TROBCIN (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 (Alergent, 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 treat-
ment of gonorrhoea. The disease can be cured by a
number of antibiotics given orally, including the
tetracyclines, chloramphenicol, erythromycin, spiram-
cyn, 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 Kan-
mycin 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
Trobcin (Actinospectacin) prepared from Strep-
tomyces 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 gonor-
rhoea were treated with a single intramuscular injection of 1.4-1.6 g. Actinospectacin (Trobcin).
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 Spain, 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 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 pedi-
culosis 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
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 nongonococcal 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>
<thead>
<tr>
<th>Follow-up</th>
<th>No. Followed</th>
<th>Satisfactory</th>
<th>NGU Infection</th>
<th>Re-infection</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>101</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1-3 days</td>
<td>89</td>
<td>11</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4-7 days</td>
<td>75</td>
<td>18</td>
<td>-</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>8-14 days</td>
<td>55</td>
<td>11</td>
<td>3</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>15-21 days</td>
<td>38</td>
<td>3</td>
<td>-</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>22-28 days</td>
<td>31</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1-2 mths</td>
<td>26</td>
<td>8</td>
<td>4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2-3 mths</td>
<td>9</td>
<td>2</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Over 3 mths</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Totals</td>
<td>89</td>
<td>56</td>
<td>11</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>Per cent.</td>
<td>100.0</td>
<td>62.9</td>
<td>12.4</td>
<td>16.7</td>
<td>7.9</td>
</tr>
</tbody>
</table>

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 Negros, 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>
<thead>
<tr>
<th>Race</th>
<th>No. Treated</th>
<th>No. Followed</th>
<th>Satisfactory</th>
<th>NGU Infection</th>
<th>Re-infection</th>
<th>Failure</th>
<th>Percent. Failing of Those Followed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negroes</td>
<td>47</td>
<td>42</td>
<td>29</td>
<td>6</td>
<td>5</td>
<td>11.9</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>54</td>
<td>47</td>
<td>27</td>
<td>9</td>
<td>9</td>
<td>2</td>
<td>4.3</td>
</tr>
<tr>
<td>Totals</td>
<td>101</td>
<td>89</td>
<td>56</td>
<td>11</td>
<td>15</td>
<td>7</td>
<td>7.9</td>
</tr>
</tbody>
</table>

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>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose</th>
<th>No. Treated</th>
<th>No. Followed</th>
<th>Failures</th>
<th>Per cent. Falling of Those Followed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trobicin</td>
<td>1·4-1·6 g.</td>
<td>101</td>
<td>89</td>
<td>7</td>
<td>7·9</td>
</tr>
<tr>
<td>Procaine penicillin</td>
<td>1·2 mega units</td>
<td>200</td>
<td>169</td>
<td>10</td>
<td>5·9</td>
</tr>
</tbody>
</table>

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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REFERENCES


Trobicin (Actinospectacin) — Un nouvel antibiotique intramusculaire contre la blennorrhagie

RÉSUMÉ

(1) Puisque les souches gonococques moins sensibles à la pénicilline et tout à fait résistantes à la streptomycine deviennent toujours plus nombreuses, et puisque quelques malades montrent une hypertolérance 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 topical 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 blennorrhagie 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 tétacycline 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 blennorrhagie, plutôt chez les sujets qui ne répondent pas aux autres antibiotiques et ceux qui y sont hypersensibles.