TRICHOMONIASIS IN A CLOSED COMMUNITY: 100% FOLLOW-UP

BY

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The scepticism with which gynaecologists and venereologists regarded the possible effectiveness of an oral trichomonacide was doubtless justified by the unsubstantiated claims that had been put forward some years ago for a chemical compound which is now happily superseded by metronidazole (" flagyl "). This does, in fact, destroy the parasite in the great majority of cases of trichomonal vaginitis. Where it fails to do so there are several possible explanations. The patient might not have taken the pills at all, or might have taken them irregularly. She might have been reinfected after being cured. The drug might in some cases not have been adequately absorbed from the gastro-intestinal tract; or, where there was no defect in absorption, the concentration of metronidazole in the blood might have been insufficient to destroy the trichomonads in the depth of the uterine cervical glands in which long-standing inflammation had led to decreased vascularity. A final theoretical possibility is that some strains of *Trichomonas vaginalis* might have a natural or acquired resistance to the drug.

I am informed (J. A. McFadzean and S. Squires, private communication) that there is little laboratory evidence of defective absorption and no evidence at all of drug-resistant trichomonads. Presumption of cure after treatment with metronidazole is arrived at after a series of negative reports of microscopical and cultural examinations of specimens taken at intervals throughout the three-months follow-up; but some patients default long before the end of that time.

It was thought that it would be of interest to ascertain the effects of oral metronidazole in a closed community in which all the patients could be kept under observation for as long as was considered desirable, and where the risk of reinfection was negligible. These conditions were found in Her Majesty's Prison, Holloway, where the 102 women who are the subjects of this report were treated. In order to save space I have listed the names of the early investigators of metronidazole only in the bibliography. I differ from those French, German, and Canadian workers who continue to give the drug in the form of vaginal suppositories as well as oral tablets. I have used the latter solely, believing that local treatment with this substance is likely to be no more successful than earlier topical applications, the use of which was followed so often by relapse. An actively trichomonicidal substance applied to the vaginal mucosa can never reach deep-seated foci of infection; and metronidazole so exhibited can cause local irritation.

The incidence of *T. vaginalis* varies in different countries. It has been reported to be as low as 8.6% among Japanese women and as high as 53.6% in French women (Gisella Perl *et al.*, 1956). Trussell (1947) has estimated that in the U.S.A. 20 to 25% of women harbour *T. vaginalis*. Figures of true incidence are difficult to obtain, since, for example, the figures of those patients treated by private practitioners are not available and most of the statistics in the past have been obtained from an analysis of special sections of the community varying from a cancer survey to a survey of Chinese cotton-mill workers, and therefore cannot be regarded as representative of the general community.

One would naturally expect figures from a V.D. clinic to be high where the majority of the female patients present themselves with a vaginal discharge, and an infestation rate of 45.6% was found by Mascall (1954). For the same reason figures of infestation obtained from gynaecological and obstetric units are high, and Burch *et al.* (1959 found 46.5% infected. Again one would expect the incidence in prostitutes to be high, and of 476 prostitutes who were routinely examined for V.D. in Holloway Prison during 1960 I found that 51% had *T. vaginalis*.

Present Investigation

For the study of metronidazole in Holloway Prison no special selection of women was made, the only criterion being that each woman would be in prison for not less than 14 weeks. It is customary to issue medicines to women in the prison twice a day, and a trial was therefore made by giving metronidazole orally in twice-daily doses, each of 300 mg., for seven days without any local treatment. Tests of cure, including wet film and culture (medium used was that of Feinberg and Whittington, 1957), were taken within one week after completion of the course of metronidazole. Tests were made for a minimum period of 12 weeks at intervals of two weeks, but care was taken to ensure that a test was always made after menstruation. All the 102 women were treated with this course of metronidazole and all of them completed the 12 weeks' surveillance.

Cases were classified as acute, subacute, and asymptomatic or carrier. *Acute infestation* was denoted by acute vulvitis, acute urethritis, acute vaginitis and cervicitis, with a profuse irritating purulent or mucopurulent discharge. *Subacute infestation* was denoted by lack of external inflammation, mild vaginitis and cervicitis, and a thin mucopurulent or mucoid vaginal discharge, irritation being intermittent, mainly after the menstrual period. In the *asymptomatic or carrier state* there were no symptoms or signs of *T. vaginalis*.

Forty-eight women had acute trichomoniasis, 51 had subacute trichomoniasis, and three were asymptomatic. Fifty-nine (58%) had previously been treated with vaginal pessaries, 18 also had gonorrhoea, and nine were pregnant. Their ages varied from 16 to over 50 years (Table I).

TABLE I.—*Age Incidence*

Age:	16–20	21–30	31–40	41–50	51–60
No. treated ..	24	50	19	7	2

Response to Treatment—Pathological Results

Of the 102 women, 92 were negative for *T. vaginalis* on film and culture after one course of treatment with metronidazole and remained negative for the following 12 weeks. Ten women became positive again at some time within the first six weeks after treatment and all of these had long histories of a vaginal discharge: five were acute cases and five were subacute.

Three of the 10 were positive on the first test, taken within six days of completion of treatment; one was positive on her first test, taken two weeks after completion of treatment and after menstruating heavily for three weeks. Three women were negative after treatment, but became positive on the second test taken

after a menstrual period ; two were negative for four weeks then became positive after the second menstrual period ; one was negative for six weeks and then became positive after her confinement.

All 10 women were re-treated immediately after relapse with the same course of metronidazole, 300 mg. b.i.d. for seven days, and they all remained negative for 12 weeks or more after this second course. Table II summarizes the pathological results of these 10 women.

TABLE II.—*Pathological Results in Weeks of the 10 Women Needing Re-treatment*

Case	Clinical State	Weeks Following Treatment										
		1	3	5	7	9	11	13	15	17	19	20
1	Acute	+	−	−	−	−	−	−	−	−		
2	,,	+	−	−	−	−	−	−	−			
3	,,	M.P.	+	−	−	−	−	−	−	−	−	−
4	,,	−	+	−	−	−	−	−	−	−		
5	,,	−	−	+	−	−	−	−	−	−		
6	Subacute	−	+	−	−	−	−	−	−			
7	,,	+	−	−	−	−	−	−	−	−		
8	,,	−	+	−	−	−	−	−	−	−	−	−
9	,,	−	−	−	+	−	−	−	−	−	−	−
10	,,	−	−	+	−	−	−	−	−			

It was noted that five of these 10 cases had chronic pelvic sepsis, and the possibility that this condition was partly the cause for relapse should be considered.

As a high rate of *T. vaginalis* has been found in prostitutes, and as in many of them the infestation is of long standing, one might expect that these women would be more difficult to treat and need a larger dosage of metronidazole ; however, this was not found to be the case. Of the 102 women, 31 were prostitutes, and of the 10 women needing two courses of metronidazole three were prostitutes ; therefore the percentage of those needing further treatment was no higher in the prostitutes than in the other women.

Clinical Response to Treatment

Of the 102 women treated, 58 showed immediate response and on examination within a week of completion of treatment the irritation had gone, all inflammation had subsided, and there was no discharge. These 58 women remained normal for the period of surveillance. In 41 women a scanty discharge remained which cleared at varying periods up to 12 weeks. In three women a mucoid discharge persisted, due to chronic cervical erosion in two and to vaginal and cervical warts in the third.

None of the 102 women ever complained of irritation after the first course of metronidazole.

Table III shows the time in weeks when a patient became free of vaginal discharge.

TABLE III.—*Clinical Response to Treatment*

No. of Women	Week when Free from Vaginal Discharge				Persisting
	1 Week	2 Weeks	4 Weeks	12 Weeks	
102	58 (57%)	19 (18%)	12 (12%)	10 (10%)	3 (3%)

Eighteen patients had gonorrhoea as well as *T. vaginalis*, and for this were given penicillin prior to the course of metronidazole. There seemed to be little difference in the duration of symptoms in those who had gonorrhoea plus *T. vaginalis* and those who had *T. vaginalis* only. This is illustrated in Table IV.

It was noted that where a cervical erosion was present the clinical response to treatment was usually slower. In cases where the cervical erosion was superficial, cure of the trichomonas infestation resulted in immediate healing of the erosion ; this was quite unexpected, and I have never seen such rapid healing with local treatment, even when the treatment has been successful in eliminating the *T. vaginalis* and the discharge.

TABLE IV.—*Clinical Response to Treatment in Patients with T. vaginalis and in Those with T. vaginalis Complicated with Gonorrhoea*

No. of Women	Disease	Week when Symptom-free				Persisting Discharge
		1	2	4	12	
84	*T. vaginalis*	48	17	9	9	1
18	*T. vaginalis* and gonorrhoea ..	10	2	3	1	2

In cases where the erosion was large, deep, and of long standing, a mucoid or white discharge persisted for some time and in two cases was still present at the end of 12 weeks (Table V).

TABLE V.—*Clinical Response. State of Cervix*

	No.	Week when Symptom-free				Persisting
		1	2	4	12	
Cervix intact ..	71	47 (66%)	11 (15%)	8 (12%)	4 (6%)	1 (<1%)
Cervix erosion	31	11 (36%)	8 (26%)	4 (13%)	6 (19%)	2 (6%)

Candida Albicans.—*C. albicans* was found in 29 of the 102 women, and four of these showed *C. albicans* prior to treatment with metronidazole. This caused no irritation and was only of pathological interest.

Toxic Reactions

Three women complained of nausea ; no other toxic reactions were observed. In two women nausea occurred on the fourth day of the first course of metronidazole, but both women completed the course with the addition of prochlorperazine ("stemetil") 5 mg. given with each 300 mg. of metronidazole. The third woman complained of nausea during her second course of metronidazole but completed the course successfully.

The number of toxic reactions was small and were of a very mild nature ; a possible reason for this could be that the women were leading a life with regular hours of eating, working, and sleeping, and having plain food and no alcohol.

Summary and Conclusions

One hundred and two women prisoners were treated for *Trichomonas vaginalis* with metronidazole. The drug had a fair test under conditions seldom available and over a period long enough to cover possible drug resistance. All the women responded to metronidazole, although 10 of them needed two courses of the drug. No resistance to the drug was found.

T. vaginalis was eliminated in all cases ; any remaining discharge was due to other conditions, such as chronic pelvic sepsis, cervical erosion, vaginal warts, etc.

As it is more practical to give the working community their medicines in twice-daily doses, and as recent trends are to provide drugs in this simple dosage if possible, it is interesting to note that the results of giving metronidazole in twice-daily doses of 300 mg. compare very favourably with the results of giving 200 mg. thrice daily.

It is to be noted also that the percentage of toxic reactions is certainly no greater.

The 102 women were a very assorted group in shape, size, age, and occupation, as they were chosen only by their length of sentence. As a toxic reaction was found only in 3% and was of a mild nature it can be assumed that it is safe and probably advantageous to give metronidazole in twice-daily doses.

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SUPERIOR MESENTERIC ARTERY OCCLUSION TREATED BY ILEO-COLIC AORTIC ANASTOMOSIS

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Complete occlusion of the superior mesenteric artery usually results in necrosis of the small gut. If, however, the obstruction is not complete the blood supply, either direct or by anastomotic channels, may be sufficient to maintain the viability of the bowel, but not be adequate during periods of increased demand, as after meals. This inadequacy may result in postprandial pain sometimes associated with malabsorption (Shaw and Maynard, 1958). Dunphy (1936) used the term "abdominal angina" to describe the syndrome. He was the first to point out that such symptoms might be a premonitory signal to the development of massive infarction, commonly preceding it by three months and in some patients by as long as two years. Abdominal angina is difficult to diagnose and the proportion of patients in whom the diagnosis is established before the development of intestinal infarction is small. In the last few years various types of operation have been performed, with success in a few cases (Shaw and Maynard, 1958 ; Morris *et al.*, 1962). Recently we have treated a patient successfully by direct anastomosis of the ileo-colic artery to the aorta. This particular type of by-pass operation does not seem to have been used before.

Case History

A 54-year-old labourer was admitted to hospital in November, 1961, for investigation of the symptom of diffuse abdominal pain. The pain was of two months' duration, worse immediately after meals, eased slightly by lying down, but was never completely relieved. Vomiting of food occasionally occurred at the height of the pain and recently there had been intermittent diarrhoea with up to eight motions a day. Neither vomiting nor defaecation relieved the pain. There was a 10-year history of angina pectoris and a three-year history of intermittent claudication.

Examination revealed a thin man looking older than his years. Blood-pressure 170/80 ; in the lower limbs no pulse was palpable distal to the femoral arteries. There was a systolic bruit over the central abdomen and both groins, but otherwise the abdominal examination was negative.

Investigations.—Faecal fat excretion: 11 g./day (three-day mean on a normal ward diet). Electrocardiogram: old anterior myocardial infarction with recent ischaemic changes. Glucose tolerance test: blood-sugar levels, 93, 144, 166, 173, and 160 mg./100 ml. fasting and at half-hourly intervals after ingestion of 50 g. of glucose. Other investigations, including barium studies of the stomach and small and large bowels, showed nothing abnormal.

In hospital severe pain was present after every meal and was not relieved by atropine, trinitrin tablets, or propantheline. The patient refused to eat more than a very small meal because of the pain. That the pain probably originated in the small intestine was demonstrated when an attempt was made to study motility by a method involving the passage of a Cantor tube. The tube was anchored by strapping to the patient's cheek. When it became taut he experienced an intense exacerbation of his pain, relieved by releasing the strapping.

Aortography showed that the superior mesenteric artery was very narrow and irregular, in its proximal 3 cm. being only 1–2 mm. in diameter. The few vessels supplying the small bowel were small in calibre and showed reduced linear flow rate. The inferior mesenteric artery was patent and had an unusually large left colic branch. The branches of the coeliac axis were substantially normal. Both renal arteries were narrow at their origins.

The patient's symptoms increased in severity so that in addition to the postprandial symptoms he complained of severe and constant abdominal pain. Because of the severity of the pain laparotomy was performed.

Operation.—Laparotomy on January 21, 1962, revealed that the small bowel was abnormally pale. No area of infarction was seen. No pulsation was seen or felt in the vessels of the small gut, although there was very little fat in the mesentery. The middle colic and right colic arteries also showed no sign of pulsation. A hard calcified area 3–4 cm. long was palpable in the superior mesenteric artery extending from its origin to a point just distal to the middle colic artery. The inferior mesenteric artery showed well-marked pulsation which extended to the sigmoid branches. The ileo-colic artery was 4 mm. in diameter and free of palpable atheroma. Arteriotomy revealed only poor retrograde flow. Direct side-to-side anastomosis was performed between the ileo-colic artery and the aorta over a length of 1.5 cm. at a site in the aorta distal to the inferior mesenteric artery (see Diagram). On release of the clamps good pulsatile flow was seen in the ileo-colic artery, and before closure of the abdomen pulsation was visible throughout the mesentery of the gut. The bowel returned to the normal pink colour.