FURTHER OBSERVATIONS ON STRAIN SENSITIVITY OF
Trichomonas vaginalis TO METRONIDAZOLE*

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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 worthwhile 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 metronidazole content of the supernatant was estimated polarographically. 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 inactivation were found, it was shown that the absorption of metronidazole, as judged by serum concentrations, 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 responded satisfactorily to 200 mg. metronidazole three times a day for 7 days and five defaulted. One patient had three cervical smears positive for
had trichomonads in the vagina, 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.

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.

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REFERENCES

HILL, J. (1968). Personal communication.


Des observations additionnelles faites au sujet de la sensibilité du T. vaginalis au métronidazole

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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