V. THE RELATIONSHIP OF COITUS TO CARCINOMA OF THE CERVIX

Milton Terris, M.D., F.A.P.H.A.; Fitzpatrick Wilson, M.D.; Harold Smith, M.D.; Evelyn Sprung, R.N.; and James H. Nelson, Jr., M.D.

THIS study of cancer of the cervix was undertaken to determine, first, whether a previous study[1] which had demonstrated an association with coitus could be confirmed in a different setting; second, whether the disease is related to circumcision status as determined by actual examination of the marital partner; and third, whether the epidemiologic characteristics of carcinoma in situ and cervical atypia are similar to those of invasive carcinoma of the cervix. The present paper is a preliminary report from a continuing study, and will be limited to data regarding the association of coitus with invasive cancer of the cervix. The data on circumcision status and on the epidemiology of carcinoma in situ and cervical atypia are still insufficient for presentation at this time.

It is recognized that there is a certain risk involved in presenting preliminary data from an incomplete study, since it may well be that the final results will be different. Nevertheless, the information available appears to be sufficient to warrant presentation and discussion of the relationships found between coitus and carcinoma of the cervix.

Methods

The previous study,[1] conducted at the Charity Hospital of New Orleans, included 122 patients with cervical carcinoma and an equal number of gynecological controls matched by race and five-year age group. All interviews were conducted by a single nurse interviewer who had no knowledge of the patient's diagnosis.

The present study includes patients from four hospitals in New York City: Kings County Hospital, Metropolitan Hospital, St. Albans Naval Hospital, and St. Johns Episcopal Hospital. For each patient with carcinoma of the cervix the control was the next patient admitted to the same gynecological service who matched by population group (Negro, Puerto Rican, Jewish, other white, and Oriental) and five-year age group (15-19, 20-24, and so on). Except for those Puerto Ricans who could not speak English and were interviewed by a Spanish-speaking nurse, all interviews were conducted by a single nurse interviewer who had no knowledge of the patient's diagnosis. The interview form was essentially the same as that used in the previous study.

Analysis of specific factors included all matched pairs for which the corresponding data were available. The matched chi-square test was used to determine the significance of differences between the pairs of patients and controls.

Results

This report includes 239 patients with histologically confirmed invasive squamous cell carcinoma of the cervix. There were 176 patients seen at Kings County Hospital, 38 at Metropolitan Hospital, 16 at St. Albans Naval Hospital, and 9 at St. Johns Episcopal Hospital. Of the 239 patients, 161 were Negro, 46 were other white, 26 were Puerto Rican, 5 were Jewish, and 1 was Oriental. The age distribution of the patients is given in Table 1.

The controls included women with a variety of gynecological disorders (Table

Table 1—Age at interview of patients

Age	Patients	
	No.	%
15–19	1	0.4
20–29	9	3.8
30–39	70	29.3
40–49	61	25.5
50–59	58	24.3
60–69	25	10.5
70 and over	15	6.3
Total	239	99.9

Table 2—Primary diagnosis of controls

Diagnosis	Controls	
	No.	%
Myoma of the uterus	68	28.5
Cystocele, rectocele, urethrocele	29	12.1
Dysfunctional uterine bleeding	23	9.6
Other benign tumor	19	7.9
Other carcinoma	17	7.1
Abortion	17	7.1
Endometrial carcinoma	13	5.4
Pelvic inflammatory disease	9	3.8
Uterine prolapse	7	2.9
Cervicitis	7	2.9
Ectopic pregnancy	4	1.7
Other	26	10.9
Total	239	99.9

Table 3—Current marital status

Status	Patients		Controls	
	No.	%	No.	%
Married to first husband	44	18.4†	76	31.8†
Married to second or later husband	35	14.6	26	10.9
Single	11	4.6*	29	12.1*
Separated	78	32.6†	47	19.7†
Divorced	15	6.3	14	5.9
Widowed	56	23.4	47	19.7
Total	239	99.9	239	99.9

* $P<0.01$
† $P<0.001$

2). There were no significant differences between patients and controls in religion, educational level, or occupation of husband and father.

The patients and controls differed markedly in their current marital status. Only 5 per cent of the patients were single as compared with 12 per cent of the controls. Also, 39 per cent of the patients were separated or divorced as compared with 26 per cent of the controls (Table 3). Since more of the patients than the controls had married before age 17 (Table 7), this factor might explain the difference in separation and divorce. Table 4 shows that the incidence of separation and divorce was higher for those marrying before age 17, and that there was no difference between patients and controls in this group. For those marrying at age 17 and over, however, the incidence of separation and divorce was significantly greater in the patients than the controls. Furthermore, this difference could not be explained by age or ethnic differences, since the patients and controls were found to be comparable in these respects in both of the age-at-marriage groups.

A history of more than one marriage was given by 35 per cent of the patients and 22 per cent of the controls (Table 5). This difference might also be explained by the earlier marriages of the patients. Table 6 shows that the incidence of multiple marriages was higher for those marrying before age 17, and that there was no difference between patients and controls in this group. For those marrying at age 17 and over, however, the incidence of multiple marriages was significantly greater in the patients than the controls. Again, this difference could not be explained by age or ethnic differences, since the patients and controls were found to be comparable in these respects in both of the age-at-marriage groups.

As previously indicated, early mar-

Table 4—Separation and divorce by age at first marriage

Age at first marriage	Patients			Controls		
	Total No.	Sep.+div. No.	Sep.+div. %	Total No.	Sep.+div. No.	Sep.+div. %
Under 17	61	28	45.9	33	13	39.4
17+	160	62	38.8*	175	48	27.4*
Total	221	90	40.7	208	61	29.3

* $P<0.05$

Table 5—Number of times married

No. times married	Patients		Controls	
	No.	%	No.	%
0–1	156	65.3	187	78.2
2+	83	34.7*	52	21.8*
Total	239	100.0	239	100.0

* $P<0.001$

riage was considerably more frequent among the patients; 28 per cent were married before the age of 17 as compared with 16 per cent of the controls (Table 7).

First coitus was also reported to have occurred at an earlier age among the patients; 53 per cent reported first coitus before age 17 as compared with 37 per cent of the controls (Table 8). There were no significant differences between patients and controls in the number of coital partners reported (Table 9).

Frequency of coitus was obtained for ten-year age periods. Where first coitus occurred during the ten-year period, the frequency recorded was that for the years following onset of coitus rather than an average for the entire period. No significant differences were found between patients and controls in the reported frequency of coitus at any age period (Tables 10-14).

Discussion

The finding that fewer cervical carcinoma patients are single is consistent with the results obtained in other studies. Dorn and Cutler[2] found in the ten-city study in the United States in 1947 that the age-adjusted incidence rates per 100,000 women were 13 for never-married whites and 35 for ever-married whites; the corresponding rates for nonwhites were 58 and 71. Haenszel and Hillhouse[3] found in New York City in

Table 6—Multiple marriages by age at first marriage

Age at first marriage	Patients			Controls		
	Total No.	2+ marriages No.	2+ marriages %	Total No.	2+ marriages No.	2+ marriages %
Under 17	61	29	47.5	33	15	45.5
17+	160	51	31.1*	175	35	20.0*
Total	221	80	36.2	208	50	24.0

* $P<0.02$

1952 that the age-adjusted incidence rates per 100,000 women for invasive epidermoid cervical carcinoma were five for never-married whites and 11 for ever-married whites; the corresponding rates for nonwhites were 28 and 46. Wynder, et al.,[4] interviewed gynecological patients in 12 hospitals in the United States; the percentage never-married was 2 per cent for white non-Jewish patients with carcinoma of the cervix and 9 per cent for their controls, while the corresponding percentages for Negroes were 4 and 10. Boyd and Doll,[5] in a study of six London hospitals, found that 3 per cent of the cervical cancer patients had never been married as compared with 7 per cent of the gynecological controls.

The finding that a higher proportion of the patients are separated or divorced is also consistent with previous reports. Lombard and Potter[6] in Massachusetts found the incidence of separation or divorce to be 21 per cent for cervical cancer patients and only 7 per cent for controls matched by age and economic status. Jones, Macdonald, and Breslow[7] in Los Angeles found that for white patients marrying before age 20, there was no difference in separation and divorce between patients and age-matched controls; for those marrying at age 20 and over, however, there was significantly more separation and divorce in patients than in age-matched controls. Boyd and Doll[5] obtained similar results, although they included death of husband as well as separation and divorce in a category of "broken marriage" in their study.

The finding that cervical cancer patients have a greater incidence of multiple marriages is consistent with their higher incidence of separation and divorce. Boyd and Doll[5] found that the greater incidence of multiple marriages in cervical cancer patients is a function of the incidence of broken marriages rather than the remarriage rate after dissolution of the first marriage. Wyn-

Table 7—Age at first marriage

Age	Patients		Controls	
	No.	%	No.	%
Under 17	53	27.6*	30	15.6*
17–19	52	27.1	51	26.6
20–24	53	27.6	70	36.5
25+	34	17.7	41	21.4
Total	192	100.0	192	100.1

* $P<0.01$

Table 8—Age at first coitus

Age	Patients		Controls	
	No.	%	No.	%
Under 17	117	52.9*	81	36.7*
17–19	69	31.2	78	35.3
20–24	26	11.8	45	20.4
25+	9	4.1	17	7.7
Total	221	100.0	221	100.1

* $P<0.001$

Table 9—Number of coital partners

No. of partners	Patients		Controls	
	No.	%	No.	%
0	2	0.9	4	1.8
1	48	21.1	61	26.8
2	58	25.4	39	17.1
3	34	14.9	39	17.1
4	25	11.0	39	17.1
5+	61	26.8	46	20.2
Total	228	100.1	228	100.1

Table 10—Frequency of coitus before age 20

Frequency	Patients		Controls	
	No.	%	No.	%
More than once a week	85	62.5	74	54.4
Once a week	18	13.2	21	15.4
Less than once a week	33	24.3	41	30.1
Total	136	100.0	136	99.9

Table 11—Frequency of coitus at age 20-29

Frequency	Patients		Controls	
	No.	%	No.	%
More than once a week	161	71.9	170	75.9
Once a week	35	15.6	21	9.4
Less than once a week	28	12.5	33	14.7
Total	224	100.0	224	100.0

Table 12—Frequency of coitus at age 30-39

Frequency	Patients		Controls	
	No.	%	No.	%
More than once a week	132	65.0	124	61.1
Once a week	36	17.7	39	19.2
Less than once a week	35	17.2	40	19.7
Total	203	99.9	203	100.0

Table 13—Frequency of coitus at age 40-49

Frequency	Patients		Controls	
	No.	%	No.	%
More than once a week	46	32.6	47	33.3
Once a week	42	29.8	45	31.9
Less than once a week	53	37.6	49	34.8
Total	141	100.0	141	100.0

Table 14—Frequency of coitus at age 50-59

Frequency	Patients		Controls	
	No.	%	No.	%
More than once a week	19	23.5	11	13.6
Once a week	13	16.0	19	23.5
Less than once a week	49	60.5	51	63.0
Total	81	100.0	81	100.1

der, et al.,[4] and Terris and Oalmann[1] have also reported a greater incidence of multiple marriages among cervical cancer patients.

The finding that early marriage is more frequent in cervical cancer patients confirms the results obtained by almost all investigators, including Terris and Oalmann,[1] Wynder, et al.,[4] Boyd and Doll,[5] Lombard and Potter,[6] Jones, Macdonald, and Breslow,[7] Rotkin[8] in Oakland, Calif., Dorn[9] in Israeli Jews, and She Ming-P'eng, et al.,[10] in Peking. Lundin, Erickson, and Sprunt[11] in Memphis found the relationship with early marriage in white women; on the other hand, the difference between Negro patients and controls did not occur for marriage before age 18, but did occur for marriage at age 18 and 19.

The finding that cancer of the cervix is associated with early coitus is in agreement with previous reports. Wynder, et al.,[4] obtained a history of coitus before age 17 in 19 per cent of white non-Jewish cervical cancer patients and 10 per cent of their controls; the corresponding percentages for Negroes were 55 and 36. Rotkin[8] found that 43 per cent of cervical cancer patients and 28 per cent of controls reported coitus before age 18. Terris and Oalmann[1] reported that 53 per cent of cervical cancer patients and 26 per cent of controls gave a history of coitus before age 17.

In the present study, no difference was found in the number of coital partners reported by patients and controls. Jones, Macdonald, and Breslow[7] found no difference between cervical cancer patients and controls in the proportions reporting more than five casual (less than six months) sexual partners.

No difference between patients and controls in frequency of coitus was found in the present study. This finding is in agreement with those of Rotkin and King[12] and Jones, Macdonald, and Breslow.[7] Boyd and Doll[5] obtained an apparent association of cervical cancer

with frequent coitus, but the difference between patients and controls proved nonsignificant ($P=0.07$) when the data were adjusted for age at marriage. Terris and Oalmann's[1] finding of an association of cervical cancer with frequent coitus in their New Orleans study is contradicted by the results obtained in the present investigation.

In evaluating these findings, it should be recognized that data on coitus may be of doubtful validity. In the first place, the individuals questioned are asked to remember events occurring years and even decades prior to interview. In the second place, there is a danger that questions regarding such sensitive areas as number of coital partners and frequency of coitus will elicit answers which are inaccurate, since they may reflect the individual's view of what is acceptable to the interviewer. It should be pointed out that in the present study the public health nurse interviewer noted some embarrassment on the part of individuals when asked the questions on number of coital partners and frequency of coitus.

The preponderance of evidence to date appears to indicate that cancer of the cervix is associated with the marital state, separation and divorce, multiple marriages, early marriage, and early coitus. If we accept data on number of coital partners and on frequency of coitus as valid, the preponderance of available evidence from retrospective studies is that many partners and frequent coitus are not associated with cancer of the cervix. On the other hand, the reports by Wynder, et al.,[4] Lombard and Potter,[6] Levin, Kress, and Goldstein,[13] and Rojel[14] that cervical cancer is associated with syphilis suggest that the disease is related to promiscuity. Rojel's[14] finding that there is a very high incidence of cancer of the cervix in prostitutes supports the hypothesis that the disease is related to frequent coitus with many partners.

There are several possible ways that coitus may be related to carcinoma of the cervix. One, suggested by Rotkin,[8] is that the adolescent cervix is more susceptible to the action of a carcinogenic agent, introduced by the male during coitus, which produces carcinoma after a latent period of many years. This hypothesis does not require a relationship of risk to the total dose of carcinogenic agent; therefore the frequency of exposure is not involved. On the other hand, the number of partners may be relevant unless it is also postulated that every male carries the carcinogenic agent. Given this latter assumption, Rotkin's hypothesis is consistent with the findings of the retrospective studies that cervical carcinoma is associated with early coitus but not with frequency or number of coital partners.

Another hypothesis has been put forward by Lundin, Erickson, and Sprunt[11] on the basis of data indicating that the primary association is with early age at first pregnancy rather than early age at first marriage. Unfortunately, they did not have data available on age at first coitus, so that they were unable to test whether the primary association is with first coitus or with first pregnancy. In any case, they suggest that some change which occurs during and after the first pregnancy may be significant in the genesis of cervical cancer. They point out, for example, that the squamo-columnar junction, which is the site of origin of almost all cases of cervical cancer, is proximal to the external cervical os in the nulliparous cervix but is situated on the vaginal surface following delivery, and they suggest that the effect of the vaginal secretions and flora might be important. Furthermore, they state that the lack of an independent association of cervical cancer with number of pregnancies is evidence against the role of pregnancy per se but does not necessarily argue against the importance of the first pregnancy.

The difficulty with this hypothesis is that it cannot stand alone. It is difficult to understand why a difference of a few years in the onset of changes due to first pregnancy should be important unless one also accepts Rotkin's hypothesis that the adolescent cervix is more susceptible to a presumed carcinogenic agent.

A third possibility is that the disease is caused by a viral agent which is carried by only a proportion of males. The risk of developing cancer of the cervix would therefore be related to the number of coital partners. The association of cervical cancer with the marital state and with multiple marriages is consistent with this hypothesis. Separation and divorce presumably tend to increase the number of partners. Early age at first marriage is associated with a greater risk of separation and divorce and therefore an increase in the number of partners. Early age at first coitus may well be related to promiscuity, while syphilis assuredly is. The rarity of the disease in nuns[15,16] and its high incidence in prostitutes would be expected. Frequency of coitus might or might not be relevant, depending on whether the individual male carries the agent all the time, sporadically, or only during a single period. Indeed, all of the known facts about the epidemiology of cervical cancer could be fitted to this hypothesis except the failure to find a relation to number of coital partners in the retrospective studies. However, as previously indicated, there is reason to question the validity of the data on number of partners in these studies.

The fourth, and most common hypothesis, is that males carry a chemical carcinogen, presumably in smegma, which causes cancer of the cervix. This hypothesis requires that the disease be associated with frequent coitus, since the risk of disease would be expected to increase with the amount of exposure to the agent. As with the viral agent possibility, almost all of the known facts about the epidemiology of cervical cancer can be fitted to this hypothesis. The additional exception here is the failure to find a relation to frequency of coitus in the retrospective studies, but again there is reason to doubt the validity of the data obtained in these studies. The smegma hypothesis is given very strong support by the fact that cervical cancer is rare in Jewish women.

Summary

In a study of 239 patients with histologically confirmed invasive squamous cell carcinoma, and an equal number of gynecological controls matched by age and population group, the disease was found to be associated with the marital state, separation and divorce, multiple marriages, early age at first marriage, and early age at first coitus. No association was found with number of coital partners and frequency of coitus, although the validity of these data is questioned. The various hypotheses concerning the specific relationship of coitus to the pathogenesis of cancer of the cervix are discussed.

REFERENCES

1. Terris, M., and Oalmann, M. C. Carcinoma of the Cervix: An Epidemiologic Study. J.A.M.A. 174: 1847–1851, 1960.
2. Dorn, H. F., and Cutler, S. J. Morbidity from Cancer in the United States. Pub. Health Monogr. No. 56. Washington, D. C.: Gov. Ptg. Office, 1959.
3. Haenszel, W., and Hillhouse, M. Uterine Cancer Morbidity in New York City and Its Relation to the Pattern of Regional Variation within United States. J. Nat. Cancer Inst. 22:1157–1181, 1959.
4. Wynder, E. L.; Cornfield, J.; Schroff, P. D.; and Doraiswami, K. R. Study of Environmental Factors in Carcinoma of Cervix. Am. J. Obst. & Gynec. 68: 1016–1052, 1954.
5. Boyd, J. T., and Doll, R. A Study of the Aetiology of Carcinoma of the Cervix Uteri. Brit. J. Cancer 18:419–434, 1964.
6. Lombard, H. L., and Potter, E. A. Epidemiological Aspects of Cancer of the Cervix: Hereditary and Environmental Factors. Cancer 3:960–968, 1950.
7. Jones, E. G.; Macdonald, I.; and Breslow, L. Study of Epidemiologic Factors in Carcinoma of the Uterine Cervix. Am. J. Obst. & Gynec. 76:1–10, 1958.
8. Rotkin, I. D. Relation of Adolescent Coitus to Cervical Cancer Risk. J.A.M.A. 179:486–491, 1962.
9. Dorn, H. F. Some Problems Arising in Prospective

and Retrospective Studies of the Etiology of Disease. New England J. Med. 261:571–579, 1959.
10. She Ming-P'eng; Ch'eng Feng-Ling; Liu T'ung-Hua; Ts'ai Hai-Ying; Liu Chih-Ming; and Wu Ai-Ju. Etiologic Survey of Carcinoma of Uterine Cervix. Chinese M. J. 82:39–45, 1963.
11. Lundin, F. E.; Erickson, C. C.; and Sprunt, D. H. Socioeconomic Distribution of Cervical Cancer. Pub. Health Monogr. No. 73. Washington, D. C.: Gov. Ptg. Office, 1964.
12. Rotkin, I. D., and King, R. W. Environmental Variables Related to Cervical Cancer. Am. J. Obst. & Gynec. 83:720–728, 1962.
13. Levin, M. L.; Kress, L. C.; and Goldstein, H. Syphilis and Cancer: Reported Syphilis Prevalence Among 7,761 Cancer Patients. New York State J. Med. 42:1737–1744, 1942.
14. Rojel, J. Interrelation Between Uterine Cancer and Syphilis. Acta path. et microbiol. scand. (Suppl. 97), 1953.
15. Gagnon, F. Contribution to Study of Etiology and Prevention of Cancer of Cervix of Uterus. Am. J. Obst. & Gynec. 60:516–522, 1950.
16. Towne, J. E. Carcinoma of Cervix in Nulliparous and Celibate Women. Ibid. 69:606–613, 1955.

Dr. Terris is professor of preventive medicine, New York Medical College (Fifth Avenue and 105th St.), New York, N. Y. 10029. Dr. Wilson, formerly clinical instructor in obstetrics and gynecology, State University of New York, Downstate Medical Center, is presently instructor in obstetrics and gynecology, College of Physicians and Surgeons, Columbia University, and coordinator, Cervical Cancer Training and Detection Program, Harlem Hospital Center. Dr. Smith is assistant clinical instructor in obstetrics and gynecology, New York Medical College. Mrs. Sprung is public health nurse, Department of Preventive Medicine, New York Medical College. Dr. Nelson is associate professor of obstetrics and gynecology, State University of New York, Downstate Medical Center, and director, Gynecological Tumor Service, Kings County Hospital, Brooklyn, N. Y.

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Fellowship in the APHA

The attention of members of APHA is drawn to Association News in the February, 1967, issue of the Journal. This sets forth the eligibility requirements for Fellowship in the APHA, explains the procedure for applying (blank forms are available from the headquarters office), and describes the privileges conferred by Fellowship.

Members are encouraged to take the initiative in applying for Fellowship. Members so interested and Fellows wishing to stimulate others to apply, are reminded that completed applications to be considered this year must be filed with the Membership Department, APHA, 1740 Broadway, New York, N. Y. 10019, no later than July 15.