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The Demonstration of the Migration of Talc from the Vagina and Posterior Uterus to the Ovary in the Rat

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Talc particles placed in both the uterine cavity and the vagina of the rat were shown to migrate to the ovary and become localized within its substance. © 1986 Academic Press, Inc.

INTRODUCTION

The presence of talc particles deeply embedded in ovarian and cervical benign and malignant tissue was reported by this Institute (Henderson *et al.*, 1971). Positive identification of the particles was achieved (Griffiths *et al.*, 1973) by replicating the surface morphology of tissue sections (Henderson, 1969) and analyzing the X-ray emission spectra of extracted foreign material with an electron microscope microanalyzer (EMMA, A. E. I. Harlow, England).

Direct communication between the external environment and the peritoneal cavity exists in the female via her genital tract. It has been demonstrated that the injection of a suspension of talc beneath the bursa of the rat ovary was followed by the development of large ovarian bursal cysts, with associated epithelial changes not inconsistent with the histological picture of premalignancy (Hamilton *et al.*, 1984). It was, therefore, of interest to see whether talc placed in the lower part of the female genital tract of the rat would migrate anteriorly to the ovary.

MATERIALS AND METHODS

In a pilot study eight female exbreeder Sprague-Dawley rats 7.5 months old were used. Under light ether anesthesia a speculum of an auroscope with the lens removed was introduced into the vagina and the cervical os illuminated. A Portex catheter (o.d. 0.75 mm) was passed a distance of approximately 2.5 cm into the cervical canal from the vagina introitus and a suspension of talc (100 mg/ml) in phosphate-buffered saline (PBS) introduced (vol 250 μ l). The animals were divided into two groups of four. Group I was sacrificed 5 days following intra-uterine instillation of the talc suspension and their ovaries were removed. The animals in Group II received further uterine instillations 6 and 15 days after the initial treatment. On Day 20, two rats from this group were killed and their ovaries removed. The remaining two rats received further treatments 22 and 30 days after their initial treatment and were sacrificed on Day 49.

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The ovaries from each animal were combined and subjected to an ashing procedure as described previously (Henderson *et al.*, 1978). Essentially this process removes organic matter by heating the organs to 550°C in the incineration chamber of a horizontal tubular muffle furnace in a stream of oxygen (250 ml/min/500 mg wet wt for 5 hr). The ashed material was then suspended in distilled water (50 μ l). Aliquots (10 μ l) were pipeted onto carbon-coated electron microscope grids and the water was evaporated. A further carbon coat was applied *in vacuo* to stabilize any particles and to dissipate heat and electrostatic charge generated by the concentrated electron beam prior to examination with the EMMA.

Twelve Sprague-Dawley exbreeder rats of a similar age to those used in the experiment described above were divided into two groups of six. Group I animals were firmly held and the louver of a 1-ml disposable microjet 501 TB syringe was introduced into the vaginal orifices and 250 μ l of a suspension of talc (100 mg/ml) in PBS was deposited into the vaginas. The animals in Group II were treated similarly except that 250 μ l of PBS was substituted for the talc suspension. Two animals from each group were sacrificed 24 hr, 48 hr, and 4 days, respectively, following initial treatment. Their ovaries were removed and treated similarly to those described in the first experiment.

RESULTS

Particles of talc were identified in the ovaries of all the animals that received intrauterine talc and in the two animals that received intravaginal talc killed after 4 days (Fig. 1a). X-Ray analysis (Fig. 1b) confirmed the chemical constitution of talc. No talc could be demonstrated in the group of rats that had received PBS intravaginally or in those animals with intravaginal talc killed after 24 and 48 hr.

DISCUSSION

Birefringent particles were first noted to be present in human ovarian carcinomas by Graham and Graham (1967) who postulated that these particles might be asbestos. Subsequent work at this Institute identified talc in ovarian cancer tissue but not asbestos (Henderson *et al.*, 1971; Griffiths *et al.*, 1973). The ease of migration of particulate material from the vagina to the peritoneal cavity (Venter and Iturralde, 1979; Iturralde and Venter, 1981) has been established.

The physiological mechanisms associated with translocation of particulate material within the genital tract are unknown but are probably operative in most mammalian species. The chemical nature of the particulate would not appear to alter its ability to be transported through the genital tract and does not elicit any selective mechanisms. Indeed it is accepted that retrograde flow of menstrual products into the peritoneal cavity via the Fallopian tubes is not an uncommon finding by laparoscopy at the time of menstruation. The rhythmic muscular contractions of the uterus that occur spontaneously and the illicit currents established by the epithelial cells of the genital tract may contribute to the translocation process.

Talc is widely used in the cosmetic and pharmaceutical industry and has been associated with the use of certain forms of barrier contraceptives. Many women apply talc to their perineal area and some to their sanitary ware (Cramer *et al.*, 1982).



FIG. 1. (a) Particles of talc in suspension of talc into the post-treatment showing the 3:1 ratio of

The association of talc with ovarian cancer (Lichtman *et al.*, 1946) and the stromal structure may lead to the

Carcinogenic activity of talc in the presence in the environment under suspicion (Longo and Cramer *et al.* (1982) suggest that ovarian cancer and the use of talc exposure to the endometrium and Mokronosova. The physical properties of talc is ac-

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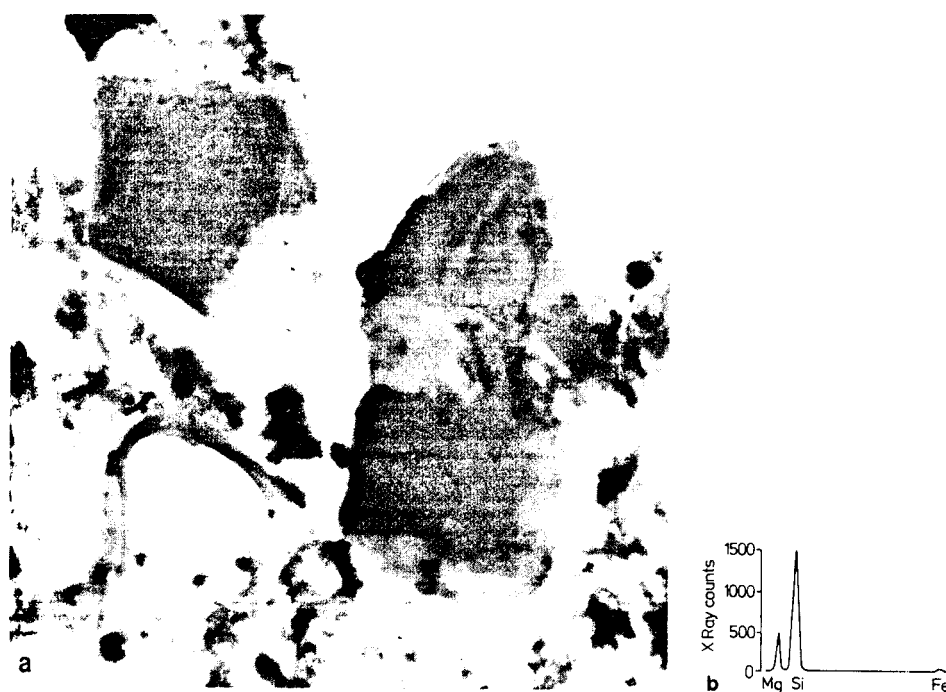


FIG. 1. (a) Particles of talc recovered from the ovary by oxygen ashing following instillation of a suspension of talc into the posterior genital tract of a rat (10,000 $\times$). (b) Spectral analysis of the particles showing the 3:1 ratio of silicon to magnesium characteristic of talc.

The association of talc with formation of granulomata is well documented (Lichtman *et al.*, 1946) and it may be speculated that disruption of normal ovarian stromal structure may lead to disturbances in steroid hormone metabolism.

Carcinogenic activity of talc has not been established although its ubiquitous presence in the environment and its elemental similarity to asbestos has brought it under suspicion (Longo and Young, 1979). However, it has been found in both normal and malignant tissue and its precise role remains unclear, although Cramer *et al.* (1982) suggested that a relationship between increased incidence of ovarian cancer and the use of talc existed. A long latent period from the initial exposure to talc to the induction of malignant change has been postulated (Katsnelson and Mokronosova, 1979), but until a greater understanding of the biological properties of talc is achieved further speculation is unjustified at this time.

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Critical Concepts Humans I

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Cadmium (Cd) was determined in 51 subjects. Controls aged between 30 and 40 years had mean values for the control group of 35.2 µg/g wet wt. The kidney cortex concentrations up to approximately 200 µg/g. The lowest liver concentrations around 30 µg/g. The critical levels for Cd exposed to environmental pollution are 200 µg/g wet wt. © 1986 Academic Press

Chronic exposure to cadmium (Cd) (Friberg *et al.*, 1974; Nogawa *et al.*, 1975) is considered as the major health hazard. It seems to be more sensitive than lead (Pb) (Friberg, 1974, 1979).

Kidney damage consists of an increase in total proteinuria, an increase in amino acids in the urine, a decrease in creatinine clearance (%TRP), decreased creatinine clearance (Friberg, 1950; Piscator, 1966; Kjellström *et al.*, 1977; Saito *et al.*, 1979b, 1980a, b, 1981c; Kawanishi *et al.*, 1979) and/or glucosuria as well as in the inhabitants of different Cd-polluted areas (Nogawa *et al.*, 1975, 1980b; Kawanishi *et al.*, 1980; Kobayashi *et al.*, 1981a, b). Tolerance to Cd-intoxication.