Spectinomycin in the treatment of gonorrhoea in males

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The sulphate salt
Spectinomycin (Trobicin; actinospectacin), an antibiotic prepared from Streptomyces spectabilis, was first used in the treatment of gonorrhoea a decade or so ago in the form of the sulphate salt. At this time cure rates of 87 to 95 per cent. were obtained using single intramuscular injections of 2 g. in males (Willcox, 1962, 1963a; Laird and Taylor, 1962; Clarke, 1964; Beekman, 1965; Tiedemann, Hackney, and Price, 1965) while good results were also reported in the female, e.g. 23 of 25 cured by Sparling, Yobs, Billings, and Hackney (1965), with single injections of 3 g.

The antibiotic was found to be ineffective in non-gonococcal urethritis (Willcox, 1963b). As with streptomycin, the doses given in gonorrhoea were mildly active against syphilis, both in the clinical (Willcox, 1962) and in the experimental infection (Clark, Yobs, and Post, 1963, 1964). The latter workers considered its possible ‘masking’ qualities, although they were able to cure rabbit syphilis using larger doses.

The dihydrochloride salt
More recently a new salt, the dihydrochloride, has been prepared and a single 2 g. dose has been reported to give highly satisfactory results in males with 90 to 100 per cent. of success as judged by the failure to recover gonococci after treatment, e.g. by Cornelius and Domescik (1970); Labowitz, Porter, and Holloway (1970); Platts (1970); Duncan, Holder, Roberts, and Knox (1972); Pedersen, Wiesner, Holmes, Johnson, and Turck (1972); Schroeter and Lucas (1972); Reyn, Schmidt, Trier, and Bentzon (1973); Stratigos, Marsellou-Kinti, Kassimatis, and Daikos (1973).

Similar or only slightly less success has been obtained by means of a single 4 g. dose in females by Platts (1970), Labowitz and others (1970), Pedersen and others (1972), and Schroeter and Lucas (1972), and the same dose proved effective in twelve of fourteen cases of rectal gonorrhoea according to Holder, Roberts, Duncan, and Knox (1972).

High maximum, average, and minimum serum levels, well above the MIC of nearly all strains of the organism, are obtained with these doses during the first 6 hours after injection (Savage, 1973). The new preparation has also proved to be extremely well tolerated and the availability of a non-toxic injectable drug able to be given to persons suspected of being allergic to penicillin is in itself extremely useful now that streptomycin has become vitally useless (Willcox, 1973). Its use has indeed already been recommended in the United States for this purpose (Savage, 1973).

Resistance patterns
Of more importance is the question of gonococcal resistance. A correlation has been noted between penicillin-resistance and spectinomycin-resistance (Pedersen and others, 1972; Reyn and others, 1973) and in a patient failing to respond to spectinomycin the organism obtained after treatment showed a high degree of resistance to the antibiotic (Reyn and others, 1973). Laird and Taylor (1962) reported unsatisfactory results using low doses of the earlier sulphate preparation. They had two examples of increased spectinomycin resistance after treatment and indeed this may likewise be induced in vitro in the laboratory (Savage, 1973). However, this was not the experience of either Duncan and others (1972) or Pedersen and others (1972) after the use of satisfactory doses of the newer salt.

There are also geographical patterns of resistance of the gonococcus to antibiotics. Reyn and others (1973) found that gonococcal strains from Odense were more sensitive to spectinomycin than those from the whole of Denmark which included a large number from the capital, Copenhagen. Certainly, with
ampicillin cure rates after a single dose of 2 g. plus
probenecid were appreciably better when ad-
ministered in Wales than in London and its environs
(Cobbald, Rees, Parker, Woodcock, John, Latto,

Now that the dihydrochloride salt of spectino-
mycin is available, and because resistance patterns
also may change with time, it was considered worth-
while to reassess the effectiveness of the antibiotic
in acute gonorrhoea in males in London and to
compare the results with those obtained in patients
examined and treated under like conditions a decade
or so previously.

Case management

Diagnosis was made routinely by Gram-stained urethral
smear in all cases before treatment when Wassermann
and VDRL serum tests for syphilis were also performed.
Both of these proved negative in all patients apart from
one West Indian in whom a weakly positive VDRL was
obtained with a negative Wassermann reaction.

All patients received a single intramuscular injection of
spectinomycin dihydrochloride pentahydrate, the 2 g.
powder being dissolved in the 3·2 ml. bacteriostatic water
containing 9 mg./ml. benzyl alcohol provided. After
treatment the patients were instructed to return after 3 to
4 days, when the urethra was examined for discharge
and the urine for haze and threads. Urethral smears and
cultures for the gonococcus on Thayer-Martin medium
were also made after treatment in 68 per cent. of those
followed and in no case was a positive culture obtained
with a negative smear. Re-treatment because of pus cells
in the urethra was discouraged at the first follow-up
visit.

Subsequently the patients were instructed to attend
again approximately 1, 3, 7, and 12 weeks later, when
the urethra was again examined for discharge (a smear
and culture being made if discharge was present) and
the urine for haze and threads; a final serum test for
syphilis was made at the last visit.

Follow-up and results

By no means all patients attended at the times
requested but sufficient time has elapsed for all to
have been able to attend for at least 3 months. The
follow-up and results so far obtained are shown in
Table I (overleaf).

Thus, of 100 patients treated, 83 were followed.
The status of 55 was satisfactory at the last visit,
twelve were treated for a non-gonococcal infection
and, judging by the presence or absence of a history
of further sexual exposure, there were nine re-
infections and seven (8·4 per cent.) suspected treat-
ment failures.

There are no satisfactory criteria to distinguish
relapse from re-infection. Curtis and Wilkinson
(1958), basing their findings on the sensitivity
patterns of the gonococcus to penicillin before and
after treatment, considered that, if all recurrences
within 1 week regardless of history were assumed to be
failures and those after this time re-infections, such a
classification would probably not be wide of the mark.
The present author has regarded 2 weeks as more
realistic. If 2 weeks is taken in the present series, the
failure rate is the same (8·4 per cent.).

One of the treatment failures was re-treated with
2·4 m.u. aqueous procaine penicillin with probenecid
and this also failed; the condition finally responded to
an injection of 2 g. kanamycin.

Patients

100 male patients with acute uncomplicated urethral
gonorrhoea were each treated with a single intramuscular
injection of 2 g. spectinomycin dihydrochloride pen-
tahydrate.

36 of these patients were born in the United Kingdom
and 64 were immigrants. Of the latter, thirty were Negroes
(27 from the West Indies and three from West Africa)
and 34 were other immigrants from 21 different countries
(five from Eire, three each from Greece and Spain, two
each from Australia, Austria, India, Iraq, and Turkey,
and one each from Ceylon, Czechoslovakia, Egypt, France,
Italy, Iran, Kenya, Lebanon, Malaysia, Morocco, Mauri-
tius, Pakistan, and the U.S.A.). Nineteen were married,
five were separated, and 76 were single. Their average
age was 27·9 years (range 17 to 55).

The urethral discharge was present before treatment for
1 to 3 days in 64 cases, 4 to 7 days in 28 cases, 8 to 14
days in five, and 15 to 21 days in two; in one case the duration
was not known. 85 patients had experienced some dysuria
and fifteen had not.

Only 45 of the patients had had no previous venereal
infection, the remaining having experienced no less than
209 previous incidents, including 129 of gonorrhoea, 51
of non-gonococcal urethritis, four of syphilis, eighteen of
other suspected sexually-transmitted conditions, and seven
of anxiety concerning venereal disease.

No less than 132 of these incidents (including 91 of
gonorrhoea and 29 of non-gonococcal urethritis) had
affected the thirty Negroes, only six of whom had never
before attended a venereal disease clinic, and who thus
between them averaged 4·4 previous incidents each
compared with 1·1 for the remainder. One West Indian
patient accounted for 31 previous incidents, including
29 of gonorrhoea, and this man and two others for no
less than 52 previous incidents.

The disease had apparently been caught from a female
stranger in 43 instances, from a female friend in 48, from
the wife in two, and from a man in six (being a friend in
four and a stranger in two cases); one man denied sexual
intercourse. The apparent incubation period was 1 to 3
days in 49 cases, 4 to 7 days in 29 cases, 8 to 14 days in
fifteen, 15 to 21 days in two, and was not known in five.
TABLE I  Follow-up and results

<table>
<thead>
<tr>
<th>Duration of follow-up</th>
<th>No. followed</th>
<th>Satisfactory</th>
<th>Non-gonococcal infection</th>
<th>Re-infection</th>
<th>Failure based on history</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-7 days</td>
<td>83</td>
<td>16</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>8-14 days</td>
<td>61</td>
<td>10</td>
<td>2</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>15-21 days</td>
<td>48</td>
<td>8</td>
<td>2</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>22-28 days</td>
<td>37</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>1-2 mths</td>
<td>30</td>
<td>9</td>
<td>2</td>
<td>3</td>
<td>—</td>
</tr>
<tr>
<td>2-3 mths</td>
<td>16</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>More than 3 mths</td>
<td>8</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>—</td>
</tr>
</tbody>
</table>
| Total                 | 83           | 55           | 12                       | 9            | 7                       | (8·4 per cent.)

*One with a rectal infection

RESULTS ACCORDING TO ETHNIC GROUPS (Table II)

More than one-half of the failures based on history arose in the Negro group which, as has already been indicated, had the highest incidence of previous venereal disease; the risk of immediate re-infection may therefore be expected to be higher in spite of the denial of further sexual exposure. In the seventy other patients the failure rate amongst those followed was only 5·1 per cent. (3 of 59 followed).

COMPARISON WITH EARLIER RESULTS USING SULPHATE SALT

In an attempt to ascertain whether the gonococcus had become less sensitive to spectinomycin in the past 10 years a comparison has been made in Table III with the earlier findings using the sulphate salt.

Whether based on history, or on all recurrences within 2 weeks regardless of history, the failure rate in London in the present series in which spectinomycin dihydrochloride was used did not differ significantly from that of a decade ago using the sulphate salt.

SIDE-EFFECTS

The drug was extremely well tolerated and no patient complained of any local or systemic side-effect.

Summary and conclusions

(1) 100 male patients with acute uncomplicated gonorrhoea in London were treated with single injections of 2 g. spectinomycin. Whether based on a denial of further sexual intercourse or on all recurrences within 2 weeks regardless of such history, there were seven failures (8·4 per cent. of the 83 patients followed).

TABLE II  Results according to ethnic groups

<table>
<thead>
<tr>
<th>Group</th>
<th>No. treated</th>
<th>No. followed</th>
<th>Satisfactory</th>
<th>Non-gonococcal infection</th>
<th>Re-infection</th>
<th>Failure based on history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negroes</td>
<td>30</td>
<td>24</td>
<td>16</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Other immigrants</td>
<td>34</td>
<td>32</td>
<td>20</td>
<td>5</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>U.K.-born</td>
<td>36</td>
<td>27</td>
<td>19</td>
<td>5</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>83</td>
<td>55</td>
<td>12</td>
<td>9</td>
<td>7</td>
</tr>
</tbody>
</table>

TABLE III  Present results compared with earlier findings using the sulphate salt

<table>
<thead>
<tr>
<th>Series</th>
<th>No. treated</th>
<th>No. followed</th>
<th>All recurrences within 2 weeks</th>
<th>Failure based on history</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No.</td>
<td>Per cent.</td>
<td>No. Per cent.</td>
</tr>
<tr>
<td>Present study (1973)</td>
<td>100</td>
<td>83</td>
<td>7</td>
<td>8·4</td>
</tr>
<tr>
<td>Willcox (1962)</td>
<td>101</td>
<td>89</td>
<td>6</td>
<td>6·7</td>
</tr>
<tr>
<td>Willcox (1963)*</td>
<td>151</td>
<td>134</td>
<td>11</td>
<td>8·2</td>
</tr>
</tbody>
</table>

*Included the 1962 patients
(2) The failure rate among the Negro patients was 16.7 per cent. (4 of 24 followed); among those born in the United Kingdom it was only 3.7 per cent. (3 of 59 followed).

(3) The results are similar to those obtained with the sulphate salt under comparable conditions a decade before.

References

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——, —— (1964) Ibid., 40, 53
CLARKE, G. H. V. (1964) Ibid., 40, 122

—— (1963a) Acta derm.-venereol. (Stockh.), 43, 399
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La spectinomycine dans le traitement de la gono-coccie masculine

SOMMAIRE

(1) A Londres, 100 hommes atteints de gonococcie aiguë non compliquée furent traités par une injection unique de 2 g de spectinomycine. En tenant compte ou non de la dénégation de tout rapport sexuel ultérieur, le total des rechutes en deux semaines fut de 7 (8,4 pour cent) sur les 83 malades suivis.

(2) Le taux d'échec chez les malades noirs fut de 16,7 pour cent (4 des 24 suivis); parmi ceux nés au Royaume Uni, il ne fut que de 3,7 pour cent (3 des 59 suivis).

(3) Ces résultats sont semblables à ceux obtenus une décennie auparavant avec le sulfate dans des conditions comparables.
Spectinomycin in the treatment of gonorrhoea in males.

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