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Diagnosis of Gonorrhoea in Women: Comparison of Sampling Sites

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Summary

A total of 250 women, 100 of them named contacts of men with gonorrhoea, were tested for infection. Each had prepared smear and culture specimens from urethra, endocervix, and vagina. The smears were Gram-stained and examined immediately. Cultures were taken using Stuart's transport medium with later inoculation of both selective and non-selective media for each specimen.

It was shown that examination of specimens from urethra and endocervix gave results superior to those found on examination of vaginal material alone. The study revealed that nearly one infected woman in three would have been missed if vaginal material only had been examined. Failure to secure a prompt scientific diagnosis has serious epidemiological implications.

Our results find support in the work of others. We conclude that the suggestion in some quarters that examination of vaginal material for the detection of gonococci is adequate should be abandoned. Any who feel unwilling to accept this view should at least supplement their testing with examination of urethral and endocervical specimens.

Introduction

Conflicting advice is offered by British gynaecological textbooks concerning the most appropriate sampling methods for the bacteriological diagnosis of gonorrhoea in women.

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Stern (1963) said: "a swab should be taken high in the vagina and cultured." Willcox (1963), however, advised that urethral and cervical specimens be taken for microscopy and culture. Jeffcoate (1967), discussing acute salpingo-oophoritis, said: "cervical (or high vaginal) and urethral swabs" should be taken; though later, when commenting on the asymptomatic nature of early gonorrhoea, he advised preparation of urethral and endocervical smears and cultures. Peel and Brudenell (1969) advised the examination of cervical smears and cultures for the diagnosis of gonorrhoea but did not mention urethral sampling. Howkins and Bourne (1971) suggested urethral with either high vaginal or cervical swabbing, though Nicol (1971) specified the urethral and cervical sites only. Baird (1969) mentioned smears and cultures but did not specify sites to be tested.

Textbooks for nurses show the same dichotomy. Catterall (1964) advised urethral and cervical examinations, while in contrast textbooks offered to student nurses in midwifery (Hallam, 1972) and gynaecology (Dodds, 1967) support the taking of vaginal swabs.

It is to be expected that the confusion of opinion expressed in these textbooks will be reflected in clinical practice. Moreover, the situation has now become further complicated by the availability of new laboratory techniques with more sophisticated ways of overcoming contamination, which could possibly make the vaginal specimen more acceptable.

To resolve these uncertainties and to establish how useful in fact the vaginal specimen can be in present circumstances, a trial was carried out comparing it with more appropriate urethral and cervical specimens.

Material and Methods

The study covered 250 women who attended the special clinic, Royal Infirmary, Sheffield, between February and August 1972.

Group 1 consisted of 150 patients, of whom 50 were named sex partners of men with gonorrhoea. Group 2 consisted of 100 patients, 50 of whom were named contacts of gonorrhoea. The patients were in no way selected, and represent in terms of age and marital status the population of the clinic.

All patients—both contacts and other new patients—were interviewed and clinically examined at their first attendance. The following investigations were then carried out: in group 1 urethral, vaginal vault, and endocervical specimens were taken. The vaginal specimens were taken from the vault under direct vision using a Cusco speculum, with the patient in the lithotomy position; in group 2 the procedure was identical apart from the method of taking the vaginal specimens. In view of the difficulty in obtaining satisfactory vaginal vault specimens from a patient lying in a hospital bed and without the use of a speculum, samples were taken blindly from the lower vagina.

Smears were made of specimens from both groups, stained by Gram's method, and immediately examined in the clinic. Cultures were similarly taken using carbon impregnated swabs and were sent to the laboratory in Stuart's transport medium. They were usually "plated out" within 24 hours. Two culture media were used for each specimen, Columbia chocolate agar (Ellner *et al.*, 1966) and trimethoprim-containing medium but without nystatin (Phillips *et al.*, 1972). Plates were incubated in 10% carbon dioxide for 36-48 hours. Positive cultures were identified by Gram stain, oxidase reaction, and appropriate carbohydrate acidification on Flynn and Waitkin's (1972) medium.

Results

In Group 1, 29 contacts were diagnosed by examination of smear and culture specimens from urethra, endocervix, or vaginal vault (see table). In one instance only was the vaginal specimen positive when the urethral and endocervical ones were negative. On no fewer than eight occasions the reverse held true. The difference is significant at the 2% level. Of the other 100 patients in group 1, 10 were found infected by examination of vaginal smears and cultures but two more were found only by urethral and endocervical smear or culture examination. This difference is not statistically significant.

Diagnosis of Gonorrhoea by Urethral and Endocervical Smear and Culture and by Vaginal Smear and Culture. (Results Concern Patients' First Attendance only)

| Patients | No. of Patients | Positive in Urethra, Endocervix, and/or Vagina | Positive in Vagina | Difference Columns 3 and 4 |
|-----------------------|-----------------|--|--------------------|----------------------------|
| Group I—High vaginal: | | | | |
| Contacts | 50 | 29 | 22* | 8* |
| Others | 100 | 12 | 10 | 2 |
| Total | 150 | 41 | 32 | 10* |
| Group II—Low vaginal: | | | | |
| Contacts | 50 | 31 | 17 | 14 |
| Others | 50 | 3 | 2 | 1 |
| Total | 100 | 34 | 19 | 15 |
| Grand Total .. | 250 | 75 | 51 | 25 |

* In one patient only the vaginal culture was positive.

In the 50 named contacts in group 2 a total of 31 positive results were obtained by all methods used. Of these only 17 yielded positive vaginal smears or cultures. This difference is highly significant ($P < 0.001$). The diagnostic abilities of the methods in group 2 "other patients" are not significantly different, but the results obtained by examination of "low vaginal" specimens were significantly inferior to those obtained with the "high vaginal" specimens ($P < 0.01$).

In terms of the grand total the diagnostic shortfall using vaginal material was nearly one in every three patients.

Discussion

Recent series like ours have all shown a significant shortfall in the diagnostic ability of the vaginal swab. Thus Olsen (1971),

who examined cultures and analysed his material on the supposition that he had found 100% of positive infections, showed that 96.2% were detected by urethral or cervical tests or both, whereas only 79.2% were found by examination of vaginal specimens. Similarly, Schmale *et al.* (1969) testing four sites—urethra, cervix, vagina, and rectum—found 93.8% of total positive diagnoses on urethral or cervical culture or both as against 77.7% from the vaginal cultures.

These results are not unexpected. The prime reason for the inadequacy of the vaginal specimen must lie in the pathology of the disease. Thus, cervical and urethral samplings are taken from the sites of infection where gonococci are actively multiplying, whereas the vaginal specimen merely detects any bacteria which may have contaminated a neighbouring area.

Two possible secondary reasons suggest themselves; either the selective media used do not inhibit contaminants or gonococci do not survive long in the vagina.

Like others, Wilkinson (1965) showed that selective media are in fact of undoubted value in preventing overgrowth of gonococci by other organisms—especially from sites such as the vagina where the presence of a dense bacterial flora is inevitable. In our series the selective medium allowed 26.1% more isolations to be made from this site than would have been possible had the non-selective medium been used alone. Thus, despite this increased testing sensitivity, in our trial the vaginal specimen still compared unfavourably.

The second contention—that delicate gonococci do not survive long in the vagina seems a much more likely explanation. In like manner, our results show that specimens taken from lower in the vagina are less likely to yield positive results than those from the vault, again suggesting a fairly short life for those gonococci in the vagina.

Gonorrhoea is now a world-wide epidemiological problem. With the advent of sexual freedom and the growing use of oral contraception, particularly in western countries, the prevalence of the disease in women is growing much faster than in men (Watt, 1964; Morton, 1970). Salpingitis is more common than all the other complications of gonorrhoea taken together and is now said to occur in no less than 10% of infected females (Rees, 1964; Rees and Annel, 1969).

The prompt and accurate bacteriological diagnosis of occult and complicated gonorrhoea in women has thus become a more urgent problem than ever before. Moreover, the highest possible yield of positive results is not only of some importance to the individual patient, it has epidemiological implications. Without a scientifically sound diagnosis of gonorrhoea, the tracing and treating of sex contacts becomes inefficient and so public health control of the infection cannot be initiated, pursued, or maintained. In the present epidemic state of gonorrhoea this aspect is of vital importance if the disease is to be kept within manageable proportions. To this end we feel it is essential that specimens are taken which maximize the possibility of arriving at diagnosis of gonococcal infection.

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Oestrogen Receptor in Human Breast Cancer Tissue and Response to Endocrine Therapy

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Summary

Oestrogen receptor determinations were done in metastatic breast cancer tissue of patients with advanced breast cancer. In 37 patients with progressive disease evaluation of the response to endocrine treatment was possible, following the criteria of the E.O.R.T.C. Co-operative Breast Cancer Group. In 20 patients with receptor-negative tumours two objective remissions were noted; in 17 patients with receptor-positive tumours 14 objective remissions were seen. There seems to be a striking correlation between the presence or absence of oestrogen receptor in tumour tissue and the clinical response to hormonal therapy.

Introduction

A correlation between the presence of a specific oestrogen receptor in breast cancer tissue and the response to endocrine treatment has been shown in rats (King *et al.*, 1965; King *et al.*, 1966; Jensen *et al.*, 1967; Trams and Maass, 1969). Evidence for a similar correlation in human breast cancer was reported by Jensen *et al.* (1972) and Maass *et al.* (1972). An increased in-vivo uptake of injected radiolabelled oestrogens by human breast cancers was also shown in patients who subsequently responded to endocrine therapy (Folca *et al.*, 1961; Braunsberg *et al.*, 1973).

In our institute oestrogen receptor determinations have been carried out since 1971 in primary breast cancers and in biopsy specimens taken from skin and lymph node metastases. In 37 patients with progressive advanced breast cancer the clinical response to endocrine treatment has now been evaluated and compared with the results of receptor determinations in metastases sampled for biopsy shortly before the start of therapy. In 20 of these patients the treatment and follow-up were part of a clinical trial of the E.O.R.T.C. Breast Cancer Group.

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Patients and Methods

The oestrogen receptor determinations were done in tissue homogenates by a charcoal separation technique (Korsten and Persijn 1972). All tissue specimens were taken from skin and lymph node metastases. In all tissue samples the presence of tumour was verified histologically. Therapy was started after the specimen had been taken but before the receptor content was known. All the patients had evidence of progressive disease and had lesions which could be evaluated objectively (skin and lymph node metastases, lung metastases, well-defined osteolytic bone metastases). The patients were investigated and followed up according to the criteria outlined in the E.O.R.T.C. Co-operative Breast Cancer Group protocol (G.E.C.A., 1967).

An objective remission was accepted when measurable regression was noted in at least half of the lesions, without progression in any lesion and without any new lesion arising anywhere. The improvement had to last for more than three months. In four patients who responded well to treatment and who had no evidence of bone metastases no follow-up skeletal x-ray films were obtained.

Endocrine therapy was thought to be indicated only when the disease was too widespread to be controlled by palliative radiotherapy or when progression was noted in irradiated areas. Nine premenopausal women underwent oophorectomy; the other 28 patients were two or more years postmenopausal and were treated with either ethinyloestradiol (Lynoral) 3 mg daily or nandrolone phenylpropionate (Durabolin) 25 mg three times a week or nafoxidine (U 11100) 180 mg daily. Nafoxidine is an oestrogen antagonist which was shown to produce remission in about 30% of cases of advanced breast cancer in type 1 and type 2 clinical trials carried out by the E.O.R.T.C. Breast Cancer Group (1972, 1973). In 35 patients this was the first endocrine treatment given. Two patients had had endocrine therapy (oophorectomy, ethinyloestradiol) previously but the biopsy specimens were taken when there was a recurrence of the progressive disease and the preceding therapy had been stopped for more than six weeks.

Results

Out of 17 patients found to have receptor in their tumour tissue 14 experienced an objective remission (table I). Of the 20 patients in whom the tumour tissue was receptor-negative only two had an objective remission (table II). Application of the X² test gave $P < 0.00001$. There seemed to be no relation between the quantity of receptor measured and the quality and duration of the remission obtained. The amounts of receptor