5. It is our impression that labour is stimulated by this technique; the contractions appear more frequently, last longer and are apparently stronger.

6. The average time of decompression (from 4 cm. or less to full dilatation) was 2 hrs. 56 minutes for primigravidas and 1 hr. 57 minutes for multigravidas.

7. All patients aided in labour by this method of decompression were carefully examined at delivery, to exclude any possible damage to the genital tract. Only one case of cervical laceration was found. This was associated with a forceps delivery and manual removal of a trapped placenta.

### SUMMARY

The principles of abdominal decompression have been discussed. A new method for decompression, using a thermoplastic chamber that fits over the breasts and abdomen, has been described. The technique gives very definite relief of pain. Sedation was not required in 45% of the cases, while in the remainder it was minimal. The first stage of labour was markedly accelerated in primigravida, and to a lesser extent in multigravida. The results are very encouraging and we feel that further trial is warranted, as this method of decompression may be a very important addition to our conduct of the first stage of labour.

We are indebted to the assistance given us by a number of people. We wish to thank: Mr. E. Lash of Transparent Garment Cover Co., Montreal, for supplying the plastic suits; Fischer Scientific Co. Ltd., Montreal, for the original vacuum pump and accessories; Canadair Ltd., who helped design and constructed the decompression dome; and Electrolux (Canada) Limited for supplying model Z-86 vacuum cleaner.

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# UROGENITAL TRICHOMONIASIS IN THE MALE: REVIEW OF THE LITERATURE AND REPORT ON TREATMENT OF 37 PATIENTS BY A NEW NITROIMIDAZOLE DERIVATIVE (FLAGYL)\*

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### INTRODUCTION

THE HUMAN habitat for Trichomonas vaginalis (Donné) is not limited to the vagina, for as early as 1883 Künstler<sup>51</sup> noted its presence in the female urinary tract. Eleven years later, Marchand<sup>57</sup> (Harburg) found the parasite in the male urogenital tract, and this was confirmed in the same year by Miura<sup>58</sup> (Tokyo) and Deck<sup>28</sup> (Ann Arbor), who found Trichomonas in the urethra and prostate.

Some decades went by before subsequent publications appeared. Among them may be mentioned those of Riba,<sup>65</sup> Smith,<sup>71</sup> Stuhler,<sup>73</sup> Allen,<sup>5</sup> Ackermann,<sup>4</sup> Drummond,<sup>29</sup> Rodecurt,<sup>67</sup> Cornell and Riba<sup>22</sup> and Karnaky.<sup>42</sup>

Chief credit is due to Bauer,<sup>8</sup> who reopened the study of the problem and who, by his magnificent presentation at Monaco,<sup>10</sup> drew the attention of the medical world to this disease, showing the importance of infestation and proving by remarkable world-wide figures that the incidence of trichomoniasis in the male was drawing close to its incidence in the female. The question was put on the agenda at the First European Symposium on Trichomonas Infestations held in Reims in 1957,<sup>2</sup> and again at the First Canadian Symposium on Non-Gonococcal Urethritis and Human Trichomoniasis, in Montreal in 1959.<sup>3</sup>

In any current study of urogenital infection by the Trichomonas, acknowledgment is due to many previous contributors to our knowledge in this field.<sup>2</sup>, 6, 8-11, 15-18, 20, 21, 24-26, 30-37, 40-44, 46-50, 52, 53, 55, 64, 67-70, 72, 76-80

### THE PARASITE

Trichomonas vaginalis is a flagellate protozoan with three to five anterior flagella, the piriform pattern of which in a fresh smear is highly characteristic. The blepharoplast from which the flagella, the undulating membrane and the axostyle originate is at the bottom of a small invagination of the cellular body situated at the point where the nucleus is closest to the periphery. The nucleus is oval and about 4 to 5  $\mu$  long, with its major axis in a radial direction; it always separates the axostyle from the undulating membrane. There are also numerous uniformly distributed chromatin grains.

When examining a *fresh smear* on a slide, the mobility of trichomonads can be observed, its zigzag movements disturbing the surrounding morphological elements.

### INCIDENCE OF TRICHOMONIASIS

According to some authors<sup>10, 35</sup> the incidence of trichomoniasis in the male approaches that of the female.

Table I shows the incidence of Trichomonas urethritis as reported by various authors. The

<sup>\*</sup>From the Department of Venercology, Notre-Dame Hospital, Montreal, and Department of Urology, Verdun General Hospital.

TABLE I.—INCIDENCE OF TRICHOMONAS URETHRITIS

Authors	Year	Incidence of Trichomonas urethritis*
· · · · · · · · · · · · · · · · · · ·		Percentage
Liston and Lees	1940	14.3
Allison	1943	15.0
Roth	1944	13.0
Whittington	1951	15.3
Sorel	1952	9.0
Lancelev.	1953	5.8
Ackermann	1953	16.0
Durel et al.	1954	12.15
Bauer	1954	30.2
Coutts and Silva-Inzunza	1955	68.0
Feo and Fetter	1956	41.0
Nicol	1957	5.5
Harkness and King	1957	15.3
Jira	1957	8.7
Durel	1959	10.4
Svlvestre, Gallai and Ethier	1959	10.8
Catterall	1959	11.0

\*Per cent of cases of non-gonococcal urethritis.

highest incidence is that given by Coutts and Silva-Inzunza,<sup>24</sup> who found the Trichomonas to be the causative agent in 68% of their patients with nongonococcal urethritis.

It is also interesting to note the number of cases of Trichomonas urethritis in the mates of women with Trichomonas vaginitis. Karnaky<sup>42</sup> found the parasite in the male mates in 25.33% of the cases, Jira<sup>40</sup> in 32%, Young<sup>80</sup> in 21.2%, Bauer<sup>10</sup> in 21.9%, Bedoya<sup>12</sup> in 76% and Siboulet<sup>70</sup> in 80%. Netter<sup>59</sup> states: "When I looked for trichomonads in the urethra of the husband, I found it in 9 cases out of 10."

It is extremely important to search systematically for Trichomonas in the husbands or mates of infected females and in males with either urethritis or prostatitis. These examinations must be very thorough and should be made not only of the urethral drop but also of the prostatic secretion (after massaging) and of the sediment from the centrifuged urine.

### METHOD OF TRANSMISSION

It can be stated that nearly all authors agree that contamination of the male takes place through sexual intercourse and that Trichomonas urethritis in the male should be considered a venereal disease.<sup>8</sup>,  $^{30}$ ,  $^{45}$ ,  $^{60}$ 

The following may be given as arguments in favour of contamination by sexual intercourse as the mode of spread and of the pathogenic role of *Trichomonas vaginalis*:

1. Appearance of urethritis in the male after sexual intercourse with a mate harbouring T. vaginalis.

2. Recurrence of discharge in the male after a reappearance of *Trichomonas vaginitis* in the mate.

3. Examination of the mates of males with Trichomonas urethitis shows that the incidence of Trichomonas vaginitis is close to 100%.<sup>12, 40, 62</sup>

Cure is effected only when the couple is freed from the parasite.

4. Trichomonas urethritis has been produced by local inoculation.<sup>9, 38, 53, 76</sup>

### CLINICAL SIGNS

In acute Trichomonas urethritis the same symptoms are occasionally noted as in gonococcal infection, namely a burning sensation on micturition, abundant discharge throughout the day and completely cloudy urine in both glasses in the twoglass test, but the discharge due to Trichomonas urethritis is not as thick or as yellowish: it is milky and more fluid.

On the other hand, in the majority of cases the clinical signs consist merely of slight mucopurulent discharge in the morning with a few filaments in the first glass of urine. Durel<sup>34</sup> emphasizes the milky nature of the discharge, which is a favourable clinical sign, but which is neither constant nor pathognomonic.

According to Lewis and Carroll<sup>54</sup> and Liston and Lees,<sup>55</sup> other Trichomonas manifestations may be seen, such as cystitis or even pyelonephritis. Bauer<sup>10</sup> found in the literature 177 cases of Trichomonas cystitis.

According to Roth,<sup>68</sup> balanitis is not rare in men with a long prepuce and he has found the parasite in the collum glandis penis.

The question of prostatic involvement was raised by Drummond,<sup>29</sup> who examined the prostatic secretion of five mates of females harbouring *Trichomonas vaginalis*, by withdrawing the fluid by puncture through the perineum; he found the parasite in four of them. Coutts *et al.*<sup>25</sup> noted three cases of Trichomonas prostatitis; Kostic<sup>48</sup> found Trichomonas in the prostatic secretion of only 24 of the 142 cases examined. On the other hand, Bauer<sup>11</sup> reports prostatic involvement in 41.5% of the cases. In our clinic, we found the prostate to be infected in 10 of 35 cases of Trichomonas urethritis; seven of these we considered to be cases of Trichomonas urethritis and prostatitis, and three of Trichomonas prostatitis only.

The proof that we were actually dealing with Trichomonas prostatis is as follows: (1) We never found trichomonads in the urethral secretion. (2) No trichomonads were found in the urine or in the sediment after centrifuging. These two control tests were made not only by examining material in the fresh condition but also by culture. (3) We consistently found trichomonads after prostatic massage in either the first four or five prostatic drops. (4) The patients complained of prostatic symptoms. (5) After Flagyl therapy, disappearance of trichomonads from the prostatic secretion and remission of symptoms were noted

Young<sup>80</sup> found Trichomonas in 53 cases out of 2500 in the centrifuged urinary sediment. We ourselves have found it in 6 of 35 cases by this technique.

# LABORATORY DIAGNOSIS

Three methods are used for detection of *Tri*chomonas vaginalis:

### 1. Examination of the Fresh Smear on a Slide

This examination requires great patience, as very frequently Trichomonas can be detected only after several minutes of observing for mobility or the least movement of its flagella.

Sampling must be done in the morning before the first micturition. The drop obtained is placed directly on a warm microscope slide, but if the secretion is thick it is preferable to dilute it with normal saline. This examination must be made immediately. If it is not possible to examine the morning discharge, the secretion obtained by prostatic massage should be examined. (In one of our patients we found the parasite only in the fifth prostatic drop.) When the above examinations are negative, the sediment from the centrifuged urine must be examined for Trichomonas. It was by this method that we found the protozoan in six of our patients.

If this first method fails to reveal the presence of Trichomonas, the second (staining) or third (culture) method should be used.

# 2. Staining

With this method it is possible to detect the presence of motionless Trichomonas, to send the smears to a specialized laboratory, and finally to diagnose Candida (Monilia) infestation. This method is more reliable than examination of the fresh smear. The May-Grünwald-Giemsa stain is used; Trichomonas is identified as a 10 to 20  $\mu$  cell with blue cytoplasm having a small elongated nucleus flanked by a blepharoplast.

Another stain that is used is the Papanicolaou stain. This, according to Rom and Demol, does not give better results than direct examination. The Papanicolaou stain is used routinely at the Hôtel-Dieu Hospital in Montreal.

# 3. Culture

Culture is the most accurate method. Its only drawback is that it takes two to three days to obtain the results. However, the method is simple and in an appropriate culture medium there is an abundant growth of the parasite.

There is a wide variety of culture media. We use the media prepared by the Ministry of Health of the Province of Quebec or by the Institute of Microbiology and Hygiene of the University of Montreal.

# TREATMENT AND RESULTS

Until recently the treatment of Trichomonas urethritis and prostatitis required several months and the results obtained were very irregular. In addition to systemic administration of such drugs as acetarsone (Stovarsol) or quinacrine, topical therapy was essential. The latter consisted either in introduction of urethral conessine jelly into the urethra after each micturition or of two to three instillations daily of a solution of methylene blue, mercurochrome, pentavalent arsenic or potassium permanganate.

Our attention was quite recently drawn to certain antibiotics and to aminonitrothiazole derivatives. Pätiälä and Vara<sup>61</sup> suggested the use of the tetracyclines; Jirovec<sup>41</sup> recommended Thiolutin; and Chappaz<sup>21</sup> advocated gramicidin and endomycin; but the results have proved unsatisfactory.

In 1954 Hosaya<sup>39</sup> isolated trichomycin, which proved highly active *in vitro* against *Trichomonas vaginalis*. This *in vitro* activity was accepted by Bertrand,<sup>14</sup> Catterall<sup>17</sup> and others, but its *in vivo* activity did not give the expected results.

Catterall<sup>17</sup> treated six patients for 14 days with a dosage of 300,000 units of trichomycin daily; Bedoya and Fernandez-Ortega,<sup>13</sup> two patients with 150,000 units daily for 10 days; and Bauer,<sup>11</sup> seven patients with 300,000 to 700,000 units daily for 14 to 24 days. All these patients continued to harbour the Trichomonas. Durel and Siboulet<sup>3+</sup> treated 17 males and obtained only one straightforward and lasting cure. In a previous publication<sup>7+</sup> we mentioned 14 cases of Trichomonas urethritis treated by trichomycin at various dosages. In this group we obtained only two cures.

Another preparation, which did not give any better results, is Tritheon (2-acetylamino-5-nitrothiazole, or aminitrozole). The in vitro, and even in vivo trichomonacidal action of this compound was discovered by Cuckler, Kupferberg and Millman.27 Its in vitro trichomonacidal activity was confirmed by Cavier et al.<sup>19</sup> and by Catterall.<sup>18</sup> Perl, Guttmacher and Raggazoni<sup>63</sup> treated 28 males with Tritheon by the oral route. Of the 28, 10 were not seen again, but Trichomonas had disappeared in 18. The dosage used was 300 mg. daily for 10 days. With the same dosage, Catterall and Nicol<sup>18</sup> treated, unsuccessfully, six cases of Trichomonas urethritis. Finally, Barnes<sup>7</sup> has reported disappointment with the results of her preliminary trials. The clinical results obtained with these preparations were therefore unsatisfactory.

Investigations were continued, and Cosar and Julou<sup>23</sup> finally developed a new nitroimidazole derivative which proved extremely potent both *in* vitro and *in vivo* against *T. vaginalis.* It is l-(2'hydroxyethyl)-2-methyl-5-nitro-imidazole, also known as RP 8823 or Flagyl.\*

The acute toxicity for the mouse is very low, the oral 50% lethal dose being 4.35 g. per kg. Durel *et al.*<sup>32-33</sup> studied the trichomonacidal activity of the serum and urine after ingestion of a single dose of 500 mg. of Flagyl and found that a 1:10 dilution of human serum prevented the growth of Trichomonas for at least  $1\frac{1}{2}$  hours; the urine seemed

<sup>\*</sup>Product of Poulenc, Ltd., Montreal.

TABLE II.—RESULTS OF TREATMENT WITH FLAGYL

	Trichomonas urethritis	Trichomonas urethritis and prostatitis	Trichomonas prostatitis	Urethritis without Trichomonas but mate harboured T. vaginalis	Total	
Disappearance of Trichomonas and of all clinical signs Disappearance of Trichomonas but persistence of a few	20	7	3	, ,,,, ,, _, ,, ,	30	
filaments in the urine	1	1		5	$\frac{2}{5}$	
Total	21	8	3	5	37	

to reach its peak activity towards the fourth hour, and it was trichomonacidal at dilutions of 1:100 to 1:1000. This finding is highly important, as this is the only compound which imparts a high trichomonacidal activity to the serum and urine.

Durel et al. <sup>32,33</sup> were the first to use Flagyl in the treatment of trichomoniasis in the male and female. They treated 13 patients who had Trichomonas urethritis and obtained 13 cures. In an earlier publication we mentioned 15 cases of Trichomonas urethritis and prostatitis which we treated by Flagyl. Cure was obtained in every case. Treatment consisted in the administration of one 250-mg. Flagyl tablet twice daily, in the morning and evening, for 10 days.

In the present study we have been treating 37 cases of Trichomonas urethritis and prostatitis. Table II shows that in every case, at the abovementioned dosage, disappearance of trichomonads was noted. In only two cases a few filaments remained in the urine. All the patients treated were therefore cured.

### DISCUSSION

The results are extremely interesting as this is the first time that such a series of cures has been obtained. The results were rigidly controlled by examination of fresh smears on slides and also by culture.

Table III shows that in 10 cases control was continued for more than three months.

TABLE III.-FOLLOW-UP CONTROL

И	'eek	8	of	fa	olle	ou	y-1	ıŗ	) (	co	n	tre	ol				1	V	ur	n	be	r	Q	f e	case	3
2 4	•••	· ·	•••	•••	•	•••	•	•••	:			•	•	 •	·			•			•	•	•	•••	; 1(	3
8 12	2 or	n.	 no	re		•••	•	•••		 			•		•	•••			•••		•	•	• •	•	14 10	ł )

The duration of the infection is also of interest. One of the patients had been suffering from urethritis and prostatitis for 18 years and after this treatment he was completely cured.

We attribute such remarkable results first of all to Flagyl, and also to the fact that in no instance did we neglect to locate the source of infection. In this way, we found the mates of 25 of our 37 patients and treated the two partners simultaneously. It is essential not to neglect the source of

contamination and to try by every possible means to locate the mate. In five cases (see Table II) we found T. vaginalis in the female partner only, but in the male partner there was morning discharge with filaments in the urine. In spite of the absence of the parasite we treated these patients with Flagyl and the clinical symptoms disappeared.

TABLE IV.—DURATION OF INFECTION

0 to 6		22
$6  ext{ to } 12 \dots \dots \dots \dots \dots \dots \dots \dots \dots \dots$		8
12 or more	• • • • • • • • • • • •	7

No intolerance to the drug was noted. No patients complained of gastrointestinal troubles or of any other side effects. In eight patients, differential blood counts were made before and 10 days after treatment, and no changes were noted.

### SUMMARY

Of 32 patients with Trichomonas urethritis and prostatitis treated by Flagyl the authors noted the disappearance of Trichomonas in all, and in 5 other patients with urethritis without Trichomonas the clinical signs disappeared. These results fully confirm those obtained by Durel et al.32-33

In our opinion, Flagyl is the most effective therapy for combating Trichomonas in the male urogenital tract.

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# L'EMPLOI DU METHOCARBAMOL DANS LE TETANOS ABORD EXPERIMENTALE ET CLINIQUE

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LE MÉTHOCARBAMOL<sup>‡</sup> a été employé pour la première fois dans le traitement du tétanos, chez un cheval du nom de Morgan.<sup>1</sup> Après quatre jours de traitements, l'animal, de couché qu'il était par les spasmes tétaniques, "s'est subitement levé et s'est précipité, la gueule grande ouverte, vers le coin de sa stalle où il s'est mis à manger avec vigueur".1

Par la suite, on a utilisé le médicament, apparemment avec succès, chez quelques humains.<sup>2, 3</sup>

On peut trouver à l'emploi du méthocarbamo! dans le tétanos, une justification pharmacologique: il semblerait bien, en effet, que la toxine tétanique déprime sélectivement l'inhibition pré-synaptique normale des neurones des réflexes pluri-synaptiques; ce qui permet ainsi à l'excitation pré-synaptique de prendre le dessus. Par contre le méthocarbamol déprime la transmission synaptique au niveau de ces mêmes neurones, diminue l'excitation pré-existante et amoindrit de ce fait les spasmes tétaniques.

TRAVAIL EXPÉRIMENTAL

Chez des lapins à qui nous avions administré environ 10,000 D.M.M. de toxine tétanique, nous avons injecté par voie intra-veineuse, 50, 75, 100 et 150 mg. de méthocarbamol par kg. de poids. La dose de 75 mg. par kg. nous a semblé la plus utile.\*

L'effet thérapeutique apparait après 15 minutes et diminue considérablement après 3 heures. Il se manifeste par une diminution en intensité et en fréquence des crises spasmodiques, par une plus grande facilité à mouvoir passivement les muscles en spasme et par un aspect plus naturel et plus éveillé de l'animal.

Nous avons aussi administré le méthocarbamol, soit localement dans le muscle en spasme, soit par voie intra-rachidienne: l'effet nous en a semblé beaucoup moins intense que par la voie intraveineuse.

Comme point de comparaison, nous avons aussi administré de la D-tubo-curarine, médication classique des spasmes tétaniques: à la dose de 0.6

<sup>\*</sup>Du Service de Médecine, Hôtel-Dieu, Québec. †Du Département de Bactériologie, Hôtel-Dieu, Quebec. ‡Fourni sous le nom de Robaxin par la maison A. H. Robbins.

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