

Occupation and Ovarian Cancer: A Case-Control Study in the Washington, DC, Metropolitan Area, 1978-1981

Patricia Hartge, ScD

Patricia Stewart, PhD

Ovarian cancer risk factors may be genetic, reproductive, or hormonal in nature. Occupational exposure to talc and other carcinogenic substances has not been studied in relation to ovarian cancer risk. We therefore examined the job histories of 296 women aged 20 to 79 who were diagnosed with epithelial ovarian cancer in the Washington, DC area in 1978 to 1981, comparing them to 343 hospital controls, matched for age and race. A blind exposure assessment, evaluating each job/industry combination for potential exposure to talc, ionizing radiation, polycyclic aromatic hydrocarbons, and solvents was conducted by an industrial hygienist blind to case-control status. Women exposed to talc had a relative risk of ovarian cancer below the null, but the confidence interval was wide and there was no evidence of a trend. Women exposed to polycyclic aromatic hydrocarbons had an elevated relative risk, also with a wide confidence interval and no evidence of a trend with duration.

Each year, more than 20,000 women in the United States develop ovarian cancer, and more than 12,000 die from it.¹ Risk of developing ovarian cancer (either invasive or of low malignant potential) is negatively correlated with number of pregnancies, years of use of oral contraceptives, hysterectomy despite ovarian preservation, and, to a lesser extent, years of breastfeeding.^{2,3,4} Risk is positively associated with a family history of ovarian or breast cancer and with a history of infertility. Use of talcum powder has been suggested but not confirmed as a modest risk factor.^{5,6}

No occupational risk factors have been established, but few studies have examined the issue. As with most case-control studies, many individual job titles are reported by so few women that it is hard to assess risk by occupation.⁷ Similarly, in many occupational cohorts, so few ovarian cancers are expected that it also would be hard to detect moderately elevated risks.

We reviewed the occupational histories in a study of ovarian cancer cases and hospital controls for two purposes. We wished to determine which jobs were reported by enough women to permit an occupational analysis in this or similar studies of women in the cancer age range. Second, examination of job histories by an industrial hygienist may reveal associations of disease with certain occupational exposures, associations that cannot be discerned by looking only at types of industries or job titles.⁸ Industries tend to have hetero-

From the Environmental Epidemiology Branch, National Cancer Institute, Rockville, MD.
Address correspondence to: Patricia Hartge, ScD, Environmental Epidemiology Branch,
National Cancer Institute, 6130 Executive Boulevard, Executive Plaza North 443, Rockville,
MD 20892.

0096-1736/94/3608-0924\$03.00/0

Copyright © by American College of Occupational and Environmental Medicine

geneous exposures that are often dependent on the job, and jobs tend to have heterogeneous exposures that are often dependent on the industry. In addition, in most case-control studies, the number of people holding any particular job is small. Even if an elevated risk is found, it is likely to have large confidence intervals, thus making the association suspect.

Having no strong hypotheses, we decided to examine occupational exposure to talc, because use of cosmetic talc has been suggested as a risk factor. We also looked at several exposures related to other malignancies or that could have been experienced in jobs held by the study subjects (eg, ionizing radiation, polycyclic aromatic hydrocarbons (PAHs),⁹ and solvents).¹⁰

Methods

Details of this study have been reported previously.⁷ Cases were 296 women diagnosed with epithelial ovarian cancer during 1978–1981 in hospitals in the Washington, DC metropolitan area. Controls were 343 women discharged from the same hospitals for conditions unrelated to any of the exposures under study and matched for age and race. All ovarian cancer cases were confirmed by pathology review. Study subjects were interviewed by trained interviewers using a standardized questionnaire that took approximately 1 hour to complete. The questionnaire included lifetime job history and a specific question about exposure to talc on the job. Each industry and occupation reported was assigned a Bureau of the Census¹¹ code by trained coders.

One of the authors (PS) conducted an industrial hygiene exposure assessment, evaluating each job/industry combination for potential exposure to talc, ionizing radiation, PAHs, and solvents blind to case-control status. Probability of exposure was assigned on a scale of 0 to 4 (definitely not, unlikely, possibly, probably, definitely), and where probability exceeded 0, level of exposure was assigned on a scale of 1 to 3 (low, medium, high). Evaluation of jobs was based on the industrial hygienist's experience.

We estimated relative risk accord-

TABLE 1
Number of Ovarian Cancer Cases and Controls Ever Employed in the 20 Job Titles Reported Most Frequently

Job Title	Cases (n = 296)	Controls (n = 343)
Secretary	80	92
Typist	36	34
Salesperson, sales clerk	34	32
Bookkeeper	27	21
Clerical worker (not otherwise specified)	28	34
Registered nurse	9	17
Waitress	12	21
Manager or administrator	18	14
Stenographer	14	10
Public administration official	18	10
Teacher (excluding elementary and secondary)	11	13
Miscellaneous clerical worker	12	16
Editor or reporter	12	7
Elementary school teacher	15	8
Cashier	10	11
Secondary school teacher	11	11
Receptionist	12	10
Telephone operator	9	11
Cleaner	7	9
Office manager	6	10

TABLE 2
Percentage Distribution of Selected Risk Factors for Cases and Controls Combined Who Worked at Least 5 Years in Four Common Occupations

	Secretary* (n = 205)	Teacher† (n = 49)	Nurse‡ (n = 28)	Cleaner§ (n = 22)
Livebirths				
0	28%	26%	21%	32%
1–2	43%	59%	32%	28%
3+	29%	14%	46%	46%
Oral contraceptives				
Never	79%	69%	79%	82%
Ever	20%	31%	21%	14%
Gynecologic surgery				
No	69%	75%	54%	59%
Yes	31%	25%	46%	41%
Infertility				
No	78%	78%	86%	91%
Yes	22%	22%	14%	9%
Menopausal estrogen use				
Never	67%	84%	75%	77%
Ever	33%	16%	25%	23%
Cigarette use				
Never	42%	57%	39%	73%
Ever	58%	43%	61%	27%

* Secretary occupation includes codes 303 (billing clerks), 325 (file clerks), 341–355 (office machine operators), 360 (payroll clerks), 370–372 (secretaries), 375 (statistical clerks), 376 (stenographers), 391 (typists), 394 (miscellaneous clerical workers), and 395 (not specified clerical workers).

† Teacher occupation includes codes 102–145 (teachers) and 382 (teacher aides).

‡ Nurse includes codes 075 (registered nurses), 925 (aides), and 926 (practical nurses).

§ Cleaner includes codes for private household cleaning: 982 (private household housekeepers), 902 (cleaners), 903 (janitors), 901 (maids), 950 (housekeepers), 983 (laundresses, private household), 984 (maids, private household), and other types of cleaning jobs.

ing to exposure with adjustment for confounders by fitting a logistic regression model.¹² The variables included race, age (in decade), parity (0, 1-2, 3 or more), gynecologic surgery (four categories), and duration of employment (none, less than 5 years, 5 to 9 years, 10 or more years) in jobs with the exposure of interest, using a probability rating of 2 to 4.

Results

A few job titles were reported very frequently, including secretarial and clerical, teaching, and nursing (Table 1). Private household cleaning was mentioned by only 16 subjects, but other types of cleaning jobs were reported, which we combined for our analysis. These common job titles were reported about as frequently by cases and controls.

For four common occupations, we combined job titles (eg, elementary, secondary, and other teachers). We compared women who had worked for at least 5 years in the occupation to women who never had, adjusting for age, race, parity, and gynecologic surgery. Secretaries and clerks had a relative risk (RR) of 1.1 (95% confi-

dence interval [CI] = 0.7 to 1.8). For teachers, nurses, and cleaners, the RRs and CIs were 1.4 (0.8 to 3.4), 0.5 (0.2 to 1.0), and 0.7 (0.2 to 2.8), respectively.

We also assessed the relation between these four common occupations and major risk factors for ovarian cancer, as well as cigarette smoking, which is probably not related to risk (Table 2). This analysis was restricted to women who had worked in the occupation for at least 5 years. Parity was highest among nurses and cleaners and lowest among teachers. Oral contraceptive use was highest in teachers and lowest in cleaners. Nurses reported more gynecologic surgery and less cigarette smoking than did women in the other jobs. Controlling for the effect of these exposures did not alter the RR estimates for these common occupations.

The relation between the selected exposures and RR is shown in Table 3. Women exposed to talc had risks below the null, but the risks were not statistically significant. In the group with 5 to 9 years of exposure to PAHs, risks of ovarian cancer were elevated, but were not statistically significant. No other risks were elevated.

Discussion

In this nonindustrial metropolitan area, working women typically held white-collar jobs with few exposures to known or suspected carcinogens. The possible role of exposures encountered in most manufacturing, agriculture, and other blue-collar occupations could not be evaluated. Nurses, waitresses, teachers, and office workers, on the other hand, were numerous, so any exposures occurring in those jobs could be assessed by the industrial hygienist. These jobs do not involve the level or variety of exposures often experienced by production jobs in manufacturing. Because no information was available on individual study subjects' exposure characteristics, it had to be assumed that exposures were homogeneous within job title (although it is known that this is not the case). Nonetheless, it is the typical occupational exposure assessment approach in most population-based case-control studies.

No indication of occupational hazard for ovarian cancer was seen in these data. This may have been because of the assumption of homogeneity or the small numbers. Nonetheless, it is still useful to have an industrial hygienist evaluate jobs for women. Women have held production jobs in manufacturing industries in World War II and today; many may experience exposures similar to men.¹³ An industrial hygiene evaluation is particularly useful in case-control studies of cancers of the ovary or other sites for which there are seldom enough women in cohort studies to estimate occupational cancer risks accurately.

References

1. Frey CM. Ovary. In: Miller BA, Ries LAG, Hankey BF, Cosary CL, Edwards BK, eds., *Cancer Statistics Review, 1973-1989*. National Cancer Institute. NIH Publication No. 92-28789, 1992.
2. Whittemore AS, Harris R, Itnyre J. Collaborative Ovarian Cancer Group. Characteristics relating to ovarian cancer risk: collaborative analysis of 12 US case-control studies. II. Invasive epithelial cancers in white women. *Am J Epidemiol*. 1992;136:1184-1203.
3. Harris R, Whittemore AS, Itnyre J. Collaborative Ovarian Cancer Group. Char-

TABLE 3

Estimated Relative Risk of Ovarian Cancer, According to Length of Occupational Exposure to Solvents, Talc, and Polycyclic Aromatic Hydrocarbons*

Exposure†	Cases	Controls	Relative Risk	95% Confidence Interval
Solvents				
None	204	231	1.0	Referent
<5 years	32	31	1.1	0.7-2.0
5-9 years	12	19	0.7	0.3-1.6
10+ years	27	35	0.9	0.5-1.6
Talc				
None	263	285	1.0	Referent
<5 years	5	11	0.5	0.1-1.4
5-9 years	2	8	0.3	0.1-1.4
10+ years	5	12	0.5	0.2-1.5
Polycyclic aromatic hydrocarbons				
None	243	277	1.0	Referent
<5 years	13	23	0.7	0.3-1.3
5-9 years	12	8	1.8	0.7-4.7
10+ years	7	8	1.1	0.4-3.3

* Relative risk estimates are from logistic regression model with terms for duration of employment, race, age, parity, and gynecologic surgery.

† Exposure = number of years in the jobs assigned probabilities of definite, probable, and possible ($P = 2-4$) exposure to these chemicals.

- acteristics relating to ovarian cancer risk: collaborative analysis of twelve US case-control studies. III. Epithelial cancers of low malignant potential in white women. *Am J Epidemiol.* 1992;136:1204-1211.
4. Whittemore AS, Harris R, Itnyre J, Collaborative Ovarian Cancer Group. Characteristics relating to ovarian cancer risk: collaborative analysis of 12 US case-control studies. IV. The pathogenesis of epithelial ovarian cancer. *Am J Epidemiol.* 1992;136:1212-1220.
 5. Harlow BL, Cramer DW, Bell DA, Welch WR. Perineal exposure to talc and ovarian cancer risk. *Obstet Gynecol.* 1992;80:19-26.
 6. Whittemore AS, Wu ML, Paffenbarger RS Jr, et al. Personal and environmental characteristics related to epithelial ovarian cancer. II. Exposures to talcum powder, tobacco, alcohol, and coffee. *Am J Epidemiol.* 1988;128:1228-1240.
 7. Hartge P, Schiffman MH, Hoover R, et al. A case-control study of epithelial ovarian cancer. *Am J Obstet Gynecol.* 1989;161:10-16.
 8. Stewart PA, Herrick RF. Issues in performing retrospective exposure assessment. *Appl Occup Environ Hyg.* 1991;6:421-427.
 9. International Agency for Research on Cancer. *IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans.* Volume 46. Lyon, France: IARC; 1985.
 10. Spirtas R, Stewart PA, Lee JS, et al. Retrospective cohort mortality study of workers at an aircraft maintenance facility. I. Epidemiological results. *Br J Ind Med.* 1991;48:515-530.
 11. Bureau of the Census. *1970 Census of Population, Alphabetic Index of Industries and Occupations.* Washington, DC: US Government Printing Office; 1971.
 12. Rothman KJ. *Modern Epidemiology.* Boston: Little, Brown and Co; 1986, 38-40.
 13. Stewart PA, Blair A. *Women in the formaldehyde industry: their exposures and their jobs.* *J Occup Med* 1994;36:918-923.