Some workers believe that the most rapid method by which to test the bacteriostatic or bactericidal properties of a drug is to select the tuberculoid cases. I am of the opinion that this may lead to erroneous conclusions, because, as I have stated, I believe that if a drug is effective then a phase is experienced in which there is evidence that the *M. leprae* is stimulated into activity. In tuberculoid leprosy such a process, because the tissues are sensitized, would be manifested in an acute tissue response; the more marked this tissue response the quicker the subsidence of the disease. Hence a trial in tuberculoid leprosy will only indicate whether a drug has the property of stimulating the bacillus. I believe a very good example of this is a drug which was first prepared by Barry in Dublin, which has been reported on by Barnes (1951), and which has been given the code number of B.283. I recently had the privilege of examining patients taking this drug in Ogoja, Western Region of Nigeria. The majority of tuberculoid cases showed much improvement, whereas the results in the lepromatous cases were disappointing. In other words, this drug has some activity, but is not powerful enough to interfere with the multiplication of the bacilli and produce any great clinical improvement in lepromatous leprosy within a reasonable time. There are many drugs of this nature.

Conclusion

I trust I have given enough evidence to indicate that the therapy of leprosy is at present at a most interesting phase. If we have not reached the stage when we can claim to have achieved complete chemotherapeutic victory, we at least can look forward to the day, perhaps not too distant, when as a result of the combined efforts of the chemists, the pathologists, and the clinicians it can confidently be asserted that leprosy as an active process can be stopped and the long-awaited cure of this disease be realized.

Even though this satisfactory result be achieved, let us ever bear in mind that our conquest is not complete so long as stigmata and sequelae of leprosy, resulting in gross deformities, remain. The time has now come for the plastic and orthopaedic surgeon to step in and complete the cure, by repairing the ravages and damage which the disease has produced and our chemotherapeutic agents have stopped.

Summary

Evidence is given that before the discovery of the sulphone preparations hydnocarpus (*chaulmoogra*) oil was used effectively in the early lepromatous case, but the more advanced lepromatous cases showed little response.

A review is given of the sulphone drugs most commonly used, and the drawbacks of the parent sulphone are mentioned. The reasons why aqueous solapsone is not broken down to diaminodiphenyl sulphone are discussed, and there is evidence to show that D.D.S. may be detoxicated in the body to a substituted form.

The opinion of Payne is cited that the monosubstituted sulphones may be active *per se*, and that there are sound reasons for advocating the parenteral use of solapsone ("sulphetrone") in a 50% aqueous solution as an alternative treatment.

The possible mode of action of the sulphone drugs is outlined. In cases of toxicity or intolerance to sulphone therapy, thiosemicarbazone is held to be a good substitute, although not so active as the sulphones.

While streptomycin and P.A.S. are active in leprosy, these drugs are not effective enough to warrant their use. The hope is expressed that isonicotinic acid hydrazide may be found effective.

The criteria of activity of a given drug in leprosy are mentioned, and tests for a critical assessment of any drug likely to be effective in leprosy are detailed.

Finally, orthopaedic and plastic surgeons are reminded of the opportunities opened up to them in this field.

I should like to express my gratitude to Dr. S. R. M. Bushby, of the Wellcome Research Laboratories, Beckenham, for kindly reading this paper, and for his valuable help and advice in its preparation.

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AETIOLOGY AND INVESTIGATION OF VAGINAL DISCHARGE*

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Vaginal discharge is a common symptom and is often accompanied by fears that may be more distressing than the complaint itself, and thoughts of venereal disease or of cancer, for example, loom large, while feelings of guilt or uncleanness are reinforced by the patient's own repeated observations. The information is not, as a rule, volunteered, and to prescribe treatment, however impressive, without a convincing examination is to ignore a large part of the patient's real need. If a discharge is bad enough to treat it is bad enough to investigate; furthermore, empirical treatment prejudices accurate diagnosis later.

The Leucorrhoea Clinic

The busy gynaecological out-patient session is not suitable for properly assessing vaginal discharge, and there is a strong case, in any large unit, for segregating these cases, after preliminary examination, into a special clinic for the following reasons. (1) Investigation and treatment can be more deliberately carried out. All the necessary equipment is readily to hand and efficient organization becomes possible. (2) Most of the treatment involves repeated out-patient attendances only, and the other diagnostic clinics are relieved of a considerable load. (3) Better facilities are afforded for clinical research.

Such a clinic, known as the "D" clinic, has been in operation at the Chelsea Hospital for Women during the past five years, and the cases investigated to date number approximately 600. It is from these that the following figures are collected.

The patients are first seen in the out-patient department before being referred, and those in whom the discharge is found to be due to surgically amenable causes, such as gross degrees of chronic cervicitis, sloughing fibroid polyp, or neoplasm, etc., are of course admitted for appropriate treatment and do not reach the "D" clinic. If diabetes

*Read in the Section of Obstetrics and Gynaecology at the Joint Annual Meeting of the British Medical Association and Irish Medical Association, Dublin, 1952.

mellitus is found to underlie a case of monilial infection the patient is referred to the consultant physician, and cases of venereal disease are sent to special departments in general hospitals outside.

It is therefore the large group of patients with neither venereal nor surgical causes of vaginal discharge which are presented; they represent the majority of cases of vaginal discharge encountered in gynaecological practice.

Exclusion of Gonorrhoea

This is of prime importance. The early acute stages are easily recognized by the profuse discharge, acute inflammation of the vulva, particularly the duct orifices of Bartholin's glands, and the presence of pus at the external urethral meatus, elicited by pressure on the urethra. The cervix is angry-looking and oedematous, and a history of recent exposure to infection can usually be obtained.

Smear preparations, simply stained with dilute carbolfuchsin, show intracellular diplococci, and Gram staining clinches the diagnosis, for no other genital disease produces Gram-negative intracellular diplococci. Very occasionally Gram-positive diplococci may appear to be Gram-negative, having lost their staining reaction as a result of death of the micro-organism within the leucocyte. This source of error is eliminated by culture, from both cervix and urethra, on McLeod's chocolate-agar medium incubated for the first 18 hours in 10% carbon dioxide and thereafter for a further 24 hours in an ordinary atmosphere.

The colonies of gonococci are small, convex, and translucent, and flooding of the culture plate with a 1% solution of tetramethylparaphenylene diamine turns the colonies rapidly bright purple. This is known as the oxidase reaction. The gonococcal complement-fixation test, more applicable to cases of systemic infection, is, in any case, unlikely to be positive in under a month.

Exclusion of Malignant Disease of the Cervix.—If speculum examination reveals the possibility of malignancy Papanicolaou smears are taken and the patient is admitted for biopsy of the suspicious areas.

Clinical Classes of Patients Comprising the "D" Clinic

These have been grouped under four main headings (Table I). The largest number of cases are due to *Trichomonas vaginalis* infection, and form the hard core

TABLE I

Infection	No. of Cases
<i>Trichomonas vaginalis</i>	219 (37.4%)
Monilial	95 (16.2%)
T.V. and monilial	45 (7.7%)
Miscellaneous	196 (33.5%)
Insufficient information	30 (5.1%)
Total	585

of the clinic because chronicity readily occurs, eradication is difficult, and relapses are frequent. Even severe cases, however, continue in good general health.

Age Incidence.—Table II shows that the peak incidence occurs at 20–29 years—that is, when ovarian activity is in its prime and the vagina, in respect both of pH and squamous health, is more resistant to infection in general than at any other time.

TABLE II.—Age Incidence

Age	T.V.	Monilial Infection
Under 20 years	16	2
20–29	91	48
30–39	63	31
40–49	37	11
50 and over	10	2
Unspecified	2	1
	219	95

Aetiology of *Trichomonas Vaginitis*

This matter is enough, in the words of Keats, to "tease us out of thought." In the 219 cases there was a history of previous attacks in 73 (33%) and 80 (36.5%) gave a definite history of acute onset, whereas only 18 (8.9%) of those with monilial infections gave such a history. Clearly, certain factors must operate to set the inflammatory process alight.

The parasite is not necessarily pyogenic in its unaided effects, for it can be found in the healthy vagina without accompanying signs of discharge. Secondary infection with a miscellany of organisms helps to establish the characteristic punctate vaginitis, and some change in the vaginal environment is probably necessary to allow it to gain a foothold—for example, an alteration in pH from the normal 4.5 to the less acid levels of 5.5–6 which favour the infection. The effects of local trauma, as will be shown, also play a part, and suitable nutriment is also necessary for maintaining the trichomonads, either from the recurrent provision of menstrual blood or some alteration in vaginal chemistry.

Sexual intercourse, including abortive attempts which leave the female still technically a virgin, is one of the principal precipitating causes. No fewer than 15 of the unmarried women gave a history of developing the infection a few days after intercourse or an attempt thereat, including one unfortunate post-menopausal woman whose only adventure in this respect it had been. It is probable that there were many more who declined to volunteer such a history. Seventy-nine of the patients were unmarried, though many were by no means virgins and six had had at least one pregnancy. One unmarried girl showed the presence of trichomonads and spermatozoa as well, and another developed the disease after an abortion procured at three months.

Table III shows that, contrary to widely held belief, trichomonas vaginitis is no more a disease of married women than is monilial infection, the incidence being

TABLE III.—Marital State

	T.V.	Monilial Infection
Nulliparous (married and unmarried; no pregnancies) ..	103 (47%)	44 (44%)
Unmarried	79 (36.1%)	23 (25.3%)
Unmarried but parous	6 (2.7%)	2 (2.1%)
Unquestionably virgines intactae ..	12 (5.4%)	6 (6.3%)

roughly the same in both. Contraction of the infection by coitus is not, however, the whole story, because at least 12 (5.4%) of the 219 patients were virgins in both the letter and the spirit, and the disease has even been recorded in babies. Intercourse may infect direct through infected semen or the outpouring of cervical mucus, or the effects of local trauma may give the latent parasite its chance. Examination of the husbands of a few of the relapsing cases did not result in finding the trichomonads, although other workers report a significant incidence of male infection. The use of a condom contraceptive should give a high degree of protection, but 16 patients regularly used this method.

Table IV enumerates the methods used: roughly, the percentage of monilial infections in patients practising contraception was twice that of the trichomonal group. One would, however, hesitate to attribute the lower incidence in the latter to contraceptive practice on the evidence of so few cases.

TABLE IV.—Contraception

	T.V.	Monilial Infection
Sheath	16	15
Pessaries	10	6
Dutch cap and chemicals	7	5
Dutch cap, sheath, and chemicals ..	—	1
Unspecified	2	1
	35 (16%)	28 (29.5%)

Many believe that infection may be autogenous from the intestinal canal, since buccal and intestinal trichomonads are common; but these organisms are nevertheless morphologically distinct from the vaginal variety, and experimental inoculation of the vagina with the intestinal species does not reproduce the disease. Exogenous infection is restricted by the inability of the trichomonads to survive drying; but damp towels, wash-rags, and baths cannot be ruled out as possible sources of infection.

Careless nursing techniques must be a serious potential danger in gynaecological departments, and the not infrequent use of the same examining glove for successive patients, punctuated by ritual immersion in bowls of antiseptic, is highly reprehensible in this and other respects; it is a dangerous and slovenly practice which no shortage of gloves or nurses can adequately excuse.

However the organism reaches the genital tract, it would appear that some local alteration in environment occurs—as a result of intercourse, instrumentation, or menstruation—which favours its survival and endows it with pathogenicity.

The Relapsing Case

This is a vexatious mystery. Of the 219 cases of trichomonas vaginitis no fewer than 50 (22.8%) relapsed while still under observation, and a longer follow-up would reveal a great many more. This relapse rate is significantly higher than in cases of monilial infection, in which it was 16.8% over a similar period. One is encouraged to believe in the existence of an encysted form which can remain dormant until conditions are once more favourable. So far only pseudocysts have been found, which cannot be cultured back into activity. Autogenous reinfection from inadequately treated sites, such as Skene's and Bartholin's glands, the urinary tract, and the cervix, is probably often responsible.

Attention has been directed to the cervix, and Table V shows the association of cervical lesions in both trichomonal and monilial cases. Somewhere between one-quarter

TABLE V.—Association of Cervical Lesions

	T.V.	Monilial Infection
Erosion	43	20
Lacerated cervix and/or cervicitis	13	9
without erosion	1	—
Cervical polyp	—	1
Erosion and polyp	1	—
Amputated cervix	—	—
	58 (26.5%)	30 (31.6%)

and one-third of the cases had some clinical evidence of cervical disease, and although it is usually hard to find trichomonads in the cervical canal, unlike the common finding of monilial spores there, the increased alkaline flow of cervical mucus alters the environment at least in the upper vagina. It would therefore seem reasonable to treat associated cervical lesions energetically, as is our practice.

Relapses most often follow a menstrual period. Trichomonas vaginitis, moreover, is relatively uncommon after the menopause; in the present series there were only 13 cases. It is much less common than monilial infections as a cause of discharge in pregnancy, and both in pregnancy and after the menopause the disease is more readily mastered. These observations, taken together, encourage the view that recurrent menstrual blood favours the persistence of the infection.

On this basis we found that in favourable cases it was possible to restrict treatment to the menstrual and immediate post-menstrual phases of the cycle, thereby allowing the patient a welcome respite during the greater part of the intermenstrual phase, provided that smear examination was satisfactory in the post-menstrual week. This suppressive treatment is continued over a series of at least three menstrual periods.

Diagnosis of Trichomonas Vaginitis

The discharge is fluid, purulent, acid to litmus paper, and often contains little gas bubbles. In acute cases the vulva is inflamed and tenderness may hamper examination. The vagina may be diffusely reddened and lustreless, or there may be scattered red spots, particularly in the fornices and on the portio vaginalis of the cervix. This punctate vaginitis is better demonstrated by swabbing with hydrogen peroxide, whereupon the white froth tends to adhere to the spotty areas.

Antiseptics and lubricants are neither necessary nor advisable before collecting a specimen with a platinum loop for microscopy. A fresh wet preparation, using a small drop of normal saline on a moderately warmed slide and covered with a coverslip, is examined immediately, as the parasite is more easily recognized while still actively motile. The size of the organism is comparable to that of a leucocyte, and it is necessary to use the $\frac{1}{2}$ objective to identify the rapidly moving flagella and undulating membrane.

From both cervix and vagina wet and dry specimens are collected for laboratory confirmation, the former in sterile pipette tubes or already mixed with saline, and the latter as smears. Smears are also taken from the urethra. Throat swabs are not satisfactory because of drying. Delay in examination often results in failure to detect both trichomonads and gonococci because of the overgrowth of other bacteria, and in the case of the trichomonads motility may have ceased owing to cooling.

The importance of examining the fresh wet specimen immediately in the clinic and without relying exclusively on subsequent laboratory diagnosis is emphasized in Table VI.

TABLE VI.—Need for Both Clinic and Laboratory Diagnosis of T.V.

T.V. found in both clinic and laboratory	87
T.V. found in clinic but not in laboratory	94
T.V. found in laboratory but not in clinic	16
T.V. found in clinic and no laboratory examination made	21
No information	1

219

Pus/Squame Ratio as an Index of Severity of Infection and Progress.—Although trichomonads can be found in vaginal secretions in all three grades of the Schröder classification, ranging from high acidity and the almost exclusive presence of Döderlein's bacilli in Grade I to the least acid secretion and mixed bacteria, mainly pyogenic, in Grade III, it is in the latter grade that their presence denotes significant infection. A very simple test, now standard practice at Chelsea, is to make a rough estimate of the ratio of pus cells to squamous cells in a saline-drop preparation examined straight away under the microscope. For ease of comparison these ratios are expressed in fractions of 10. For example, a pus/squame ratio of 0/10 signifies very satisfactory progress, a healthy vaginal state, and a good prognosis, whereas a pus/squame ratio of 8/2 is definitely unfavourable, regardless of the actual number of parasites seen, and it often presages a symptomatic relapse, usually after the next period.

Monilial Infections

As causes of vaginal discharge the yeast fungi are nowadays increasingly recognized. The yeasts include the *Candida* (*Monilia*) parasites, of which there are many species, but of these only *Candida albicans* is pathogenic in humans. It may infect the mouths of babies, the external skin, the nail-folds, and the respiratory tract, as well as the cervix and vagina. It can be dormant in the genital tract for long periods and be found on routine examination of patients without symptoms. When the patient, however, is afflicted she develops a discharge which is either flaky, like damp bread, or glairy. Pruritus vulvae is often out of all

proportion to the amount of discharge, and vulvitis and secondary eczematization occasionally reduce the patient to a state of sleepless misery.

The organism thrives in a highly acid medium. Its association with pregnancy is therefore common. Glycosuria, whether diabetic or not, also favours its growth. Of our 95 cases of moniliasis, six were pregnant, and a higher pregnancy incidence would have been shown save for the fact that this hospital does not deal with midwifery.

The clinical appearances often suggest the diagnosis, which, however, can be made with certainty only from stained smears from both vagina and cervix, when *C. albicans* will be seen under high-power magnification either as mycelial threads (Fig. 1), or more often as spores, particularly in cervical specimens.

FIG. 1.—Photomicrograph showing spores and a mycelial thread of *Candida albicans* in a case of vaginal thrush.

The resistant case with intense pruritus might well be investigated for gastric achlorhydria. Two of our cases were found to be lacking in this respect, and the response to treatment with dilute hydrochloric acid by mouth was dramatic (Figs. 2, 3, and 4).

FIG. 2.

FIG. 3.

FIG. 4.

FIG. 2.—A case of vulvitis secondary to vaginal moniliasis; gastric achlorhydria. State of vulva before administration of dilute HCl by mouth. FIG. 3.—Same case as in Fig. 2, seven months later, HCl still being given. FIG. 4.—Same case, seven months later than Fig. 3, after conclusion of HCl.

The double infection of monilial infection and trichomonas vaginalis is by no means uncommon, and accounted for 7.7% of all our cases.

Miscellaneous Group

This group, as shown in Table I, consisted of 196 cases (33.5%). They are summarized in Table VII. The most significant figure is the last one, the number of patients

TABLE VII.—Summary of Miscellaneous Group

	No. of Cases	Percentage of Total
Cervical lesions (erosion, ectropia, laceration and infection, polyps)	86	14.7%
Postmenopausal state (natural, artificial, surgical)	20	3.4%
Gonorrhoea previously missed	1	
Syphilis	1	
Foreign body	1	
Recent colporrhaphy	2	
Prolapse	1	
No pathological condition found	84	14.4%
	196	

in whom no pathological condition was ever found, and in 49 of whom no trace of discharge was visible. A further five cases had a normal pregnancy.

Summary

It is necessary to distinguish between pathological vaginal discharges and vaginal moisture that may be no more than an exaggerated physiological phenomenon if the patient is to be spared treatment which is either inappropriate or unnecessary and therefore psychologically harmful.

In hospital practice there are very good grounds for segregating these cases into a special leucorrhoea clinic, in which they can be properly assessed. The clinical material of the "D" clinic of the Chelsea Hospital for Women is presented under four main groupings:

- (1) trichomonas vaginitis; (2) monilial infections; (3) double infections with *Trichomonas vaginalis* and monilia; and (4) miscellaneous conditions.

Cases amenable to surgical treatment are not included in the clinic, but are admitted for operation, and cases of venereal disease are also referred elsewhere.

The trichomonal cases form the hard core of the clinic, not only because they are common but because relapse is frequent (22.8%), and various sources of infection are reviewed, particularly with regard to sexual intercourse or attempts theret. Over one-third of the cases quoted were unmarried, and a significant number contracted the infection as a result of their indiscretions.

The need for examination of fresh wet specimens is illustrated, and the importance of the ratio of pus cells to squamous cells is presented as an index both of prognosis and of progress under treatment. The well-known tendency to relapse after a menstrual period encourages a new approach to the timing of treatment.