FILE NAME: Talc (TALC)

DATE: 1979

DOC#: TALC051

DOCUMENT DESCRIPTION: Journal Article - Cosmetic Talc and Ovarian Cancer

able, economically justifiable, and effective, as well as being acceptable and helpful to the families at risk of HC

We thank Dr Charles Webb, consultant neurologist, University Hospital of Wales, Mrs P. L. Jones, field worker, and the many clinicians in Wales who have been involved in this work.

This work has been supported by grants from the Welsh Office and DHSS and from the Committee to combat Huntington's Chorea (COMBAT).

Requests for reprints should be addressed to P. S. H.

REFERENCES

1. Squires J, Phillips R. Huntington's Chorea in South Wales. *Quart J Med* 1937; 6: 403–23.
2. Harper PS, Walker DA. The social, personal and economic burden of Huntington's Chorea in South Wales. *Brit J Psychiat* (in press).

# Controversy

## COSMETIC TALC AND OVARIAN CANCER

D. L. LONGO R. C. YOUNG

*Medicine Branch, Division of Cancer Treatment, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20205, U.S.A.*

*Summary* The causes of ovarian cancer are unknown. The increased incidence in industrialised countries suggests an environmental influence. Epidemiological, experimental, and clinical data seem to link asbestos and talc with ovarian cancer. Direct passage of talc or asbestos-contaminated talc through the female reproductive tract to the ovarian surface may play an ætiological role. Further systematic evaluation of talc and asbestos as ovarian carcinogens is needed.

### INTRODUCTION

OVARIAN cancer, the most commonly fatal gynæcological malignancy, has been increasing in frequency over the past 40 years. Unlike cervical and endometrial cancer, for which epidemiological correlations have led to a better understanding of risk factors and pathogenesis, little is known about the causes of ovarian cancer.[1]

A role for environmental factors in the origin of ovarian cancer has been inferred from its higher incidence in industrialised countries. The products of industry upon which most attention has been focused are asbestos and talc. Whereas the carcinogenic properties of asbestos are undisputed, there is still controversy over talc.[2–4] Although conclusive data are lacking, various lines of evidence make it difficult to absolve cosmetic talc as a possible carcinogen, co-carcinogen, or promoter of malignant transformation.

### ORIGIN OF OVARIAN TUMOURS

The ovarian epithelium is derived from specialised mesothelial cells in the peritoneal cavity. Ovarian tumours tend to grow by local extension and uncommonly metastasise through the bloodstream. In this regard they are similar to tumours of the mesothelium of both pleural and peritoneal origin as well as animal tumour models of foreign-body tumorigenesis.[5] Often the histological distinction between ovarian tumours, peritoneal mesotheliomas, and carcinomatosis peritonei is difficult. Thus, where epidemiological studies have drawn distinctions between these entities they may be arbitrary because these tumours may have similar origins.

### ASBESTOS AND TALC

The case against asbestos is persuasive. It promotes bronchogenic lung carcinoma[6] and mesothelioma,[7] and ovarian cancer has been found in increased incidence in women with asbestosis.[8] Female asbestos workers studied by Newhouse[9] had an unusually high number of peritoneal neoplasms. Women exposed to asbestos only indirectly as members of households of asbestos employees have been found to have a ten-fold increased risk of mesothelioma.[10] Direct intrapleural injection of asbestos in rats produces a high frequency of mesotheliomas.[11] Strong evidence of a link with ovarian cancer was found by Graham and Graham,[12] who injected mice, hamsters, guineapigs, and Dutch rabbits with tremolite asbestos. The mice and hamsters showed no lesions, presumably because of a protective layer of peritoneum surrounding their ovaries which is absent in the guineapigs and rabbits. Both guineapigs and rabbits developed an atypical papillary pattern of ovarian epithelial hyperplasia which the authors suggested was similar to early ovarian epithelial tumours in women. Furthermore, they observed birefringent bodies in sections of four out of twelve ovarian tumours and none of nine normal controls. These bodies were thought to be asbestos, although no rigorous proof was provided. Although asbestos fibres can be demonstrated in lungs, they are difficult to identify in mesothelial tumours, and their presence would not be mandatory to establish an association.

The case against talc began as guilt by association with asbestos. Mineral talc is closely related to asbestos, and the two substances are often found together in mineral deposits. The pulmonary lesions of talc millers and miners[13] were virtually indistinguishable from those due to asbestos but the latent period was about 20 years longer. Pleural and peritoneal tumours were found at three to four times the expected frequency until particulate-exposure control measures were instituted in 1950 in the U.S.A. A follow-up study[14] showed that these measures had returned risks to normal. An Italian study[15] of talc millers and miners working a deposit less contaminated by asbestiforms showed no increase in lung or peritoneal tumours. Thus, epidemiological data could be interpreted as showing that the risk of developing cancer from an occupational talc exposure was due to contaminating asbestos.

### EPIDEMIOLOGICAL STUDIES

The epidemiological assessment of the risk due to talc is hampered by several factors. Firstly, talc exposure is so widespread that control groups are difficult to identify. Talc is used in dusting powders, deodorants, chalks, crayons, textiles, pills (including two of the six common brands of contraceptive pills), soap, insulating materials, paints, asphalt filler, paper, and condoms and contraceptive diaphragms. It is also used extensively in food

cessing. Secondly, consumer talc products marketed before 1973 were variably contaminated by asbestos. Rohl et al.[16] studied twenty products, half of which contained detectable amounts of tremolite (up to 14% by weight). Two brands had detectable chrysotile fibres. In October, 1976, the Cosmetic, Toiletry and Fragrance Association (C.T.F.A.) revised their guidelines for talc and recommended that no sample containing asbestos detectable by X-ray diffraction and optical microscopy with dispersion staining should be sold. Therefore, data collected on populations exposed before 1976 may reflect the hazard of contaminating asbestos rather than talc. Unfortunately, adherence to the revised C.T.F.A. guidelines is voluntary and monitoring of samples is left to individual manufacturers; so that, even now, commercial talcs are not certain to be asbestos-free. Finally, the epidemiological assessment of risk of talc exposure is seriously affected by the long latency of presumed talc-induced disease. A prospective study might take more than forty years. Newhouse[17] has reported no evidence of health hazard among the predominantly female employees in a British talc factory in a study which needs to be continued another ten years[4] to be confident in the negative result. Information from epidemiological studies of talc exposure thus far must be considered inconclusive.

## EXPERIMENTAL STUDIES

Animal studies on the effects of talc have been reviewed by Hildick-Smith.[3] Talc was not found to be mutagenic in vitro, but neither is asbestos.[18] In-vivo tests and several acute and chronic exposure models failed to show any carcinogenic potential over a wide dose range. Though these studies were conducted with talcs of undefined chemical and physical characteristics, their uniformly negative results provide the basis for Hildick-Smith's conclusion that "concern . . . about the possible health hazard from consumer exposure to cosmetic talc is unwarranted". Yet data on the cellular response to talc are sparse. Allison[19] observed that talc—like other agents of chronic inflammation, including asbestos[20]—is ingested by macrophages with attendant release of lysosomal hydrolases. Lung fibroblasts take up talc particles up to 10 μm in diameter,[21] and these particles penetrate the cell membrane but not the nuclear membrane. Chrysotile asbestos fibres are handled in a similar way. No studies of the effects of talc on cell metabolism have been reported. Intratracheal instillation of talc in Syrian golden hamsters has been shown not to induce respiratory tumours, though fibrosis was not uncommon.[22] Benzo(a)pyrene alone also failed to induce respiratory-tract tumours.[23] However, talc and benzo(a)pyrene together induced tumours in 80% of hamsters treated. Whereas the bulk of evidence suggests that talc is not an independent carcinogen, it may act as a co-carcinogen or promoter. None of the animal studies has clarified what talc does at the cellular level.

## CLINICAL EVIDENCE

Clinical data provide the bulk of evidence for a role for talc in human disease. The development of fibrous adhesions from talc has been known since 1933, and for this reason talc has been used to obliterate pleural cavities in diseases causing chronic effusions. In a granulomatous lesion Lichtman et al.[24] found talc which had been deposited there 36 years earlier. They also observed tremendous variation in the response to talc of different tissues and the same tissue in different species, some lesions developing central necrosis within five days in the absence of a polymorphonuclear response. Talcosis, a diffuse lung disease characterised by peribronchial fibrosis, was an occupational pneumoconiosis until exposure limits were enforced in the U.S.A. Talc bodies in sections of diseased lung, as with asbestos bodies in asbestosis, suggest that talc elicits a strong defensive reaction in man. Pulmonary intravascular granulomas caused by intravenous injection of talc-containing drug formulations can lead to vascular thrombosis and sclerosis with pulmonary hypertension.[25] Thus, there is little doubt that talc is not as inert in man as in some animal species which have been used to assert its benignancy. The most provocative evidence of a specific association between talc and ovarian cancer was that reported by Henderson et al.,[26] who found talc particles 0·1–2 μm in diameter deeply embedded in 75% (10 of 13) of ovarian tumours studied, as well as some cervical and endometrial tumours. No asbestos fibres were identified. Uncertainties about applicability of the technique used in that report have cast some doubt on the validity of the findings, but several subsequent papers from the same group[27–31] lend weight to the original contentions. Access of talc to the peritoneal cavity is most likely through the vagina. Studies of the transport of particles in the human female reproductive tract[32] have shown that non-motile inert carbon particles deposited in the vagina can be recovered 30 to 35 min later in the Fallopian tubes.

## TALC AND OVARIAN CANCER

We suggest that cosmetic talc can be deposited in the vagina through repeated application to the perineum or through use of a talc-dusted diaphragm or condom during intercourse. As it is carried through the female reproductive tract most particles are removed by local defence mechanisms, but an occasional particle can be deposited on the surface of the ovary. Possibly stimulated by gonadotrophins and/or ovarian hormones, the talc (perhaps contaminated with asbestos) alters the responsiveness of the ovarian epithelium, which ultimately proliferates autonomously.

This hypothesis seems to be consistent with the known facts about ovarian cancer. With talc exposure beginning in infancy, hormonal stimulation with menarche, and assuming a 20–40 year latency period, peak incidence of ovarian cancer might be expected in the 40–60 year age group. This is, in fact, the observed age-group of peak incidence. The hypothesis would predict the observed high incidence of bilaterality. It would also predict that anything interrupting the patency of the female reproductive tract should protect against ovarian cancer. An epidemiological report from the Mayo Clinic[33] shows that hysterectomy is associated with a lower risk of ovarian cancer. Similarly, patients with a history of tubal disease (e.g., scarring from pelvic inflammatory disease) should have a lower incidence of ovarian cancer. Although this prediction has not been directly assessed, data suggesting a lower attack-rate in sexually active women may indirectly support the

hypothesis. The observed increased risk of ovarian cancer in late-primiparous and nulliparous women[35] can be explained by implicating uninterrupted cyclical hormone influences in the genesis of ovarian epithelial neoplasia.

## CONCLUSION

The risk of cosmetic talc has not been fully evaluated. Enforcing the removal of detectable asbestos from talc is a first step to protecting consumers from potential hazard. Investigators should focus on detecting the effects of talc on cells in general and hormonally responsive cells specifically. Primates should be used in experimental studies because their hormonal cycles and epithelial trophisms most closely parallel those of women. Efforts to identify particles in ovarian-cancer specimens should be intensified. The epidemiological study of Newhouse and her colleagues[17] in Great Britain on the risks of systemic exposure in female talc workers should be repeated in another geographical location. Furthermore, a study on the risks of local use of talc in the genital region should be undertaken. Finally, clinicians should collect data on the use of cosmetic talc by their patients with ovarian cancer. Data obtained from such an approach may justify the absolution of talc which has already been claimed.[3,4] But until such information is collected *The Lancet*'s statement that "it seems unlikely that future exposure to cosmetic talc of the specifications now agreed to by major manufacturers will present a health hazard" must be taken on faith alone.

Requests for reprints should be addressed to R. C. Y.

## REFERENCES


1. Bergman CH. Etiology of cancer of the human ovary: a review. *J Nat Cancer Inst* 1974, 53: 1603–18.
2. Boyer HP, Arlon R. Talc, a possible occupational and environmental carcinogen. *J Occup Med* 1973, 15: 92–7.
3. Heidelberger GY. The biology of talc. *Br J Indust Med* 1976, 33: 227–29.
4. Anonymous. Cosmetic talc powder. *Lancet* 1977, i: 1348–9.
5. Brand KG, Johnson KH, Buoen LC. Foreign body tumorigenesis. *CRC Crit Rev Toxicol* 1976; 4: 353–94.
6. Doll R. Mortality from lung cancer in asbestos workers. *Br J Indust Med* 1955, 12: 81–6.
7. Wagner JC, Sleggs CA, Marchand P. Diffuse pleural mesothelioma and asbestos exposure in North Western Cape Province. *Br J Indust Med* 1906. 17: 260–71
8. Keal EE. Asbestosis and abdominal neoplasms. *Lancet* 1960, ii: 1211–6.
9. Newhouse ML, Berry G, Wagner JC, Turok ME. A study of the mortality of female asbestos workers. *Br J Indust Med* 1972; 29: 134–41.
10. Vianna NJ, Polan AK. Non-occupational exposure to asbestos and malignant mesothelioma in females. *Lancet* 1978; i: 1061–3.
11. Wagner JC, Berry G. Mesotheliomas in rats following inoculation with asbestos. *Br J Cancer* 1969; 23: 567–81.
12. Graham J, Graham R. Ovarian cancer and asbestos. *Environ Res* 1967; 1: 115–28.
13. Kleinfeld M, Messite J, Kooyman O, Zaki MH. Mortality among talc miners and millers in New York State. *Arch Environ Health* 1967; 14: 663–7.
14. Kleinfeld M, Messite J, Zaki MH. Mortality experiences of talc workers: a follow-up study. *J Occup Med* 1974, 15: 345–9.
15. Rubino GF, Scansetti G, Piolatto G, Romano CA. Mortality study of talc miners and millers. *J Occup Med* 1975; 18: 186–93.
16. Rohl AN, Langer AM, Selikoff IJ, et al. Consumer talcums and powders: mineral and chemical characterization. *J Toxicol Environ Health* 1976, 2: 255–84.
17. Newhouse ML, Miner BF, Moore WKS. Paper given at seminar on Biology of Talc in Health Products, Cardiff, May, 1976, cited in 5.
18. Ames BN. unpublished observations.
19. Allison AC. Paper given at seminar on Biology of Talc in Health Products, Cardiff, May, 1976.
20. Schorlemmer HU, Davies P, Hylton W, Gugig M, Allison AC. The selective release of lysosomal acid hydrolases from mouse peritoneal macrophages by stimuli of chronic inflammation. *Br J Exp Pathol* 1977, 58: 315–26.
21. Henderson WJ, Blundell G, Richards R, et al. Ingestion of talc particles by cultured lung fibroblasts. *Environ Res* 1975; 9: 173–8.
22. Steinbach F, Rowland I. Role of talc and benzo[a]pyrene in respiratory tumor formation. *Scand J Respir Dis* 1978; 59: 130–40.
23. Kuschner M. The J. Burns Amberson lecture: the causes of lung cancer. *Am Rev Respir Dis* 1968, 98: 573–97.
24. Lichtman AL, McDonald JR, Dixon CI, Mann FC. Talc granulomas. *Surg Gynecol Obst* 1946, 83: 531–58.
25. Hopkins GB, Taylor GD. Pulmonary talc granulomatosis. *Am Rev Resp Dis* 1970, 101: 194–8.
26. Henderson WJ, Joslin CAF, Turnbull AC, Griffiths K. Talc and carcinoma of the ovary and cervix. *J Obstet Gynaecol Br Comm* 1971, 78: 266–72.
27. Henderson WJ. The use of analytical electron microscopy in the study of foreign and naturally occurring minerals in biological tissues. *Microsc Acta* 1979, 3: 131–3.
28. Griffiths K, Henderson WJ, Chandler JA, Joslin CAF. Ovarian cancer: some new analytical approaches. *Postgrad Med J* 1973, 49: 68–72.
29. Henderson WJ, Chandler JA, Blundell G, Griffiths C, Davies JD. The application of analytical electron microscopy to the study of diseased biological tissue. *J Microscopy* 1973; 99: 183–92.
30. Henderson WJ, Griffiths K. Identification of particles in ovarian tissue. In Brush MG, Taylor RW, eds. Gynecological malignancy: clinical and experimental studies. Baltimore: Williams and Wilkins, 1975. 225–40.
31. Henderson WJ, Hamilton TC, Griffiths K. Talc in normal and malignant ovarian tissue. *Lancet* 1979, i: 499.
32. Egli GE, Newton M. The transport of carbon particles in the human female reproductive tract. *Fertil Steril* 1961; 12: 151–5.
33. Annegers JF, Strom H, Decker DG, Dockerty MB, O'Fallon WM. Ovarian cancer, incidence and case-control study. *Cancer* 1979; 43: 723–9.
34. Beral V, Fraser P, Chilvers C. Does pregnancy protect against ovarian cancer? *Lancet* 1978; i: 1033–6.


# Round the World

*From our Correspondents*

## *United States*

### THE PUBLIC'S RIGHT TO KNOW

IF there is one thing that distinguishes the U.S. from the U.K. it is the publicity that surrounds crimes and those accused of committing them. In Britain the discussion in the media of sub-judice matters is sharply circumscribed. In the U.S. comment has been very free, far too free some would argue. In a notorious or scandalous case there may be enormous publicity on every aspect, including every detail of the accused, before the case even comes to trial. All this is defended by the media as part of the public's right to know, embedded in that sacrosanct document, the U.S. Constitution.

But the Supreme Court has been busy in these last few weeks. It decided in the Weber case that affirmative action was permitted in favour of minorities, the victims of inequality in the past, even if other racial groups were thereby disadvantaged. The case differed from the Bakke case in that no specific quota was involved. The Court ordered extensive "busing" to enforce racial balance in schools (though whether the fuel will be available—or well spent—is another matter). Finally, to the fury of the media and the libertarians the Court decided, by a majority, that a judge, if both sides agreed, could exclude the Press and other media from the courts in criminal and civil cases. The judgment came, as so often happens, from a relatively trivial legal fracas in New York State. But, by implication, it could have extensive repercussions. Justice, it is said, may certainly be done, but it certainly will not be seen to be done under this dispensation, and the public will not know. We can expect considerable hubbub to develop over this decision.

The public right to know has been in the foreground since the Watergate affair, when the public were denied this right by deliberate concealment. It led to the Freedom of Information Law by which public access to all Government documents is now permitted. In theory this is admirable, and scornful fingers are pointed at Britain, where so much secrecy prevails. There are also some undesirable aspects which are now coming to the fore, particularly those involving the F.B.I. and similar archives. Every little crook and nanny, as it were, is searching every little nook and cranny of these archives (of course, at the taxpayers' expense) for something or other. Some are looking for the names of those who informed on them to the police or betrayed Party comrades; others are looking for opportunities