
FURTHER OBSERVATIONS ON STRAIN SENSITIVITY OF
Trichomonas vaginalis TO METRONIDAZOLE*

BY
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Squires and McFadzean (1962) reviewed the
question of strain sensitivity of Trichomonas vaginalis
to metronidazole. Since then examinations of the
sensitivities of strains isolated from occasional
patients who had apparently not responded to
treatment with metronidazole have been continued.
The results of these examinations are described.

It was also thought worth while to examine the
strain sensitivities of random cultures of the
parasite lest there had been a change which was
not as yet reflected by therapeutic failures. At the
same time, in view of the observation by Nicol,
Evans, McFadzean, and Squires (1966) that
organisms of the genus Mimae could “inactivate”
the drug, the vaginal flora of these patients were
also examined for the presence of organisms capable
of inactivating the compound.

Methods
The techniques for isolation and sensitivity testing of
the parasites in the case of patients who had apparently
failed to respond to treatment were as described by
Squires and McFadzean (1962). In the case of the
random samples, which came from the London Hospital,
the Middlesex Hospital, and St. Thomas’ Hospital, the
initial media used for isolating the organisms did not
contain antibiotics. Subsequent subcultures were made
into medium containing antibiotics before determining
the sensitivities of the trichomonads to metronidazole.
The initial cultures were also plated out on blood agar.
The bacteria were subsequently inoculated into tryptose
phosphate medium containing 10 and/or 100 μg./ml.
metronidazole. After incubation for 24 hours at 37°C,
the tubes were centrifuged at 4,000 r.p.m. for 10 minutes,
the supernatant was removed and was sterilized by
being held at 100°C for 20 minutes, and the metroni-
dazole content of the supernatant was estimated polaro-
graphically. These procedures were undertaken initially
with the mixed flora present. If inactivation occurred,
the bacterial species were then separated, identified
where possible, and tested individually for their abilities
to inactivate the compound.

Results
45 cultures were submitted from different parts
of Great Britain over the period 1962 to 1968, from
patients who had apparently not responded to
treatment with metronidazole. Trichomonads were
isolated and cultured from 25 (56 per cent.) of these
and all were found to be sensitive to 0-5 to 1 μg./ml.
metronidazole. Trichomonads were not grown from
twenty samples, and in eleven of these there was no
evidence of trichomonads having been inoculated
as shown by the absence of dead organisms in
centrifuged deposits of the cultures.

22 of the specimens were also examined for the
presence of organisms capable of inactivating
metronidazole. Of these, eleven (50 per cent.) had
organisms present which inactivated the drug, as
assessed polarographically. In these instances the
organisms were not identified. In some cases,
however, where no organisms capable of inactiva-
tion were found, it was shown that the absorption
of metronidazole, as judged by serum concentra-
tions, was poor.

84 random inocula were made from patients with
trichomonal vaginitis attending outpatient clinics of
three London hospitals; T. vaginalis was grown
from 55 (65 per cent.) of these and in all instances
the sensitivities were within the normal range.

56 (67 per cent.) of the 84 inocula contained
bacteria. These were not directly related to those
from which T. vaginalis was grown. Sixteen out of
the 56 (28 per cent.) were capable of inactivating
metronidazole (see Table): it so happened that no
one patient harboured more than one organism
capable of inactivating the compound. Seven of the
isolates were Strep. faecalis, four were E. coli, three
were Gram-positive cocci, one was a Proteus sp.,
and one a Klebsiella sp. It was possible to follow-up
eleven of the sixteen patients. Of these, five re-
plied satisfactorily to 200 mg. metronidazole
three times a day for 7 days and five defaulted.
One patient had three cervical smears positive for

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had in the yet, undetermined.

metronidazole. obtained at some years. We are grateful to Dr R. D. Catterall, of the Middlesex Hospital, Dr C. S. Nicol, of St. Thomas’ Hospital, and Dr P. Rodin, of the Whitechapel Clinic, the London Hospital, for kindly submitting cultures of trichomonads from their patients. We are also grateful to Mr M. J. Parnell for the polarographic estimations.

T. vaginalis after the standard treatment with metronidazole.

Discussion

There is still no evidence of the development of resistance of the trichomonad to metronidazole after widespread use of the compound in this country for some 8 years.

The question of the importance of the presence in the vagina of organisms capable of inactivating metronidazole has yet to be resolved. One patient had trichomonads present in cervical smears after treatment, but the reliability of identification of the parasite in the smears is in doubt (Hill, 1968).

Summary

The sensitivities to metronidazole of 25 strains of T. vaginalis isolated from patients who had apparently failed to respond to treatment with metronidazole, and the sensitivities of 55 isolates obtained at random, showed no evidence of the development of resistance to this compound.

The importance of the presence of bacteria in the vagina capable of inactivating the compound is, as yet, undetermined.

### Table

**Details of the Random Samples Which Contained Micro-Organisms Capable of Inactivating Metronidazole**

<table>
<thead>
<tr>
<th>Isolate No.</th>
<th>Contaminating Organism</th>
<th>Percentage Inactivation of Metronidazole (10 µg/ml)</th>
<th>Percentage Inactivation of Metronidazole (100 µg/ml)</th>
<th>Response to Treatment with Metronidazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST 7</td>
<td>E. coli</td>
<td>100</td>
<td>60</td>
<td>3 cervical smears positive for T. vaginalis after treatment</td>
</tr>
<tr>
<td>ST 9</td>
<td>E. coli</td>
<td>65</td>
<td>60</td>
<td>Defaulted</td>
</tr>
<tr>
<td>M 5</td>
<td>S. faecalis</td>
<td>—</td>
<td>70</td>
<td>Defaulted</td>
</tr>
<tr>
<td>M 11</td>
<td>E. coli</td>
<td>100</td>
<td>100</td>
<td>Satisfactory</td>
</tr>
<tr>
<td>M 15</td>
<td>S. faecalis</td>
<td>100</td>
<td>40</td>
<td>Defaulted</td>
</tr>
<tr>
<td>M 16</td>
<td>S. faecalis</td>
<td>100</td>
<td>70</td>
<td>Defaulted</td>
</tr>
<tr>
<td>M 17</td>
<td>S. faecalis</td>
<td>100</td>
<td>65</td>
<td>Satisfactory</td>
</tr>
<tr>
<td>M 19</td>
<td>S. faecalis</td>
<td>100</td>
<td>70</td>
<td>Satisfactory</td>
</tr>
<tr>
<td>M 31</td>
<td>Proteus sp.</td>
<td>—</td>
<td>45</td>
<td>Defaulted</td>
</tr>
<tr>
<td>M 38</td>
<td>Klebsiella sp.</td>
<td>—</td>
<td>40</td>
<td>Satisfactory</td>
</tr>
<tr>
<td>M 40</td>
<td>S. faecalis</td>
<td>100</td>
<td>40</td>
<td>Unknown</td>
</tr>
<tr>
<td>ST 1</td>
<td>E. coli</td>
<td>100</td>
<td>60</td>
<td>Unknown</td>
</tr>
<tr>
<td>M 23</td>
<td>S. faecalis</td>
<td>100</td>
<td>75</td>
<td>Unknown</td>
</tr>
<tr>
<td>M 34</td>
<td>Gram-positive cocci</td>
<td>—</td>
<td>70</td>
<td>Unknown</td>
</tr>
<tr>
<td>M 49</td>
<td>S. faecalis</td>
<td>—</td>
<td>30</td>
<td>Unknown</td>
</tr>
<tr>
<td>M 52</td>
<td>E. coli</td>
<td>—</td>
<td>40</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

We are grateful to Dr R. D. Catterall, of the Middlesex Hospital, Dr C. S. Nicol, of St. Thomas’ Hospital, and Dr P. Rodin, of the Whitechapel Clinic, the London Hospital, for kindly submitting cultures of trichomonads from their patients. We are also grateful to Mr M. J. Parnell for the polarographic estimations.

**References**

HILL, J. (1968). Personal communication.

**Résumé**

La sensibilité au métronidazole de 25 souches de T. vaginalis isolées de malades qui n’avaient pas apparentement répondu au traitement par le métronidazole, et la sensibilité de 55 souches obtenues au hasard ne montrait aucun signe de développement d’une résistance à ce médicament.

L’importance de la présence de bactéries dans le vagin capables de rendre ce médicament inactif reste jusqu’ici non établie.
Further observations on strain sensitivity of Trichomonas vaginalis to metronidazole.

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