was assessed by the tube-dilution method. Resistance or sensitivity to streptomycin, kanamycin, sulphafurazole, erythromycin, and doxycycline was tested by the disc method (Oxoid multo disc). Positive cultures found during surveillance were subjected to the same tests as those used for diagnosis.

### Results

Approximately 14 per cent. of the strains were relatively resistant to penicillin—strains requiring a minimum inhibitory concentration of penicillin of 0.1 µg./ml. or more being regarded as relatively resistant.

Sixteen strains were resistant to streptomycin and four to sulphafurazole, and one was slightly resistant to doxycycline. The particular patient harbouring the last strain was, however, cured by doxycycline (Table I).

The results of treatment are set out in Table II (opposite).

Twelve patients did not return after their initial treatment, and of the 103 who did, eleven had post-treatment gonorrhoea; six of these cases were considered to be treatment failures and five to be re-infections, giving a failure rate of six out of 103 cases (5.8 per cent.). The full surveillance period of 4 weeks was completed by 74 patients.

TABLE I *Initial sensitivities of the infecting organisms*

Minimum inhibitory concentration of penicillin G (µg./ml.)	No. of strains	Resistance to		
		Streptomycin	Sulphonamides	Doxycycline
0.03	82			
0.06	17	3	1	
0.12	3	3		
0.15	8	5	3	
0.3	3	3		1
0.6	2	2		
Total	115	16	4	1

**Discussion**

As with all therapeutic trials, default complicated the accurate assessment of success or failure. Hewitt (1969) suggested a formula to calculate possible failure rates among defaulters, but did not stipulate at which point during surveillance, whether immediately following treatment or after a certain period of time. In this series the last treatment failure was diagnosed on Day 4, well within the 2-week period within which failures appear according to Putkonen and Rouhunkoski (1951).

At 2 weeks, 82 cases were satisfactory, six had been withdrawn as failures, and three were considered to be re-infections; 91 in all. Two more patients were re-infected by the end of the third week.

Differentiation between failure and re-infection is always difficult (Table III) and will remain so until typing of the various strains of *N. gonorrhoeae* becomes a more practical and standardized procedure. We regarded admission of re-exposure, either as a 'ping-pong' infection from a regular consort or from a different untreated consort, together with marked changes in the antibiogram as suggestive of re-infection. In our cases, a 5- or 10-fold alteration in the penicillin sensitivities was involved (Table III). In all our treatment failures, positive cultures were

found at the first post-treatment examination: in those patients thought to be re-infected all the immediate post-therapy cultures were negative—only to become positive at a later visit.

Of the six treatment failures, two developed complicated infections; one had salpingitis and the other Bartholinitis. A further two patients had vomited within 10 minutes of taking the capsules, and their smears and cultures remained positive the next day.

The side-effects of doxycycline were minimal and confined to nausea and vomiting. Four patients were nauseated and four others vomited, but all were cured except the two women who vomited within 10 minutes of taking their capsules. In our experience, if vomiting is delayed for only half an hour, enough of the drug will have been absorbed to effect a cure. Vomiting can usually be prevented if the capsules are taken with a drink of milk; 50 ml. fresh milk being preferable to the reconstituted variety.

Vaginal candidosis was not a problem as it appeared in only two patients after treatment with doxycycline, nor does the drug in a single dose of 300 mg. appear to suppress *T. pallidum*. One of us (C.B.S.S.) gave this dose to a patient suffering from secondary syphilis.

TABLE II *Results of treatment*

Day	No. on surveillance	Last attendance	Reason for withdrawal from trial		Treatment failure
			Default	Re-infection	
1	115	12	12		
2	103	3			3
4/5	100	11	7	1	3
8	89	5	5		
15	84	5	3	2	
22	79	5	3	2	
29	74	74			
Total		115	30	5	6

TABLE III *Post-treatment gonorrhoea*

Marital status	Age (yrs)	Promiscuous	Antibiogram		Re-exposure	Day of surveillance	Classification
			Initial	Post-treatment			
Sep. <sup>a</sup>	34	Yes	0.12	0.12	No	4	Treatment failure
M <sup>b</sup>	26	No	0.03	0.12	No	2	
M <sup>c</sup>	25	No	0.03	0.03	No	2	
S <sup>c</sup>	18	Yes	0.3*	0.15	No	2	
M	35	No	0.03	0.03	No	4	
S	19	Yes	0.03	0.03	No	4	Re-infection
S	24	Yes	0.03	0.3*	Yes	22	
M	22	No	0.06	0.3*	Yes	15	
S	38	Yes	0.03	0.15*	Yes	15	
M	29	No	0.03	0.15	Yes	5	
Div.	23	Yes	0.15	0.03	Yes	22	

<sup>a</sup>Developed salpingitis after treatment  
<sup>c</sup>Bartholinitis apparent on Day 2

<sup>b</sup>Vomited within 10 minutes of taking capsules  
 \*Resistant to streptomycin

An unemployed man, aged 61 years, attended about 3 months after infection. He had a generalized papular syphilide with inguinal adenitis and perianal moist papules, serum from which revealed *T. pallidum* on darkground examination.

Serological tests gave the following results: VDRL positive 1/128; CWR positive; RPCFT positive.

The patient agreed to take the three capsules of Vibramycin so that we could assess if they had any effect on his syphilis, although he knew they were not expected to cure him. He was admitted to our ward and barrier nursed. Further darkground examination of serum from the moist papules revealed *T. pallidum* after 24 and 48 hours, the rash being unchanged throughout. After the second examination treatment was started with procaine penicillin, 1 million units daily for 10 days, and this was followed by rash fading and the moist papules drying within a week.

The main advantage of doxycycline is that it is curative for gonorrhoea in women in a single oral dose. Administration is easy and painless and so far no allergic effects have been reported. It is the logical choice of treatment for patients who are afraid of injections.

### Summary

115 female patients suffering from uncomplicated gonorrhoea, confirmed by culture, were treated with 300 mg. doxycycline (3 capsules of Vibramycin). The failure rate was 5.8 per cent., six of 103 cases followed-up.

The only side-effect was occasional nausea and vomiting, and it was found that this could usually be suppressed by giving the capsules with a drink of milk. Post-treatment vaginal candidosis was not a problem. A 300 mg. dose of the drug had no effect on *T. pallidum* in one case of secondary syphilis.

Doxycycline has the advantage over other oral preparations in that it is given in one dose which can easily be supervised. We believe that it has a definite place in the treatment of gonorrhoea in women, particularly in patients who are 'needle-shy'.

### References

- DOMESCIK, G., McLONE, D. G., SCOTTI, A., and MACKEY, D. M. (1969) *Publ. Hlth Rep. (Wash.)*, **84**, 182  
 HEWITT, A. B. (1969) *Brit. J. vener. Dis.*, **45**, 40  
 PUTKONEN, T., and ROUHUNKOSKI, S. (1951) *Acta derm.-venereol. (Stockh.)*, **31**, 391  
 SYLVESTRE, L., and GALLAI, Z. (1968) *Un. méd. Canad.*, **97**, 639

### La doxycycline HCl (Vibramycine) employée en une seule dose dans la gonococcie de la femme

#### SOMMAIRE

115 femmes atteintes de gonococcie non compliquée confirmée par culture furent traitées par 300 mg. de doxycycline HCl (3 capsules de Vibramycine). Le taux d'échec fut de 5,8%, soit 6 des 103 cas suivis. Le seul effet secondaire fut l'existence de nausées et de vomissements; l'on constata que ceci pouvait être empêché en faisant prendre les capsules avec un verre de lait. L'apparition de candidase vaginale post-thérapeutique ne constitua pas un problème. Une dose de 300 mg. du produit n'eut pas d'effet sur *T. pallidum* dans un cas de syphilis secondaire. L'avantage de la doxycycline sur les autres préparations buccales réside dans le fait qu'elle peut être donnée en une dose unique dont on peut facilement contrôler la prise. Les auteurs croient que cette technique a une place indiscutable dans le traitement de la gonococcie féminine, en particulier chez les malades qui 'craignent l'aiguille'.