VAGINAL MONILIASIS AFTER TREATMENT OF TRICHOMONAL INFECTION WITH "FLAGYL"*

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There is some difference of opinion regarding the incidence of vaginal thrush following the treatment of trichomonal vaginitis with the new oral trichomonicide, metronidazole ("Flagyl"). Rees (1960) and Rodin, King, Nicol, and Barrow (1960) concluded that metronidazole neither encouraged nor inhibited the growth of the fungus concerned. Watt and Jennison (1960) found coincident monilial infection unaffected by treatment. Moffett and McGill (1960), on the other hand, noted that *Candida* might be encouraged; three of their 42 patients showed the fungus after treatment, and symptoms were severe or moderately severe in two. Whitehouse and Porteous (1962) stated that several cases of monilial vulvo-vaginitis had been seen after treatment of *Trichomonas vaginalis* infection with an oral trichomonicide, presumably "Flagyl".

None of these reports compares the incidence of moniliasis before and after metronidazole treatment, and this retrospective study attempts to fill this gap. The incidence of vaginal moniliasis, before and after Flagyl or local Stovarsol treatment, is compared, and comparison is also made with a control group.

Material

The study comprises three groups of female subjects:

- (1) One hundred consecutive patients treated with Stovarsol pessaries;
- (2) One hundred consecutive patients treated with metronidazole orally;
- (3) A control group of one hundred women, almost half being contacts of male patients with urethritis seen during 1959-1962.

The age groups and marital status of the female patients are shown in Tables I and II respectively; there was a higher incidence of young single women in the metronidazole group.

TABLE I
AGE GROUPS OF PATIENTS AND CONTROLS

Age Group (yrs)	Flagyl	Stovarsol	Control
Under 20	39	29	25
20-29	44	47	56
30-39	13	17	10
40 and Over	4	7	9
Total	100	100	100

TABLE II
MARITAL STATUS OF PATIENTS AND CONTROLS

Marital Status	Flagyl	Stovarsol	Control
Single	65	50	42
Married	29	42	49
Widowed, Separated, or Divorced	6	8	9

The reason for attendance is shown in Table III.

TABLE III
REASON FOR ATTENDANCE OF PATIENTS AND CONTROLS

Reason for Attendance	Flagyl	Stovarsol	Control
Contact of Male Gonorrhoea Case	45	26	31
Contact of Male Non-Specific Urethritis Case	8	20	15
Other Reasons (Symptomatic) ..	47	54	54

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Methods

All 300 patients were examined for gonococcal infection. Gram-stained smears and cultures were made from urethral and cervical material in each case. Vaginal secretion was examined by dark-ground microscopy for *Trichomonas vaginalis*. Vaginal smears were also routinely prepared and stained by Gram's method.

The diagnosis of *Candida albicans* was made from these specimens by recognizing the Gram-positive hyphae or buds, or both, of the fungus. The hyphae of *C. albicans* must be differentiated from the Gram-positive lacto-bacillus. Hyphae are irregular in length usually broader than the bacillus and with rounded ends. Not infrequently they show spore holes. The lacto-bacillus, on the other hand, is fairly regular in length with almost square ends. Confusion may arise when bacilli are found end to end or terminally bulbous, giving the appearance of hyphae.

All these laboratory procedures were carried out initially and at each and every follow-up examination. A follow-up of 3 months was the aim in all cases.

Results

Table IV shows the main complaints of the women comprising the whole series. A complaint of vaginal discharge is often elicited only after leading questions. Nevertheless the symptomatic percentage, which is roughly the same in each group, is worthy of note.

TABLE IV
INITIAL COMPLAINT

Presenting Symptom	Flagyl	Stovarsol	Control
Nil	25	31	39
Vaginal Discharge	62	54	34
Vulval Irritation	10	7	9
Other	3	8	18

Table V shows the initial laboratory findings and the cumulative incidence of moniliasis on follow-up. Initially there were four and six cases respectively in the Flagyl and Stovarsol groups, compared with twelve in the control group. The final total incidences of moniliasis were found to be 23, 19, and 15 per cent. in the Flagyl, Stovarsol, and control groups respectively. In all cases in which monilia was found initially it persisted after the treatment of the trichomonal infection.

TABLE V
LABORATORY FINDINGS

Laboratory Findings		Flagyl	Stovarsol	Control
On Initial Examination	<i>T. vaginalis</i> Only ..	53	70	—
	Gonococci Only ..	—	—	33
	<i>T. vaginalis</i> + Gonococci	43	24	—
	Monilia Only	—	—	12
	Monilia + <i>T. vaginalis</i>	3	4	—
	Monilia + <i>T. vaginalis</i> + Gonococci	1	2	—
	Nil	—	—	52
Monilia Found Subsequently ..		19	13	3
Total Incidence of Monilia ..		23	19	15

The follow-up period in the various groups is shown in Table VI.

TABLE VI
LENGTH OF FOLLOW-UP

Follow-up		Flagyl	Stovarsol	Control
Default after first attendance ..		17	22	23
Surveillance	Up to 2 wks ..	83	78	77
	2 wks to 1 mth ..	62	64	55
	1 mth to 2 mths	45	55	39
	3 mths and Over	22	35	15

Symptoms of moniliasis were absent or minimal in all cases.

Unfortunately the incidence of *C. albicans* in pregnancy could not be fully determined. Only fifteen patients were pregnant, six in the Flagyl group, four in the Stovarsol group, and five in the control group. From each group one patient only was found to have moniliasis on follow-up.

The failure-recurrence rate as regards trichomonal infection was highest in the Stovarsol group (17 per cent.); in the Flagyl group it was only 6 per cent.

Each of the three groups of course included patients receiving penicillin treatment for gonorrhoea, and a few receiving other antibiotics for other conditions, e.g. cystitis. Of the control group 33 were so treated, and vaginal thrush was subsequently found in more of them. In the Flagyl and Stovarsol groups likewise antibiotic therapy made no apparent difference to the post-treatment incidence of moniliasis.

Discussion

The incidence of *C. albicans* in the female population is generally accepted to be about 20 per cent.

(Jeffcoate, 1957). It is not surprising, therefore, to find the final total percentage in the three groups near to this figure.

The low initial incidence in those infected with *T. vaginalis* suggests that the parasite may well swamp the fungus, making its demonstration by the method used impossible or nearly so. Whether culture would improve this percentage is not clear from the literature. Watt and Jennison (1960), reporting six positive monilial cultures in 39 cases of trichomonal vaginitis, did not make it clear at which stage of treatment the trichomonad was found. Other writers do not mention whether smear or culture methods were used.

The elimination of the protozoon from the vagina allows the fungus to return to its original percentage incidence. There is no suggestion, however, that it encourages the fungus to increase or that it masks symptoms of monilial infection. The small percentage addition to the control group on follow-up supports this view. The variation in follow-up incidence of moniliasis in the Stovarsol and Flagyl groups suggests that a high rate of positives depends on the elimination of the protozoon. One point is clear, *i.e.* that metronidazole has no fungicidal properties *in vivo*.

According to the figures presented, one woman in five may manifest vaginal moniliasis after the successful treatment of trichomonal vaginitis with Flagyl. There would appear to be good reason to anticipate this in all cases, and with this in mind the local application of gentian violet or some other fungicide at the initiation of metronidazole therapy should be considered.

Summary and Conclusions

Two separate groups, each of one hundred women, were treated for trichomonal infection with Flagyl and Stovarsol respectively, and have been studied as regards the incidence of vaginal moniliasis. The findings have been compared with those in a control group of one hundred.

The pre-treatment incidence of moniliasis of the vagina was low in those infected with *T. vaginalis*, but follow-up studies brought the level of incidence up to or above the control group level, *i.e.* to about that generally recognized as average.

The higher cure rate of trichomonal infection associated with Flagyl probably accounts for the higher post-treatment incidence of moniliasis as compared with the Stovarsol group. This is believed to be an index of cure rather than a side-effect.

One woman in five treated with Flagyl was subsequently found to have moniliasis. The use of preventive measures is suggested.

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REFERENCES

- Jeffcoate, T. N. A. (1957). "Principles of Gynaecology", p. 313. Butterworth, London.
 Moffett, M., and McGill, M. I. (1960). *Brit. med. J.*, **2**, 910.
 Rees, E. (1960). *Ibid.*, **2**, 906.
 Rodin, P., King, A. J., Nicol, C. S., and Barrow, J. (1960). *Brit. J. vener. dis.*, **36**, 147.
 Watt, L., and Jennison, R. F. (1960). *Brit. med. J.*, **2**, 902.
 Whitehouse, W. L., and Porteous, C. R. (1962). *Lancet*, **1**, 506.

La moniase du vagin après l'emploi du Flagyl dans le traitement de l'infestation trichomonale

RÉSUMÉ

Deux groupes, chacun de cent femmes infestées par le *Trichomonas vaginalis*, furent traités, l'un avec le Flagyl et l'autre avec le "Stovarsol". L'incidence de moniase a été comparée avec celle d'un groupe de cent témoins.

Où trouva la moniase chez très peu des 200 femmes infestées, mais après le traitement l'incidence approcha ou dépassa le niveau normal des 100 témoins, surtout chez les femmes qui avaient reçu du Flagyl. Ce développement de la moniase doit donc être vu plutôt comme un signe de guérison que comme une réaction inattendue.

Une femme sur cinq parmi celles traitées avec le Flagyl fut atteinte ensuite de moniase. Il semble donc qu'il faudrait prendre des mesures préventives.