

The relationship between perineal cosmetic talc usage and ovarian talc particle burden

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OBJECTIVE: Epidemiologic studies support the hypothesis of a dose-related risk of epithelial ovarian cancer with perineal talc exposure. Frequency and duration of talc usage has not been previously correlated with ovarian talc content.

STUDY DESIGN: Ovaries were studied from 24 women undergoing incidental oophorectomy who were interviewed regarding talc usage. Twelve subjects reported frequent perineal talc applications; the twelve controls reported no use. Ovarian tissue blocks were digested and analyzed by polarized light microscopy and analytic electron microscopy to identify and quantify talc.

RESULTS: Talc was identified in all 24 cases by either light or electron microscopy. Talc particle counts were completely unrelated to reported levels of perineal talc exposure.

CONCLUSIONS: The detection of talc in all ovaries demonstrates that it can reach the upper genital tract. Widespread exposure to talc during diapering may contribute to the ubiquitous presence of talc in ovarian tissue. (AM J OBSTET GYNECOL 1996;174:1507-10.)

Key words: Talc, ovary

Epidemiologic evidence suggests that perineal exposure to talc is associated with an increased risk of epithelial ovarian cancer in a dose-related fashion.¹⁻³ Other epidemiologic studies have shown no increased risk of ovarian cancer associated with talc.⁴⁻⁷ Studies show access of particulate matter into the female peritoneal cavity through the transvaginal route.⁸⁻¹⁰ A few reports have identified talc in ovarian tissue,^{11,12} both benign and malignant, but these data were not correlated with an exposure history. Other potential genital tract exposures in a woman's life include surgical gloves,¹³ condoms, and diaphragms. Diapering with talc during infancy is another potential exposure. Epidemiologic studies have not linked these exposures to an increased risk of ovarian cancer.^{1,2}

If transvaginal transport of perineally applied talc occurs, women with the heaviest exposures may show the largest talc particle burdens in their ovaries. Tissue digestion techniques are an accepted analytic adjunct in the identification and quantification of asbestos in the lungs of occupationally exposed individuals^{14,15} and are useful in the identification and quantification of talc as well.

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The goal of this pathoepidemiologic study was to correlate the history of perineal talc usage with the talc particle burden found in the ovaries.

Material and methods

In a case control study of benign ovarian neoplasms at Columbia Presbyterian Medical Center, women undergoing surgery from 1992 to 1993 were interviewed regarding various factors, including talc usage. Subjects were also questioned regarding possible occupational exposures to asbestos, and mothers were contacted regarding diapering history whenever feasible.

Subjects were categorized for talc exposures as follows. Women who reported no direct application of talc to the perineum or to underwear were considered unexposed. For women who reported talc application to underwear or the perineum, the total number of lifetime applications was estimated as the average frequency of use times the number of years of use. For instance, a woman who reported perineal talc application twice per day for 10 years was considered to have 7240 applications. To simplify the classification of exposed and unexposed women, subjects who reported tubal ligation, diaphragm use, or feminine hygiene spray use were excluded from this analysis.

Interviewed subjects from the parent case control study who had a normal contralateral ovary in the surgical specimen were eligible for this substudy. Sections of normal ovary from the 12 women who reported the largest number of perineal talc applications were analyzed. For each of these subjects the unexposed woman closest in age was selected as a control. In addition, the ovaries of two stillborn fetuses were analyzed as negative controls.

Table I. Talc particle counts in women who reported perineal cosmetic talc usage

Subject No.	age (yr)	Lifetime talc applications*	EM talc particle counts†	Polarized light microscopic counts†	Asbestos detected	Talc use with diapering
1	49	4,784	1,600,288	96	No	Yes
2	49	5,475	0	54	No	Unknown
3	57	6,552	0	100	Yes	No
4	31	8,144	0	114	No	Unknown
5	43	10,556	0	464	Yes	Unknown
6	45	11,284	151,300	300	No	Yes
7	50	11,648	236,406	345	No	Yes
8	57	15,600	0	75	No	Yes
9	66	18,980	0	250	Yes	Yes
10	47	21,840	1,576,000	111	No	Unknown
11	44	23,660	0	348	No	Yes
12	44	39,312	7,565,000	26	Yes	Unknown

EM, Electron microscopy.

*Frequency of use × Years of use.

†Per gram wet tissue weight.

Ovarian tissue in blocks was deparaffinized, rehydrated, blotted dry, and weighed. Digestion with 5% potassium hydroxide was performed at 70° C for 2 to 4 hours. After complete digestion, the tissue was centrifuged at 12,000 revolutions/min for 20 minutes. The potassium hydroxide was removed, leaving a pellet to which approximately 20 ml of distilled water was added. The pellet was resuspended by use of a microultrasonic cell disrupter at 50 W for 5 seconds. Centrifugation, distilled water wash, and microultrasonic cell disrupter were repeated three times. The distilled water was removed, and the pellet was resuspended in 5 to 10 ml of distilled water. Drops of 10 µl of the final suspension were placed on nickel formvar and carbon-coated locator grids and air-dried. Transmission electron microscopy to identify particles and their size was performed. The identity of the particles was determined by energy-dispersive spectroscopy and confirmed by electron diffraction. Grids were viewed at both 10,000 and 19,000 diameters. All talc particles observed were counted. Cytospin slides for polarized light microscopy were prepared from the same final suspension as the electron microscopy grids. Polarized light microscopy counted larger talc particles (limits of detection approximately 1 µm), whereas electron microscopy detected smaller ones (limits of detection approximately 0.5 nm).

Routinely, all solutions are checked for detectable limits of contaminating particles; all places where particles could have contaminated the specimen, such as paraffin, are also controlled for.

Associations between talc exposure and talc particle count in the 12 exposed subjects were assessed with Spearman's rank correlation coefficient.

Results

Detailed results can be seen in Tables I and II. The mean age of the patients was 49 years (range 29 to 66

years). For eight exposed subjects, a control was found who was within 4 years of her age. Talc particle counts were not related to age in either the exposed or unexposed subjects ($p > 0.25$). The mean number of lifetime exposures for the women reporting perineal talc use was 14,820 (range 4784 to 39,312). Talc was detected in all ovaries by either polarized light or electron microscopy. There was a wide range of values, as shown by the large SDs. Table III shows that talc particles were observed to a similar extent with both exposed and unexposed subjects.

Neither the light microscopic nor electron microscopic values correlated with reported perineal talc usage (p values 0.37 and 0.45). There was a negative correlation between the values obtained by light microscopy and electron microscopy ($r = -0.34$, $p = 0.05$). An attempt to contact mothers of subjects was successful for 11 of the 24 subjects. Ten of these reported using talc to diaper their babies, which indicates that lifetime talc exposure may be underestimated for nearly all the subjects. Analyses of two fetal ovaries and a pair of surgical gloves was completely negative for talc.

In one subject we studied both ovaries; on the right side we detected no talc by electron microscopy and 556 particles by light microscopy, and on the left side we detected 1,669,000 particles per gram of wet weight by electron microscopy and 6 particles by light microscopy. Hematoxylin-eosin stained slides from the analyzed sections of tissue were examined. There was no evidence of response to talc, such as foreign body giant cell reactions or fibrosis in the tissue. Asbestos was detected in ovaries of five of the subjects with no talc exposure and in four ovaries of the talc-exposed subjects.

Comment

If transvaginal transport of perineally applied talc occurs, we would expect women with the heaviest exposures to show the largest talc particle burden in their ovaries.

Table II. Talc particle counts in women without history of perineal cosmetic talc usage

Subject No.	Age (yr)	Reported exposure history	EM talc particle count*	Polarized light microscopic talc particle counts*	Asbestos detected	Talc use with diapering
1	63	0	1,350,000	89	No	Yes
2	57	0	315,250	111	No	Yes
3	29	0	0	12	No	Unknown
4	48	0	1,669,000	6	Yes	Unknown
5	59	0	315,208	166	Yes	Yes
6	40	0	0	69	Yes	Yes
7	43	0	0	566	Yes	Unknown
8	64	0	0	420	Yes	Yes
9	49	0	0	53	No	Unknown
10	54	0	0	1139	No	Unknown
11	32	0	63,042	2200	No	Unknown
12	58	0	472,813	0	No	Unknown

EM, Electron microscopy.

*Per gram wet tissue weight.

Table III. Comparison of particle burdens between reported exposed and nonexposed subjects

Talc exposure	No. of subjects with talc by EM	No. of subjects with talc by light microscopy	Mean EM particle count*	SD	Mean light microscopic particle count*	SD
Reported talc use (n = 12)	5/12	12/12	927,416	2,174,888	190	144
No reported talc use (n = 12)	6/12	11/12	348,776	570,055	405	655

EM, Electron microscopy.

*Per gram wet tissue weight.

Tissue digestion techniques have been used to identify and quantify particle burdens of various organic materials in human tissue. The most notable use of this technique is in the identification of asbestos in the lungs of occupationally exposed individuals.¹⁴⁻¹⁵ Other studies have examined other organs as well. In the 1979 report of Henderson et al.¹¹ ovaries were studied after an oxygen incineration procedure. They found 6900 to 55,100 talc particles per gram of wet weight in three normal ovaries, 17,400 to 24,300 in three cystic ovaries, and 6400 to 24,500 in three ovarian adenocarcinomas. No exposure histories were stated.

Our study attempted to correlate ovarian talc particle burden with exposure history. Our results do not support a linear dose-related ovarian talc particle burden. However, the mean electron microscopic particle count was much higher in talc users. Perhaps perineal talc does contribute to the ovarian particle burden; however, factors other than dosage may contribute. Other factors to consider include method of application, type of talc, and the possible contribution of inhaled talc particles. The range of talc particle values obtained in this study was wide, as evidenced by the large SDs. This spread of values was also present in the study of Henderson et al.¹¹ and in much of the asbestos fiber burden literature. Talc may be unevenly distributed throughout the ovarian paren-

chyma. This is supported by the discrepant counts we obtained on the one subject who had analysis of both ovaries. The lack of correspondence between polarized light and electron microscopy counts was due to measurement of different size particles.

Undocumented exposures to talc may partly explain the lack of correlation between adult histories of perineal cosmetic talc applications and ovarian burdens. Although both examination and surgical gloves in the past were dusted with talc, we cannot document this exposure. The gloves we currently use are talc free, according to the company and to our analyses. Ten of the 11 available mothers reported using talc while diapering their babies; this ubiquitous exposure may also contribute to the ovarian particle burdens.

Talc as a possible etiologic agent in the development of epithelial ovarian cancer may be related to asbestos exposure in several ways. Aside from the chemical similarities between the two, many cosmetic talcs contained significant amounts of asbestos, particularly before 1976.¹ Although tremolite asbestos has been documented as a contaminant of some talc preparations, the types of asbestos detected here are more commonly associated with an environmental (chrysotile) or occupational (chrysotile and crocidolite) exposure.¹⁶

The detection of talc in all the ovaries demonstrates

that talc can reach the upper genital tract. However, the quantity detected in this study did not correlate well with the reported exposure. Further study is required to elucidate whether the presence of talc in ovarian tissue is pathogenic.

REFERENCES

1. Cramer D, Welch W, Scully RE. Ovarian cancer and talc: a case control study. *Cancer* 1982;50:372-6.
2. Harlow B, Cramer D, Bell D, Welch W. Perineal exposure to talc and ovarian cancer risk. *Obstet Gynecol* 1992;80:19-26.
3. Harlow B, Weiss N. A case-control study of borderline ovarian tumors: the influence of perineal exposure to talc. *Am J Epidemiol* 1989;130:390-4.
4. Longo D, Young R. Cosmetic talc and ovarian cancer. *Lancet* 1979;2:349-51.
5. Scully RE. Ovarian tumors—a review. *Am J Pathol* 1977;87:686-720.
6. Hartge P, Stewart P. Occupation and ovarian cancer: a case-control study in the Washington DC metropolitan area 1978-81. *J Occup Med* 1994;36:924-7.
7. Tzonou A, Polychronopoulou A, Hsieh CC, et al. Hair dyes, analgesics, tranquilizers and perineal talc application as risk factors for ovarian cancer. *Int J Cancer* 1993;55:408-10.
8. Egli G, Newton M. The transport of carbon particles in the human female reproductive tract. *Fertil Steril* 1961;2:151-5.
9. Henderson W, Hamilton T, Baylis M, Pierrepont CG, Griffiths K. The demonstration of the migration of talc from the vagina and posterior uterus to the ovary in the rat. *Environ Res* 1986;40:247-50.
10. Scully RE. Atlas of tumor pathology, second series, fascicle 16: tumors of the ovary and maldeveloped gonads. Washington, DC: Armed Forces Institute of Pathology, 1979.
11. Henderson W, Hamilton T, Griffith K. Talc in normal and malignant ovarian tissue. *Lancet* 1979;5:499.
12. Henderson W, Joslin C, Turnbull A, Griffiths K. Talc and carcinoma of the ovary and cervix. *J Obstet Gynaecol Br Commonw* 1971;78:266-72.
13. Henderson W, Melville-Jones C, Barr W, Griffiths K. Identification of talc on surgeons' gloves and in tissue for starch granulomas. *Br J Surg* 1975;62:941-4.
14. Heller D, Gordon R. Demonstration of asbestos fibers in a ten year old sputum sample. *Am J Ind Med* 1991;20:415-9.
15. Roggli V, Pratt P. Number of asbestos bodies on iron-stained tissue sections in relation to asbestos body counts in lung tissue digests. *Hum Pathol* 1983;14:355-61.
16. Heller D, Gordon RE, Westhoff C, Gerber S. Asbestos exposure and ovarian fiber burden. *Am J Ind Med* (in press).