Treatment of trichomoniasis in females with and without gonorrhoea

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Summary
46 women with trichomoniasis and gonorrhoea were treated with nimorazole (300 mg twice daily for 7 days) and a trichomonal cure rate of 90-2 per cent. was noted.

In addition, 53 of 112 patients with trichomoniasis but without gonorrhoea, were treated with metronidazole (200 mg three times a day for 7 days) and 59 with nimorazole (300 mg twice daily for 7 days) in a randomized trial. The cure rates were 96 and 90-5 per cent. respectively. There was no significant difference in the results noted in the two groups.

Neither the trichomonal infection itself nor the result of antitrichomonal therapy was affected by antgonococcal therapy (one-day treatment with ampicillin or single-dose therapy with doxycycline).

No increase was noted in the frequency of candidiasis after antitrichomonal therapy (in patients without gonorrhoea) or after antigonococcal therapy, but there was substantial variation between consecutive specimens in the prevalence of C. albicans.

Introduction
In a one-year study of female patients attending a venereal disease clinic, the frequency of Trichomonas vaginalis was found to be 20 per cent. (Eriksson and Wanger, 1975).

Good results in the treatment of trichomoniasis have been obtained with metronidazole. During the last few years other potent antitrichomonal agents have been produced, one of these being nimorazole. In our investigation of women with T. vaginalis, we have studied (a) the effect of treatment with nimorazole, (b) the comparative effect of metronidazole and nimorazole, and (c) the effect, if any, of the treatment of T. vaginalis on Neisseria gonorrhoeae and Candida albicans.

Patients and methods
All women attending the clinic were examined at all visits for the presence of N. gonorrhoeae, T. vaginalis, and C. albicans during the period November, 1971, to October, 1972.

Diagnosis
N. gonorrhoeae was detected by direct microscopy and/or culture. Specimens were taken from the urethra, cervix, and rectum, and were cultured on Thayer-Martin medium. T. vaginalis was identified by direct microscopy and/or culture during the first half of the investigation, and by culture alone during the second half. Cultures were done by the method of Diamond (1957).

C. albicans was identified by culture on Sabouraud agar plates. Eriksson and Wanger (1975) have described the diagnostic procedures in detail.

Treatment
Patients with uncomplicated gonorrhoea were treated either with 2 g ampicillin (Doktaclin®, Astra Läkemedel AB, Sweden) administered orally in two doses with a 5-hour interval or with 0-3 g doxycycline (Vibramycin®, Pfizer AB, Sweden) in a single oral dose.

Patients with T. vaginalis were treated differently depending on the presence or absence of N. gonorrhoeae.

(a) Patients with trichomoniasis and gonorrhoea Trichomoniasis was treated with nimorazole 300 mg twice daily for 7 days. Every third patient was excluded from treatment.

(b) Patients with trichomoniasis alone These patients were treated in randomized series with metronidazole (Flagyl®, AB Leo, Sweden) 200 mg three times a day for 7 days or, alternatively, with nimorazole 300 mg twice daily for 7 days. The randomization was carried out in groups of ten patients, five being treated with metronidazole and five with nimorazole. The investigator did not know which preparation each patient received.

Treatment for trichomoniasis was not given until gonorrhoea was diagnosed or excluded. In patients in whom both gonorrhoea and trichomoniasis were diagnosed and treated at the same visit, antitrichomonal treatment was started the day after the antigonococcal treatment.

Patients in whom trichomonal cultures became positive during the follow-up period, after antitrichomonal therapy, were not treated again.

All pregnant patients were excluded from the study, and it was not usually possible to treat the sexual partners...
of the patients with trichomonal infestation. Blood
specimens were collected for white blood cell counts and
liver function tests before and immediately after treat-
ment.

Patients with candidiasis Patients with candidiasis were
not treated until other therapeutic procedures and
follow-up examinations had been completed.

Follow-up
Patients were asked to return for follow-up examinations
at weekly intervals. Our aim was to recall patients treated
for trichomoniass for at least three visits. At these visits
the patients were asked about subjective symptoms and
complaints, and any side-effects of the drugs.

Results
During the period of investigation specimens were
collected from 1,347 women, and at the first visit
N. gonorrhoeae was found in 506 cases (38 per cent.),
T. vaginalis in 272 (20 per cent.), and C. albicans in
233 (17 per cent.).

The frequency of infection, the relationships of
the different pathogens, and their symptomatological
significance have already been reported (Eriksson and
Wanger, 1975), as well as the results of the antitrichomonal treatment (Enfors and Eriksson, 1975).

Patients with trichomoniass and gonorrhoea
In this group, 46 patients were treated with nimo-
razone (Table). Among the patients in whom anti-
trichomonal treatment failed, three were noted at the
first follow-up visit and one at the second.

In 26 patients the gonorrhoea was treated with
ampicillin and in twenty with doxycycline. Neither
ampicillin nor doxycycline therapy affected the
results of the antitrichomonal therapy, nor was any
difference noted in the therapeutic results if the
antitrichomonal therapy was initiated at the same
time as the antitrigonococcal therapy or later.

Patients with trichomoniass alone
In this group, 112 patients were treated—53 with
metronidazole and 59 with nimosazole (Table).

Among the patients registered as failures, two,
treated with metronidazole, were noted at the first
follow-up, and four, treated with nimosazole, at the
second follow-up. One patient treated with nimosazole
was noted as a failure at the third follow-up.

The results of the tests of cure are presented in the
Table. In the group of patients with trichomoniass
but without gonorrhoea who were treated with
metronidazole, 48 out of 50 (96 per cent.) were
cured, while 48 of 53 (90.5 per cent.) treated with
nimosazole were cured. Thus there was no significant
difference ($\chi^2_1=0.49$; $P=0.5$). In the group of
patients with trichomoniass and gonorrhoea, 37 out
of 41 (90.2 per cent.) were cured. There was no
difference in the results of treatment with nimosazole
in patients with or without gonorrhoea.

Side-effects of antitrichomonal therapy
Four patients treated with metronidazole developed
raised S-GOT and S-GPT. (The rise was slight in
two, two-fold in one, who was an alcoholic, and
marked in one, who proved to have hepatitis). Two
patients treated with metronidazole complained of
nausea. One patient treated with nimosazole com-
plained of dizziness, one (treated for gonorrhoea one
week before antitrichomonal therapy) of nausea, and
one developed a rash. None of the patients in the
study had to discontinue treatment because of
side-effects.

Correlation between antitrichomonal therapy and the
prevalence of candidiasis
The prevalence of C. albicans was studied at visits
before and at the first follow-up examination after
antitrichomonal therapy (in patients without go-
norrhoea). Out of a total of 103 patients, two who had
been previously negative had positive results to
C. albicans cultures after therapy; both had been
treated with metronidazole.

Correlation between antitrigonococcal therapy and the
prevalence of other pathogens
To provide a control group for the study of the effect,
if any, of antitrigonococcal therapy on T. vaginalis and
vice versa, every third patient (a total of 22) was
excluded from treatment when antitrichomonal
therapy was started. However other patients were
left untreated during the period of investigation for
various reasons, such as lack of co-operation, and the
control group eventually contained fifty patients.

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<td>Patients with gonorrhoea</td>
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During the follow-up of the gonococcal infection all of these showed persistence of *T. vaginalis*.

The treatment for trichomoniasis had no demonstrable effect on the results of the antgonococcal therapy, but the number of failures in the treatment of gonorrhoea, with both ampicillin and doxycycline, was very low (Enfors and Eriksson, 1975), so that a very large series would have been required to demonstrate any such effect.

No increase in the frequency of *C. albicans* was observed after the antgonococcal therapy.

In 552 patients without any treatment, 404 had no finding of *C. albicans* at the first and second visit, thirty had negative findings at the first visit and positive at the second, and in 29 patients the opposite results were obtained.

**Discussion**

A trichomoniasis cure rate of about 90 per cent after one week of treatment with metronidazole has been reported by Rodin, King, Nicol, and Barrow (1960) and Csonka (1963). Similar good therapeutic results have been reported for nimorazole (Cohen, 1971; Moffet, McGill, Schofield, and Masterton, 1971).

In a comparative study of randomized treatments, McClean (1972) obtained equivalent results with both preparations (cure rate 82 per cent.) whereas Evans and Catterall (1971) and McCann, Mahony, and Harris (1972) obtained less satisfactory results with nimorazole than with metronidazole.

In our study we found no difference in the results of treatment with metronidazole and nimorazole (cure rates of 96 and 90 per cent. respectively), and both can be regarded as very good. The number of defaulters was comparatively low, but the observation period was fairly short.

**Possible causes of therapeutic failure in the treatment of trichomoniasis**

The risk of re-infection is high as the patients who attend a venereal clinic are sexually active and the possibility of re-infection will increase during long observation periods.

Patients may not complete the prescribed course of treatment. A demonstration of the significance of these factors was provided by Keighley (1971), who obtained a cure rate of 98 per cent among patients in prison with supervised medication.

Poor absorption of the drug, conversion into inactive metabolites, and inactivation of the vaginal flora have been suggested as causes of therapeutic failure (Kane, McFadzean, and Squires, 1961; Cohen, 1971; Nicol, Evans, McFadzean, and Squires, 1966). McFadzean, Pugh, Squires, and Whelan (1969) found no evidence of primary or acquired resistance after 8 years of treatment with metronidazole. According to de Carneri (1970), experimentally produced metronidazole-resistant strains were still sensitive to nimorazole, whereas Benazet and Guillaume (1972) demonstrated cross-resistance. The good therapeutic results with metronidazole provide evidence that no clinically important resistance develops. In assessing cure, cultures have proved to be superior to microscopy, particularly in cases with occasional trichomonads (Eriksson and Wanger, 1975).

**Correlation between antitrichomonal therapy and the prevalence of C. albicans**

Antitrichomonal therapy has been considered to be one of the contributory factors in the increasing frequency of *C. albicans* (Csonka, 1963; Catterall, 1971; Keighley, 1971; Ross, 1973), but we have not observed any such increase in the prevalence of *C. albicans* after antitrichomonal therapy in our series.

**References**

Benazet, F., and Guillaume, L. (1972) *Lancet*, 1, 597
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