Genital herpes simplex virus infection and gonorrhoea

Association and analogies

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The association of genital herpetic infections with gonorrhoea and other venereal diseases has been noted since the latter part of the 19th century (Diday and Doyon, 1886). Recently, Beilby, Cameron, Catterall, and Davidson (1968) in England have suggested the possibility that gonorrhoeal infection may trigger recurrences of herpetic cervicitis. To test this hypothesis, the present study was conducted in a population of women attending a venereal disease clinic in Atlanta, Georgia. Cultures were obtained to permit the detection of both *N. gonorrhoeae* and genital herpes simplex virus. Serological tests, to determine whether a genital herpetic infection was primary or recurrent, were also performed.

In order to evaluate the prevalence of cervical cellular atypia in women attending a venereal disease clinic, Papanicolaou cervicovaginal smears were also obtained.

Material and methods

STUDY GROUP

The series comprised 132 women attending the venereal disease clinic of the Fulton County Health Department in Atlanta. About half of these women came to the clinic because they were contacts of men with gonorrhoea. The other women came to the clinic with various complaints, including vaginal discharge, gross genital lesions, pruritis, and dysuria. Their ages ranged from 15 to 57 years (median 20). 85 per cent. were Negro and the rest Caucasian.

LABORATORY STUDIES

For the detection of *N. gonorrhoeae*, cervical and rectal cultures were obtained with cotton-wool swabs, plated immediately on Thayer-Martin medium, and processed

as described elsewhere (Schmale, Martin, and Domescik, 1969). For the detection of herpes simplex virus (HSV), material from the endocervix and exocervix was obtained with a cotton-wool swab, placed in Hanks's balanced salt solution, and cultured immediately, or after refrigeration within 6 hrs, on primary rabbit kidney tissue culture. Additionally, if vesicular and/or ulcerative vulvar lesions were present, specimens for virus culture were obtained from the lesions and processed as above. Type identification of HSV isolates was performed by techniques previously reported (Nahmias, Chiang, del Buono, and Duffey, 1969a). A serum specimen was obtained from each woman at the time of entry into the study. Those patients in whom HSV was isolated had a second serum specimen obtained 3 to 8 weeks after the first. Serological tests included micro-neutralization HSV type differentiation studies (Nahmias, Josey, Naib, Luce, and Duffey, 1970).

Papanicolaou smears, obtained from cervico-vaginal and cervical scrapings of 127 women in the study, were stained and examined by routine methods. The frequency of cervical cellular atypia in the study group was compared with that in a group of women of similar age, race distribution, and socioeconomic level attending Grady Memorial Hospital in Atlanta.

Results

Table I presents the association found between genital HSV infection and gonorrhoea in the 132 women in the study group. Eighty women yielded positive gonococcal cultures; ten from rectal specimens only. Of the eighty women with positive gonococcal cultures, four (5 per cent.) also had positive cultures for HSV; one had external lesions. Of the 52 women with negative gonococcal cultures, three (5.8 per cent.) had HSV isolated from the genitalia; all three had external lesions.

All seven HSV isolates were found to be Type 2. One of the four women with both gonorrhoea and genital herpes, and one of the three women with genital herpes but no gonorrhoea, had serological evidence of a primary Type 2 herpetic infection.

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TABLE I Association of genital herpes with gonorrhoea in women—VD clinic

Gonococcal cultures	Genital herpes cultures		
	Positive	Negative	Total
Positive C*+R**+	2	27	80
C+R-	1	40	
C-R+	1	9	
Negative	3	49	52
Total	7	125	132

*C = cervical culture for gonococcus

**R = rectal culture for gonococcus

Table II presents the results of cytological screening for cervical neoplasia in 127 women in the study group. 21 (16.5 per cent.) of the women had evidence of mild to severe cervical atypia. This rate is approximately three times that (5.7 per cent.) found in the population of women of similar socioeconomic level, age, and racial distribution attending the municipal hospital.

Comment

Although the occurrence of both genital herpes and gonorrhoea in the same individual has been noted by several workers (Diday and Doyon, 1886; Hutfield, 1968; Barile, Blumberg, Kraul, and Yaguchi, 1962; Amstey and Balduzzi, 1970; Jeansson and Molin, 1971), systematic studies on the association between these two infections have been carried out in only two other venereal disease clinics—one in London, England (Beilby and others, 1968), and one in Stockholm, Sweden (Jeansson and Molin, 1971). The results of our studies in a venereal disease clinic

in Atlanta are compared in Table III with those obtained by the European investigators. The British group observed a much higher recovery rate of genital HSV in women with gonorrhoea than in those without gonorrhoea (13 per cent. *v.* 0.6 per cent.). On the other hand, little difference in the percentage of genital HSV isolations between women with gonorrhoea and those without the latter infection was noted in either the Swedish study (10.6 per cent. *v.* 6.4 per cent.) or in our study (5 per cent. *v.* 5.8 per cent.). Part of the difference in results might be attributed to the fact that none of the British women had external genital herpetic lesions, whereas two of the ten Swedish patients and four of the seven women in our clinic had external lesions.

Neither the British nor Swedish studies attempted to ascertain whether the genital herpetic infection was primary or recurrent. In our study, one of the four women with both gonorrhoea and genital herpes had a primary Type 2 HSV infection. In view of this finding, as well as the observed prevalence of genital herpes without concomitant gonorrhoea in the Stockholm and Atlanta studies, it appears unlikely that gonococcal infection triggers a recurrence of genital herpes. It would seem more plausible that the two infections are coincidental in the same patient. It is well known that two or more venereally transmitted agents are often present in the same individual. Thus, in the present study, three cases of gonorrhoea were associated with syphilis and two others with vulvar condyloma acuminatum.

The venereal communicability of HSV Type 2 infection has been best documented by contact studies in Atlanta (Nahmias, Dowdle, Naib, Josey, McLone, and Domesick, 1969b) and Houston (Rawls,

TABLE II Papanicolaou cervico-vaginal screening of women at the VD clinic and at a Municipal hospital

No. of women	Screened	With cervical atypia	Percentage with cervical atypia
VD clinic	127	21	16.5
Municipal hospital	45,829	2,610	5.7

TABLE III Association of genital herpes with gonorrhoea in women—Comparison between VD clinics in Great Britain, Sweden, and U.S.A.

Clinics	Great Britain (London)		Sweden (Stockholm)		U.S.A. (Atlanta)	
Herpes positive Gonococcus negative	1 (0 ^a) 155	(0.6 per cent.)	5 (2 ^a) 78	(6.4 per cent.)	3 (3 ^a) 52	(5.8 per cent.)
Herpes positive Gonococcus positive	7 (0 ^a) 54	(13.0 per cent.)	5 (0 ^a) 47	(10.6 per cent.)	4 (1 ^a) 80	(5.0 per cent.)
Case ratio Herpes:Gonorrhoea	1:7		1:5		1:11	

^aexternal lesions suggestive of genital herpes

Gardner, Flanders, Lowry, Kaufman, and Melnick, 1971) of women exposed to males with penile herpes. Those studies have demonstrated a high communicability rate for genital herpes, with at least three out of four female contacts showing evidence of herpetic infection. This is a similar rate to that which has been observed for female contacts of males with gonorrhoea (Thin, Williams, and Nicol, 1971).

Although the population of women attending the VD clinics in London, Stockholm, and Atlanta might differ in some characteristics, the findings summarized in Table III suggest that when a diagnosis of gonorrhoea is made in a woman, there is a 5 to 13 per cent. likelihood of the patient having a concomitant genital herpetic infection. The 1:11 ratio of cases of genital herpes to cases of gonorrhoea in women attending the Atlanta VD clinic is very similar to the 1:14 ratio noted in a previous study performed several years earlier in the same clinic (Nahmias and others, 1969b). Taken together with the results obtained in the two European VD clinics, these observations suggest that for every five to fourteen cases of gonorrhoea in women attending a venereal disease clinic, it should be possible to detect one case of genital herpes.

Genital Type 2 HSV infection and gonorrhoea have a number of epidemiological and clinical features in common (Josey, Nahmias, and Naib, 1968, 1972; Goss, 1971; Johnson, Holmes, Kvale, Halverson, and Hirsch, 1969; Allison and Sanders, 1971). The two infections occur in similar populations and have their greatest prevalence in adolescents and young adults. Both infectious agents affect the cervix most commonly and are usually subclinical in women. Whereas re-infection with gonorrhoea and recurrences with genital herpes are well established, it is not clear at present whether some of the recurrences of genital herpes may be due to re-infection from an exogenous source. Both genital herpes and gonorrhoea can affect extragenital sites, *e.g.* anorectal and oral sites. Both infectious agents can cause skin lesions and meningitis and are occasionally recovered from the blood. Another analogy is that the major source of neonatal infection with both agents is the mother's infected birth canal.

The frequency of cervical cellular atypia noted on Papanicolaou cervico-vaginal screening in the women attending a venereal disease clinic was about three times that found for the general population of women of similar socioeconomic level, age, and racial characteristics attending a municipal hospital (Table II). It is well known that there is a high incidence of cervical neoplasia in promiscuous women (Josey and others, 1968). It is reasonable, therefore, to suggest that venereal disease clinics might serve as key areas

for routine Papanicolaou screening for the detection of cervical cancer. Javert and Ayre (1972) have recently emphasized the possible coexistence of gonorrhoea, herpes simplex virus infection and precancerous cervical changes. These authors suggest that gonococci may be activating agents that affect the squamocolumnar junction of the cervix allowing viruses to produce dysplasia, cancer *in situ*, and invasive cervical cancer.

Summary

Cultures for both *N. gonorrhoeae* and herpes simplex virus (HSV) were obtained in 132 women attending a venereal disease clinic in Atlanta. Of eighty women with positive gonococcal cultures, four (5 per cent.) had genital Type 2 HSV infection (one primary case); of 52 women with negative gonococcal cultures, three (5.8 per cent.) had genital Type 2 HSV infection. These findings do not support the recently proposed hypothesis that gonorrhoea triggers recurrences of genital herpes. Results of this and two other studies indicate that 5 to 13 per cent. of women with gonorrhoea have concomitant genital herpetic infections, and that for every five to fourteen cases of gonorrhoea, one case of genital herpes would be expected.

The frequency of cervical cellular atypia in women attending the VD clinic was approximately three times that detected in women attending a municipal hospital, suggesting that VD clinics are key areas for cervical cancer screening.

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Infection due au virus de l'herpès simplex génital et gonococcie

SOMMAIRE

Pour 132 femmes, s'étant présentées à une clinique vénéréologique d'Atlanta, des cultures furent entreprises

à la fois pour *N. gonorrhoeae* et pour le virus de l'herpès simplex (VHS). Parmi les 80 femmes ayant une culture positive pour le gonocoque, 4 (5 pour cent) avaient une infection par le VHS génital type 2 (1 cas primaire). Parmi les 52 femmes avec des cultures négatives pour le gonocoque, 3 (5,8 pour cent) avaient une infection par le VHS génital type 2. Ces constatations ne soutiennent pas l'hypothèse récemment proposée que la gonococcie déclenche des rechutes de l'herpès génital. Ces résultats et ceux de deux autres études indiquent que 5 à 13 pour cent des femmes atteintes de la gonococcie ont des infections herpétiques génitales concomitantes et que, pour chaque 5 à 14 cas de gonococcie, on peut s'attendre à un cas d'herpès génital.

La fréquence des atypies cellulaires du col chez les consultantes de la clinique vénéréologique fut à peu près trois fois celle trouvée chez les consultantes d'un hôpital municipal; ceci suggère que les cliniques vénéréologiques occupent une situation-clef pour la recherche systématique du cancer du col.