DIAGNOSIS AND MANAGEMENT OF TRICHOMONIASIS IN MEN AND WOMEN*

BY

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Trichomonas vaginalis is commonly found in the genito-urinary tracts of men and women. Studies of different groups of women have shown an incidence varying from nil in virgins (Jírovec, Breindl, Kučera, and Šebek, 1942) to high levels in sexually active women presenting with vaginal discharge. Buxton, Weinman, and Johnson (1958) found no evidence of trichomoniasis in 157 female undergraduates of whom only 10 were married, but they found that 70 per cent. of 221 female prisoners were infested; 6·3 per cent. of married female employees of an insurance company were found to be infested compared with 1·4 per cent. of unmarried female employees.

In the Whitechapel Clinic during the year beginning July 1, 1960, routine tests for trichomonal infestation were positive in 449 (31·5 per cent.) of 1,424 women and in 92 (5·6 per cent.) of 1,646 men with non-gonococcal urethritis (Wisdom and Dunlop, 1965). Search for *T. vaginalis* is therefore of importance in the investigation of patients exposed to sexually transmitted disease. The diagnosis is made by finding *T. vaginalis* in wet smear or in culture.

Investigation of Women

Smears.—Material taken by gently scraping the mucosal surface of the posterior fornix of the vagina with a sterile platinum loop is mixed with an equal quantity of normal saline on a slide. Specimens may be taken from the urethra or other sites using a similar technique. A cover-slip is placed on the slide and the specimen examined microscopically using a $\frac{1}{8}$ -in. objective with the iris-diaphragm partly closed, or using a $\frac{1}{2}$ -in. oil-immersion objective and dark-field illumination. The parasite is recognized by

the presence of jerky movements from the four flagella which protrude from the blunt end of its pear-shaped body. The organism measures from 10 to 30 microns in length. Gentle warming of the slide may facilitate identification by increasing the motility of the parasite. It is important that specimens should be examined immediately after they have been taken because movement may soon become sluggish or cease. Repeated smears may be necessary to find the parasite, particularly in the cases of patients who have been douching or using other local therapy. All such treatment should stop during investigation for trichomoniasis.

Cultures.—When the presence of *T. vaginalis* is suspected, but cannot be demonstrated in wet smears, material for culture may be obtained by rubbing a Stuart's swab (Stuart, Toshach, and Patsula, 1954) on the mucosa of the vaginal vault or the urethra, or by soaking it in discharge from para-urethral glands or Bartholin's ducts. The swab is then placed in a bijou bottle of appropriate culture medium (Feinberg and Whittington, 1957; see Appendix). Alternatively, material may be obtained by gentle scraping with a sterile platinum loop and placed in the culture medium, or by scraping with a sterile mustard-spoon on a holder; the spoon and the material it contains are then placed in a tube of the medium. In addition, the first 20 ml. of urine should be collected in a sterile container. This urine should be either centrifuged or filtered. If it is to be centrifuged, this should be carried out at about 1,500 r.p.m. for five minutes and the deposit then withdrawn with a pipette before the supernatant fluid is poured away. The culture medium should be inoculated with a drop of the deposit, and a further drop used for making a wet smear. If a centrifuge is not available, the urine should be filtered through a

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small funnel (approximately 3 in. in diameter) containing a plug of sterile cotton-wool. After filtration the plug is removed with sterile forceps; a wet smear should be made by squeezing a drop from the plug on to a slide, and the plug is then placed in a tube of culture medium.

Investigation of Men

Smears.—Even if there is no urethral discharge, a wet smear made by gentle scraping of the urethra with a platinum loop should be examined. If the patient is uncircumcised a similar wet smear should be made from the sub-preputial mucosa.

Cultures.—If trichomoniasis is suspected, but the parasite cannot be found in smears, material should be obtained from the mucosa of the urethra, and also from the sub-preputial sac if the patient is uncircumcised, using a Stuart's swab or a platinum loop. This material should then be cultured in Feinberg-Whittington medium.

Further Investigations.—Should these tests show no evidence of infestation in men suspected of harbouring the parasite, the urethra should be re-examined and tested by wet smear and culture after the urine has been retained overnight. A series of wet smears of the fluid obtained by massage of the prostate and seminal vesicles (Oates, 1958) should also be examined microscopically. After the massage the urine is voided and the first 20 ml. collected and filtered. A drop from the filter-plug is examined by wet smear and the filter-plug then cultured in Feinberg-Whittington medium, as described above.

Treatment

(1) *By Mouth.*—Metronidazole ("Flagyl", May & Baker) has proved highly effective since successful clinical trials were first reported by Durel, Roiron, Siboulet, and Borel (1959, 1960). Toxic reactions so far reported have been few and slight, taking the form of mild gastro-intestinal disturbances, dizziness, or transient skin rashes. Rodin, King, Nicol, and Barrow (1960) reported depression of the blood polymorphonuclear leucocyte count in 3 of 41 cases in which serial white cell counts were done. The depression was asymptomatic and reversed spontaneously. No case of agranulocytosis has yet been reported despite wide use of the drug. It is apparent, however, that this imidazole-ring compound should only be prescribed when clearly indicated. Indiscriminate use, without diagnosis and follow-up, should be avoided. Further studies of its effects on the bone marrow are required, and routine white cell counts of the blood should be performed

during prolonged or repeated courses of this drug. Although there is no evidence that metronidazole can cause foetal abnormalities it appears a reasonable precautionary measure at the present time to withhold the drug in the first trimester of pregnancy (*Lancet*, 1963).

One tablet (200 mg.) 3 times a day after meals for 7 days produces an immediate cure rate of 90 per cent. or more in both men and women, and follow-up studies have shown that some 70 to over 90 per cent. of patients observed for three months or more after treatment have remained free from infestation (Csonka, 1963; Rodin and others, 1960; Watt and Jennison, 1962; Wisdom and Dunlop, 1965). It seems that many of the apparent failures that occur are due to re-infestation, which emphasizes the importance of the investigation of the sexual partners as soon as the diagnosis is made. Failure of treatment may be due to irregular or insufficient dosage, poor absorption, the presence of local structural abnormalities, or possibly infestation with a drug-resistant strain of *T. vaginalis*. Further research into this problem is needed.

(2) *Local.*—Antiseptic douches and pessaries of many kinds have been employed, but relapses are common. Such treatment is unlikely to be permanently effective because it cannot be applied to all sites of infestation. About 75 per cent. of women suffering from trichomonal vaginitis have, in addition, infestation of the lower urinary tract, and related glands may be affected (Whittington, 1957). Local treatment is applied to the vagina and, when discontinued, re-infestation of the vagina from adjacent structures is likely. Of all the preparations used, acetarsol pessaries ("S.V.C.", May & Baker), have the advantage of being cheap, and they are strongly trichomonocidal. Toxic reactions are rare but even minimal dosage, in patients sensitive to arsenic, may cause severe illness. Death has been reported (Bowen, Lewis, and Edwards, 1961). Local treatment is often unsuccessful for men because inaccessible sites such as the prostate or seminal vesicles may be affected. Trichomonal balanoposthitis may be treated by careful washing of the sub-preputial sac with soap and water twice a day, careful drying, and then applying a preparation such as "Penotrane" (Ward Blenkinsop), which is an organic mercurial compound, in the form of ointment or dusting powder for a period of 10 days; alternatively, the sub-preputial sac may be irrigated with Lotio Hydrarg. Perchlor. 1/8,000. Even in these apparently uncomplicated cases, however, systemic treatment with metronidazole is to be preferred to local therapy because of the difficulty of excluding

infestation of a site inaccessible to local measures. Urethral stricture is often found in association with trichomonal urethritis in males (Allison, 1943; Hancock, 1959); in such cases dilatation of urethral strictures is an essential part of treatment.

(3) *Sexual Contacts*.—Sexual contacts of patients with trichomoniasis should be investigated as outlined above. If *T. vaginalis* is found, treatment should be given to both partners, preferably concurrently, before permission is given to resume sexual intercourse. If, after full investigation, *T. vaginalis* cannot be found in the sexual partner many clinicians nevertheless offer the partner a course of metronidazole as a precautionary measure. However, there is no evidence at this time to indicate that such a course, given to a consort in whom exhaustive tests have shown neither *T. vaginalis* nor evidence of “non-specific” genital infection, reduces the incidence of recurrence in the infested partner. Further work on this problem is needed.

Follow-up

Patients should be advised to refrain from passing urine for at least three hours prior to each attendance.

Women

(1) At the end of treatment a wet smear of vaginal scrapings is examined microscopically and a culture is made from vaginal material. A wet smear and a culture may also be made from the urine.

(2) Fourteen and 21 days after the start of treatment, and after the succeeding menses (or at monthly intervals) until three months have elapsed, wet smears of vaginal scrapings are examined microscopically.

(3) Three months after the start of treatment final tests are completed by repeating the procedure carried out at the end of treatment.

Men

(1) At the end of treatment a wet smear of urethral scrapings is examined microscopically and a urethral culture is made.

(2) Fourteen days after the start of treatment a wet smear of urethral scrapings is examined microscopically.

(3) Twenty-one days after the start of treatment a wet smear of urethral scrapings, and wet smears of the prostatic-vesicular secretions, are examined microscopically. Cultures are made of urethral material and of urine. Urethroscopy is required if there was any evidence of urethritis, prostatic-vesiculitis, or urinary infection before treatment, or

any history of these conditions without subsequent urethral examination.

(4) At monthly intervals until three months after the start of treatment a wet smear of urethral scrapings is examined microscopically.

(5) Three months after the start of treatment final tests are completed by repeating the procedure carried out at the end of treatment.

Failure of Treatment

Failure may be due to the fact that treatment has not been followed as prescribed or to re-infestation from a sexual partner. These possibilities should first be excluded. In patients who have been treated with local measures only, failure may be due to re-infestation from sites inaccessible to local therapy and systemic treatment with metronidazole is indicated.

In patients who have already been treated with metronidazole in adequate dosage, whose consorts are not infested, and who have no anatomical abnormality such as urethral stricture in the male, further studies are indicated. The level of metronidazole in the blood should be estimated during therapy, to determine whether effective levels of the drug are being attained; the sensitivity to metronidazole of the infesting trichomonad should also be measured. In the absence of this information further treatment is empirical. Re-treatment with metronidazole has proved successful using the same daily dosage as before, either for the same period or for 10–14 days, or using a higher dosage such as 800 mg. to 1 g. daily for 7–10 days. In women the use of vaginal pessaries of metronidazole concurrently with tablets by mouth has also proved effective in some cases.

In the rare cases where systemic metronidazole cannot be used it is advisable to render the urine alkaline, for example, by means of Potassium Citrate Mixture BPC by mouth throughout the duration of treatment with local remedies. For local treatment of women two acetarsol pessaries (“S.V.C.”, May & Baker) may be inserted nightly for two to four weeks, and the patient should attend weekly for observation during this treatment. For men with trichomonal urethritis, daily urethrovaginal irrigations may be given for 10 days with a solution of 1 in 10,000 oxycyanide of mercury or of potassium permanganate 1 in 10,000. If trichomonads are found in the prostatic-vesicular fluid, daily irrigations should be used for two weeks and, on two occasions in each week, the irrigations should be preceded by massage of the prostate and seminal vesicles. The treatment of trichomonal balanoposthitis has already been considered.

Summary

Investigations to detect the presence of *Trichomonas vaginalis* in men and women are outlined.

Management and treatment are discussed. The most successful therapy is systemic, and a course of metronidazole by mouth, 200 mg. 3 times a day for 7 days, is recommended. Sexual consorts must be investigated, and treated where necessary; the treatment of sexual partners should be concurrent.

Follow-up and the management of patients in whose cases treatment has failed are discussed.

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APPENDIX

Laboratory Techniques

(1) Cultures

(a) *Preparation*.—Two points must be emphasized:

- (i) after inoculation, tubes of culture medium should be placed in an incubator with as little delay as possible; (ii) the larger the inoculum the greater is the chance of growing trichomonads when the infestation is light.

The tubes of culture medium should have cotton-wool plugs and should be warmed to blood heat before inoculation; 4 ml. of the medium is a convenient quantity to receive several loopfuls of vaginal material or the deposit from centrifuged urine or the cotton-wool plug from filtered urine.

The inoculated tubes are cultured at 35–37°C. for 5 days.

(b) *Examination*.—After incubation for 2 days the cultures are centrifuged at about 1,500 r.p.m. for 5 minutes; a drop of the deposit is taken from each tube with a pipette, placed on a clean slide, and covered with a cover slip. This wet smear is then examined microscopically. If no trichomonads can be found in a 2-day-old culture, incubation should be continued and the examination repeated after a further 3 days. It is important to remember that if a culture contains only a few trichomonads, these may escape detection in a sample taken without adequate centrifugation.

(2) Transport of Specimens

Trichomonads will remain alive in moist secretion at room temperature for several hours. If facilities

for microscopical examination are not immediately available, the interval between taking the specimens and examining them is likely to be longer than this. In such cases a swab impregnated with the material to be tested can be placed in Stuart's transport medium (Stuart and others, 1954) and sent by post to the laboratory. The swab should be received within 48 hours of inoculation. It is removed from the Stuart's medium with sterile forceps and placed in a tube of Feinberg-Whittington medium, which is then incubated in the usual way. Before centrifuging these cultures prior to microscopy, liquid should be squeezed out from the swab into the culture medium and the swab discarded.

(3) Preparation of Feinberg-Whittington Medium

Proteolysed liver BPC	..	25.0 g.
Sodium chloride	..	6.5 g.
Dextrose	..	5.0 g.
Inactivated horse serum	..	80.0 ml.
Distilled water	..	1,000 ml.
Penicillin	..	1,000,000 units
Streptomycin	..	500,000 units

The solid components are dissolved in the distilled water, the horse serum is added, and the pH is adjusted to 6.4 with N/1NaOH. The medium is sterilized by Seitz-filtration and distributed in about 4-ml. amounts in sterile 3 in. × $\frac{1}{2}$ in. plugged tubes or in sterile bijou bottles. It should be stored in a refrigerator at 4°C. Under these conditions the medium keeps for at least three months.

**Diagnostic et traitement de l'infestation à trichomonas
chez l'homme et la femme**

RÉSUMÉ

On expose les procédés de détecter le trichomonas vaginalis chez l'homme et chez la femme.

Le traitement le plus efficace est par voie générale et on recommande une cure de metronidazole oral: 200 mg., 3 fois par jour, pendant 7 jours. Les partenaires sexuels doivent être traités en même temps.

On discute la façon de suivre et de traiter les malades chez qui cette thérapeutique a échoué.