INCIDENCE OF GONOCOCCI RELATIVELY RESISTANT TO PENICILLIN

OCCURRING IN THE SOUTHAMPTON AREA OF ENGLAND
DURING 1958 to 1965*

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In 1957, there began in Southampton a sustained increase in the number of cases of gonorrhoea in which there was a failure of response to treatment by the then standard dose of 300,000 units of penicillin aluminium monostearate (PAM). In conjunction with Dr Irene Hutchinson of the Public Health Laboratory, it was decided to study the sensitivities to penicillin of gonococci isolated during a survey intended to last for several years, meanwhile relating these laboratory findings to the clinical and bacteriological response in several groups of cases treated with differing amounts and preparations of penicillin. This paper presents the results obtained during the years 1958 to 1965.

Throughout this period tube dilution sensitivity tests were carried out by Dr Hutchinson on all gonococcal isolates; the number of patients whose response to treatment could be assessed and related to the laboratory findings amounted to 1,143. The criteria for deciding on failure of treatment were the detection of gonococci in the genital secretions within the week following treatment coupled with the absence of a history suggesting re-infection (post-treatment gonorrhoea). In view of the occasional occurrence of cases of persisting asymptomatic infection with minimal signs, all patients making a first return visit were re-examined by urethral smear and culture. Four methods of treatment were used.

**Group 1** Aqueous procaine penicillin, a single injection of 900,000 units.

The results could be assessed in 204 cases and post-treatment gonorrhoea was recognized in thirty (14·7 per cent.). 38 of the 204 laboratory isolates were shown to have a penicillin sensitivity level of between 0·06 and 0·5 unit per ml. and 22 of the cases of treatment failure fell into this group. 166 isolates showed a sensitivity of 0·03 unit per ml., and eight of the cases of treatment failure fell into this group.

**Group 2** Penicillin aluminium monostearate, a single injection of 600,000 units.

The total of patients assessed was 291 and post-treatment gonorrhoea occurred in 45 (15·5 per cent.). 64 of the 291 isolates showed a sensitivity to penicillin of between 0·06 and 0·5 unit per ml. and forty cases of treatment failure fell into this group. There were 227 isolates showing sensitivity to 0·03 unit per ml. and there were five cases of treatment failure in this group.

**Group 3** Penicillin aluminium monostearate, one injection of 600,000 units together with streptomycin one injection of 1 g.

558 patients were assessed and post-treatment gonorrhoea was recognized in 62 cases (11·3 per cent.). 68 of the 558 isolates showed a sensitivity to penicillin of 0·06 to 0·5 unit per ml. and forty of the cases of treatment failure occurred in this group. There were 490 isolates showing sensitivity to 0·03 unit of penicillin per ml. and in this group there were 22 cases of treatment failure. Tests for streptomycin sensitivity were not carried out.

**Group 4** "Triplopen", a single injection of 1·25 mega units (benethamine penicillin 500,000 u., procaine penicillin, 250,000 u., and benzyl penicillin sodium, 500,000 u.) Ninety patients were assessed and post-treatment gonorrhoea occurred in six (6·7 per cent.). Eighteen of the ninety isolates showed a sensitivity to penicillin of between 0·06 and 0·5 unit per ml. and five cases of treatment failure fell into this group. 72 isolates showed sensitivity to 0·03 unit per ml. and there was one case of treatment failure.

These findings are condensed in the Table (opposite).

In addition to the major investigation an attempt was made to determine whether cases of infection contracted overseas yielded a different proportion of partially-resistant strains of gonococci from that yielded by cases of infection contracted in the United Kingdom. 404 cases were studied. In 281 cases infection had been contracted in the Southampton region, in 68 cases infection had originated elsewhere in the United Kingdom, and there were 55 cases from overseas. Thirty (54·5 per cent.) of the organisms cultured in the overseas infection group showed partial resistance in the range of 0·06 to 0·5 unit per ml. as against an incidence of 17·1 per cent. for the local infections and 32·4 per cent. for the infections contracted elsewhere in the United Kingdom.
Kingdom. These differing rates of incidence are statistically significant.

These findings give support to the contention that when dealing with infections contracted overseas it is prudent straightway to use doses of penicillin substantially in excess of those usually given. This empirical approach seems to be justifiable also in those cases of gonorrhoea in short-stay patients who contract their infections elsewhere in the United Kingdom. Steps might also be taken to give advice along these lines to those responsible for treatment of gonorrhoea in patients on the high seas.

Summary

The occurrence of strains of gonococci relatively resistant to penicillin among cases of gonorrhoea seen in a major sea-port of England was studied during 1958 to 1965. Tube sensitivity tests were carried out on all cases before treatment and the findings were related to the numbers of cases of post-treatment gonorrhoea (PTG) detected in four groups of patients, each receiving differing schedules of penicillin treatment, “Triplopen” (benethamine penicillin 500,000 u., procaine penicillin 250,000 u., and benzyl penicillin sodium 500,000 u.) yielded the lowest failure rate (7 per cent.) and PAM 600,000 u. intramuscularly the highest (15·5 per cent.). There was a close association between the numbers of cases of PTG and the numbers of isolates of gonococci relatively resistant to penicillin. Additionally, it was shown that there was a significantly higher incidence of partially-resistant organisms isolated from cases of infection contracted overseas compared with the number of such organisms causing infections contracted in the Southampton area. It is suggested that patients contracting gonorrhoea abroad should receive doses of penicillin substantially in excess of those usually given.

L’Incidence des gonocoques partiellement résistants à la pénicilline

La présence de souches de gonocoques partiellement résistants à la pénicilline chez les malades atteints de blennorragie rencontrés dans un très grand port de l’Angleterre a été étudiée pendant les années 1958 à 1965. Des tests de sensibilité in vitro ont été faits sur tous les cas avant de les traiter et les conclusions étaient en rapport aux cas de blennorragie vus après traitement et découverts dans quatre groupes de malades, chacun ayant reçu une posologie différente de pénicilline. Le “Triplopen” (benéthamine pénicilline 500,000 unités, procaine pénicilline 250,000 unités, et benzyle pénicilline sodique 500,000 unités) avait donné le taux le plus faible d’insuccès (7 pour cent) et le “PAM” (600,000 unités) par injection intramusculaire avait donné le taux le plus élevé d’insuccès (15,5 pour cent). Il y avait une étroite association entre le nombre de cas de blennorragie après traitement et le nombre de gonocoques isolés et relativement résistants à la pénicilline. De plus, il a été démontré qu’il y avait une incidence plus forte et bien définie de gonocoques partiellement résistants qui avaient été isolés des cas d’infections contractées outre-mer comparée au nombre des gonocoques qui causent les infections contractées dans la région de Southampton. Il a été suggéré que les patients qui avaient contracté la blennorragie à l’étranger devraient recevoir des doses de pénicilline bien en excès de celles données généralement.

### Table

**POST-TREATMENT GONORRHOEA RELATED TO TREATMENT METHODS AND TO IN VITRO SENSITIVITIES TO PENICILLIN**

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>No. of Cases Assessed</th>
<th>Cases of PTG* No.</th>
<th>Cases of PTG* No.</th>
<th>Cases of PTG* No.</th>
<th>Cases of PTG* No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Procaine Penicillin 900,000 u. Intramuscular</td>
<td>204</td>
<td>30</td>
<td>15</td>
<td>38</td>
<td>22</td>
</tr>
<tr>
<td>(2) P.A.M. 600,000 u. Intramuscular</td>
<td>291</td>
<td>45</td>
<td>15</td>
<td>5</td>
<td>64</td>
</tr>
<tr>
<td>(3) P.A.M. 0·6 m.u. Streptomycin 1 g.</td>
<td>558</td>
<td>62</td>
<td>11</td>
<td>68</td>
<td>40</td>
</tr>
<tr>
<td>(4) Benethamine Penicillin 0·5 m.u. Procaine Penicillin 0·25 m.u. Benzyl Penicillin Sod., 0·5 m.u.</td>
<td>90</td>
<td>6</td>
<td>7</td>
<td>18</td>
<td>5</td>
</tr>
</tbody>
</table>

*Post-treatment gonorrhoea within 7 days of treatment, though our normal routine of 3 months follow-up was aimed at in all cases.*

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(Revised and translated for clarity and accessibility.)