

# TROBICIN (ACTINOSPECTACIN) A NEW INJECTABLE ANTIBIOTIC IN THE TREATMENT OF GONORRHOEA\*

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Numerous workers in many countries (Willcox, 1961) have reported increasing failure rates in the treatment of gonorrhoea both with penicillin and with streptomycin (Alergant, 1958). Evidence is accumulating of an increased number of strains of gonococci which are less sensitive to these antibiotics than formerly (Cradock-Watson, Shooter, and Nicol, 1958; Curtis and Wilkinson, 1958). Although "resistance" to penicillin is only relative—and failures will still respond if sufficient penicillin is given—that to streptomycin is virtually absolute (Durel, 1961; Reyn, 1961).

In addition, sensitivity reactions to penicillin have become a world-wide problem in recent years (Idsøe, Guthe, and Willcox, 1958). The most effective available method of avoiding such reactions is to refrain from giving penicillin (or streptomycin) to persons known to have had previous sensitivity reactions to these antibiotics, or to persons with a history of allergy, especially of asthma.

These hindrances have emphasized the need of an effective alternative drug to penicillin for the treatment of gonorrhoea. The disease *can* be cured by a number of antibiotics given orally, including the tetracyclines, chloramphenicol, erythromycin, spiramycin, and penicillin—but these drugs are not only considerably more costly but nearly all usually require repeated dosing. Orally administered drugs are inherently unsatisfactory for the treatment of venereal diseases as patients frequently do not take them as instructed. Moreover when the urethral or vaginal discharge has apparently subsided, they may keep the unconsumed tablets for self-medication on a future occasion (with all that this implies), and a "black market" in the tablets may be created by unscrupulous persons.

Of the drugs other than penicillin which may be given by injection, chloramphenicol is out of favour

on account of haemopoietic side-effects and Kanamycin requires a number of injections to achieve success and is also, like streptomycin, ototoxic. The injectable tetracycline preparations so far tried are not sufficiently effective in curing gonorrhoea by a single injection in doses which can be tolerated locally.

The present paper concerns a new antibiotic Trobicin (Actinospectacin) prepared from *Streptomyces spectabilis*. It is stated to have a wide antibacterial spectrum and to be as active against the gonococcus as chloramphenicol. It is well tolerated and a single intramuscular injection is capable of curing gonorrhoea even in cases in which failure has been noted with other antibiotics.

## Case Material

101 male patients with acute uncomplicated gonorrhoea were treated with a single intramuscular injection of 1.4–1.6 g. Actinospectacin (Trobicin).

47 of them were Negroes (44 from the West Indies and three from West Africa), and of the remainder 28 were from the United Kingdom, eight from Eire, four from Cyprus, four from Italy, two from France, and one each from Austria, Canada, Germany, Iraq, New Zealand, Spain, Switzerland, and Yugoslavia. Their average age was 26.9 yrs (range 16 to 60). 23 were married and 78 were single.

45 patients (including 20 Negroes) had had no previous venereal incident. The remainder had had 98 previous attacks of gonorrhoea, twelve of non-gonococcal urethritis, one of syphilis, one of penile boil, one of balanitis, one of condylomata acuminata, one of pediculosis pubis, and three of venerophobia—a total of 118 previous incidents. 65 of these (63 of gonorrhoea and two of non-gonococcal urethritis) had been contracted by the 47 Negroes, making an average of 1.4 previous attacks for this group compared with an average of one previous attack for the remainder.

The duration of the discharge before treatment was 1 to 3 days in 74 patients, 4 to 7 days in seventeen, 8 to 14

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days in seven, and 15 to 21 days in two; one patient had had his discharge, apparently without much inconvenience, for 6 weeks. All but thirteen patients had noted some dysuria.

The disease had apparently been caught from a stranger in 55 instances, from a friend in 38, from a male in four, and from the wife in two, while two persons denied exposure to risk. In one instance the disease had been contracted in the West Indies and had been imported into Britain by air.

The apparent incubation period was 1 to 3 days in 48 cases, 4 to 7 days in 28, 8 to 14 days in sixteen, 15 to 21 days in three, 22 to 28 days in one, and more than 4 weeks in two; in three cases it was unknown.

In all cases gonococci were found by urethral smear before treatment. The routine Wassermann reaction and V.D.R.L. (or Kahn) test were both negative before treatment in 92 cases, the Wassermann reaction negative and the V.D.R.L. test positive in three, and both tests reactive in six. All but one of the reactive sera were found in West Indian patients, doubtless because of a past yaws infection in some instances. The gonococcal complement-fixation test was negative in all but two of 37 patients tested, one of the two reactive sera being from a West Indian patient.

#### Case Management

The first 44 patients were given single injections of 1.4 g. and the remainder had 1.6 g. With the first batch the powder, which was dissolved in 10 ml. distilled water (a special diluent being used for the first thirteen doses), was divided between the two buttocks. Latterly a single injection was used.

The patients were instructed to attend again after 2 to 3 days and subsequently at 1, 2, 4, 8, and 12 weeks from treatment. At each visit the urethra was examined for discharge (a smear being taken if present) and the urine was inspected for haze and threads. It was planned to examine the prostatic secretion for pus on two occasions during surveillance and to perform final serum tests for syphilis at 3 months.

Not all patients attended at the times requested but sufficient time has elapsed for all of them to be observed for at least one month after treatment.

#### Results

Of 101 patients treated, 89 were followed and the status at the last visit was satisfactory in 56 (Table I). Eleven patients had a subsequent infection with non-gonococcal urethritis, fifteen were re-infected with gonorrhoea, and there were seven failures (7.9 per cent). No satisfactory criteria exist to distinguish relapse from re-infection apart from a history of further sexual exposure; it is noteworthy that all

but one of the fifteen suspected re-infections were noted 15 days or longer after therapy.

TABLE I  
RESULTS OF TREATING 101 CASES OF ACUTE UNCOMPLICATED GONORRHOEA WITH TROBICIN (ACTINOSPECTACIN)

Follow-up	No. Followed	Result				
		Satisfactory	NGU Infection	Re-infection	Failure	
0	101	—	—	—	—	
1-3 days	89	11	2	—	1	
4-7 days	75	18	—	1	1	
8-14 days	55	11	3	—	3	
15-21 days	38	3	—	3	1	
22-28 days	31	2	1	1	1	
1-2 mths	26	8	4	5	—	
2-3 mths	9	2	—	1	—	
Over 3 mths	6	1	1	4	—	
Totals	No. 89	56	11	15	7	
	Per cent.	100.0	62.9	12.4	16.7	7.9

The results obtained in the white and Negro patients are contrasted in Table II, which shows that the failure rates in this series were higher in the Negroes, who also had an appreciably greater number of previous infections. It is likely, therefore, that some of the so-called failures in this group were in fact re-infections. In the 54 white patients treated, the failure rate in those followed was only 4.3 per cent.

TABLE II  
RESULTS IN WHITE AND NEGRO PATIENTS

Race	No. Treated	No. Followed	Results				Per cent. Failing of Those Followed
			Satisfactory	NGU Infection	Re-infection	Failure	
Negroes	47	42	29	2	6	5	11.9
Others	54	47	27	9	9	2	4.3
Totals	101	89	56	11	15	7	7.9

#### Results following Failure with Other Antibiotics

In two of the cases treated there had been previous repeated failures with other antibiotics.

In one case, failure had occurred after two single injections of 1.2 mega units aqueous procaine penicillin, 2.4 mega units procaine penicillin with aluminium monostearate, and 1 g. streptomycin sulphate. Tetracycline tablets (1 g. daily) had also been prescribed for this man but were apparently not taken.

In the other case, failure occurred after single

injections of 900,000 and 1·2 mega units of aqueous procaine penicillin, and again after 4 g. tetracycline spread over 4 days.

In both cases the response to Trobicin was immediate and there was no further relapse.

One of the other patients in this series was known to be sensitive to penicillin, having had a marked urticaria on an earlier occasion. No adverse reactions were noted in this patient following Trobicin.

**Comparison with Penicillin.**—Table III compares the results obtained with single injections of 1·2 mega units aqueous procaine penicillin G in other patients treated during the same period, and demonstrates that Trobicin given in single intramuscular injections compares well with penicillin for the treatment of acute gonorrhoea in the male.

TABLE III  
COMPARISON OF RESULTS OBTAINED WITH TROBICIN AND WITH PENICILLIN

Antibiotic	Dose	No. Treated	No. Followed	Failures	Per cent. Failing of Those Followed
Trobicin ..	1·4-1·6 g.	101	89	7	7·9
Procaine penicillin	1·2 mega units	200	169	10	5·9

**Tolerance.**—No systemic side-effects were noted with the dosage given and no complaints of local pain were noted irrespective of whether one or two buttocks were injected, indicating that Trobicin compares favourably in this respect with the other injectable antibiotics—penicillin and streptomycin.

#### Summary and Conclusions

- (1) In view of the emergence of increasing numbers of strains of gonococci less sensitive to penicillin and completely resistant to streptomycin, and of the fact that some persons are allergic to these antibiotics, there is an increasing need for alternative drugs in the treatment of gonorrhoea.
- (2) Although the tetracycline antibiotics are effective in appropriate dosage by mouth, injectable tetracycline preparations have not achieved the necessary local tolerance which would make them satisfactory in single injections. There is a need, therefore, for an effective and well-tolerated preparation which can be given by a single intramuscular injection.
- (3) A new antibiotic Trobicin (Actinospectacin), prepared from *Streptomyces spectabilis*,

offers considerable promise in this direction.

- (4) 101 male patients with acute gonorrhoea were given single intramuscular injections of 1·4 to 1·6 g. Trobicin. In 89 followed, there were seven failures (7·9 per cent.). If Negro patients were excluded, the failure rate was only 4·3 per cent. These results compare well with those obtained with single injections of 1·2 mega units aqueous procaine penicillin.
- (5) Two of the successfully-treated patients had previously received repeated injections of penicillin and streptomycin and/or tetracycline by mouth. Another patient was known to be allergic to penicillin.
- (6) Trobicin was well tolerated in the doses given and no adverse side-effects, local or general, were reported.
- (7) It is considered that a single injection of Trobicin offers a suitable alternative to penicillin or streptomycin in the treatment of gonorrhoea. It is especially indicated in patients who fail to respond to those antibiotics, or who are allergic to them.

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#### Trobicine (Actinospectacine) — Un nouvel antibiotique intramusculaire contre la blennorrhagie

##### RÉSUMÉ

(1) Puisque les souches gonococciques moins sensibles à la pénicilline et tout à fait résistantes à la streptomycine deviennent toujours plus nombreuses, et puisque quelques malades montrent une hypersensibilité à ces antibiotiques, on a grand besoin d'autres médicaments contre la blennorrhagie.

(2) Les tétracyclines sont efficaces par voie buccale, mais elles provoquent une réaction topique qui empêche leur emploi intramusculaire. On cherche alors un médicament qui sera efficace et bien toléré en une seule dose parentérale.

(3) Un antibiotique nouveau, la Trobicine (Actinospectacine), préparée à partir de l'organisme *Streptomyces spectabilis*, semble donner la réponse à ce problème.

(4) 101 mâles atteints de blennorragie aigüe ont reçu une seule injection intramusculaire de 1,4 à 1,6 g. de Trobicine; 89 cas furent suivis et on constata 7 (7,9%) échecs. Les malades nègres à part, il n'y eut que 4 échecs.

Ce résultat est à peu près égal à celui obtenu avec une seule injection de 1,2 unités de la pénicilline procaine aqueuse.

(5) Deux des malades guéris avaient reçu auparavant

plusieurs injections de pénicilline, et de streptomycine ou de la tétracycline par voie buccale sans amélioration. Un autre malade était connu comme hypersensible à la pénicilline.

(6) La Trobicine fut bien tolérée dans la dose employée, et on n'a pas vu de réaction inattendue, topique ou générale.

(7) On conclut que les injections uniques de Trobicine peuvent remplacer la pénicilline et la streptomycine comme remède spécifique contre la blennorragie, plutôt chez les sujets qui ne répondent pas aux autres antibiotiques et ceux qui y sont hypersensibles.