Int. J. Cancer: 71, 948–951 (1997)

Publication of the International Union Against Cancer
Publication de l'Union Internationale Contre le Cancer

TUBAL STERILISATION, HYSTERECTOMY AND DECREASED RISK OF OVARIAN CANCER

Adèle GREEN[1]*, David PURDIE[1], Christopher BAIN[2], Victor SISKIND[2], Peter RUSSELL[3], Michael QUINN[4], Bruce WARD[5] and THE SURVEY OF WOMEN'S HEALTH STUDY GROUP

[1]*Queensland Institute of Medical Research, Brisbane, Queensland, Australia*
[2]*Department of Social and Preventive Medicine, University of Queensland, Brisbane, Queensland, Australia*
[3]*Department of Anatomical Pathology, King George V Memorial Hospital, Sydney, New South Wales, Australia*
[4]*Department of Obstetrics and Gynaecology, Royal Women's Hospital, Melbourne, Victoria, Australia*
[5]*Department of Obstetrics and Gynaecology, University of Queensland, Brisbane, Queensland, Australia*

We have examined the effect of tubal sterilisation and hysterectomy on risk of ovarian cancer in a large case-control study in eastern Australia involving 824 women aged 18–79 years, diagnosed with epithelial ovarian cancer between 1990 and 1993, and 855 controls randomly selected from the electoral roll. Relative risks for ovarian cancer were estimated using multiple categorical regression to adjust for age, parity, oral contraceptive use and other risk factors. Tubal sterilisation was associated with a 39% reduction in risk of ovarian cancer (RR 0.61, 95% CI 0.46–0.85) and hysterectomy with a 36% reduction (RR 0.64, 95% CI 0.48–0.85). Risk remained low 25 years after surgery and was reduced irrespective of sterilisation technique, and estimates were similar among various types of epithelial ovarian cancer. The greatest reduction (74%) was observed among women with primary peritoneal tumours. Pelvic infection and use of vaginal sprays or contraceptive foams were not related to ovarian cancer, while use of talc in the perineal region slightly but significantly increased risk among women with patent fallopian tubes. Reportedly heavy or painful menses, perhaps associated with retrograde flow, were associated with ovarian cancer, and reduction in risk of disease after hysterectomy was greatest among women who had heavy periods. Our findings support the theory that contaminants from the vagina, such as talc, and from the uterus, such as endometrium, gain access to the peritoneal cavity through patent fallopian tubes and may enhance the malignant transformation of ovarian surface epithelium. Surgical tubal occlusion may reduce the risk of ovarian cancer by preventing the access of such agents. *Int. J. Cancer* 71:948–951, 1997.

Although the factors that cause epithelial ovarian cancer are unknown, there are several discretionary factors that appear to protect against it. Oral contraception is associated with up to 70% reduction in risk after 10 or more years of use compared with never-use (Purdie *et al.*, 1995), the protection presumably reflecting long-term suppression of ovulation. A 30–50% reduction in risk has been observed (Booth *et al.*, 1989; Hankinson *et al.*, 1993; Irwin *et al.*, 1991; Whittemore *et al.*, 1992), though not consistently (Chen *et al.*, 1992; Risch *et al.*, 1994; Shu *et al.*, 1989), after tubal sterilisation, and this is independent of childbearing and oral-contraceptive use. A similar inverse association is found between hysterectomy with ovarian conservation and ovarian cancer (Hankinson *et al.*, 1993; Hartge *et al.*, 1989; Irwin *et al.*, 1991; Risch *et al.*, 1994; Weiss and Harlow, 1986).

Explanations include blocking the ascent into the peritoneal cavity (Woodruff, 1971) of carcinogenic agents such as talc (Henderson *et al.*, 1979), asbestos (Graham and Graham, 1967), viruses (Wahlberg, 1994) or contraceptive foams or gels (Silver, 1994) through surgical closure of the fallopian tubes or post-surgical compromise of ovarian circulation (Cattanach, 1985) associated with decreased ovarian function. Alternatively, the negative associations between pelvic surgery and ovarian cancer may be secondary to sub-fertility (Mori *et al.*, 1992) or may be the result of surveillance bias since women whose ovaries have been screened for malignancy during surgery will have a reduced risk of cancer for several years compared with women not screened in this manner (Weiss and Harlow, 1986). Available data are largely inconclusive about these alternatives since the studies have involved small numbers of women reporting tubal sterilisation and hysterectomy and details regarding timing of surgery often were lacking. In the largest case-control study of its kind, we have studied in greater detail the possible effect of tubal sterilisation or hysterectomy on a woman's risk of developing epithelial ovarian cancer, specifically investigating most of the associated factors that have been postulated to date.

SUBJECTS AND METHODS

Incident cases of primary epithelial ovarian cancer diagnosed between August 1990 and December 1993 and registered in gynaecological-oncology treatment centres in 3 Australian states, New South Wales, Victoria and Queensland, were ascertained. Tissue used to establish original diagnoses was reviewed by an independent pathologist in each state. Full details have been presented elsewhere (Purdie *et al.*, 1995). Briefly, cases aged 18–79 years were invited to participate in the study with their doctors' consent, and a response rate of 90% was obtained. Control women, frequency-matched for age and urban/rural district of residence, were randomly chosen from the electoral roll (enrolment to vote is compulsory in Australia), and a letter explaining the study and inviting participation was sent to them. Women who gave a history of ovarian cancer or bilateral oophorectomy were excluded, and the response rate was 73% among eligible controls. In a face-to-face interview, identically trained interviewers administered a standard questionnaire, asking about personal details such as education, height and weight, smoking history, details of menstrual cycles and family history of ovarian cancer. Full histories of pregnancies and lactation were obtained, and by means of a calendar, each woman's contraceptive practices between the ages of 15 and 50 years were elicited. Questions also were asked about history of pelvic infection, abdominal surgery and use of talc. If tubal sterilisation or hysterectomy had been performed, women were asked about date and place of surgery and name of surgeon. Confirmation and details

Contract grant sponsors: Australian National Health and Medical Research Council; Queensland Cancer Fund.

*Correspondence to: Queensland Institute of Medical Research, Post Office, Royal Brisbane Hospital, Qld., 4029, Australia. Fax: 61-7-3362 0101. e-mail: adeleG@qimr.edu.au

The Survey of Women's Health Study Research Group is comprised of the following collaborators: S. Campbell, C. Dalrymple, A. Day, A. Ferrier, K. Free (deceased), P. Grant, N. Hacker, P. Harnett, P. Harvey, R. Houghton, T. Jobling, Peter MacCallum Cancer Institute, R. Planner, T. Proietto, R. Rome, J. Solomon, B. Susil, G. Wain and G. Wright. Research Assistants: C. Birks, P. Brisley, P. Candlish, S. Clarke, K.-A. Lockwood, L. Luck, R. Patterson, L. Potter, A. Ward, M. Watson and M.-E. Yarker.

Received 2 December 1996; revised 27 January 1997

of operative procedures were then sought from the relevant medical practitioners with each woman's written consent.

To test the theory that tubal occlusion prevents entry of foreign agents to the peritoneal cavity through the fallopian tubes, we assessed exposures to vaginal sprays, contraceptive foams and douches, possible talc lubricant on the surface of condoms (Kasper and Chandler, 1995) and talc used specifically in the perineal region. It also was postulated that if peritoneal irritants were to play a role in the development of epithelial ovarian cancers, then this would apply to primary peritoneal cancers in particular, with a consequent substantial reduction in risk to this sub-group after tubal occlusion. Duration of exposure was calculated from age at first use to earliest age at pelvic surgery, if any, and age at last use (age at diagnosis or at interview if use was continuing). In addition, we investigated whether tubal occlusion might prevent retrograde menstruation, which may be damaging to the ovary. To this end, associations between ovarian cancer and painful or heavy periods were assessed on the assumption that these symptoms identified women who may have experienced retrograde menstruation (Smith, 1991) to a greater degree than women without these symptoms.

Crude odds ratios (ORs) with 95% confidence intervals (CIs) were calculated as estimates of the relative risk (RR) of ovarian cancer. Multivariate RRs were estimated using multiple categorical logistic regression to simultaneously adjust for parity and duration of oral contraceptive use and for other possible confounders, such as age (in years), education, body mass index, smoking and history of ovarian cancer in a first-degree relative. Multivariate RRs are presented in this report except when stated otherwise. All analyses were performed using the SAS (Cary, NC) statistical package.

RESULTS

Tubal sterilisation

Of 824 women with incident ovarian cancer and 855 controls, there were 104 cases (13%) and 194 controls (23%) who reported tubal sterilisation. Among a random sample of 64 women for whom surgical records could be located, there was 100% agreement with the women's self-reports of tubal sterilisation (Green *et al.*, 1997). Among control subjects, women who had had a tubal sterilisation tended to have had more children more often than those who had not had tubal sterilisation (Table I). Risk of ovarian cancer was appreciably reduced in women after tubal sterilisation compared with other women (RR 0.61, 95% CI 0.46–0.85) (Table II). Among a random sample of 20 cases and 58 controls for whom information about method of tubal sterilisation was available from either surgical records or women's general practitioners, decreased risk of ovarian cancer was observed irrespective of sterilisation technique, with crude RRs of 0.15, 95% CIs 0.02–1.3 after occlusion by tubal rings; 0.20, 0.04–0.95 after bipolar diathermy; 0.23, 0.07–0.84 after application of clips; and 0.48, 0.24–0.94 after tubal ligation.

TABLE I – PREVALENCE OF POSSIBLE RISK FACTORS AMONG CONTROLS WITH AND WITHOUT SURGICAL OCCLUSION OF THE FALLOPIAN TUBES, STANDARDIZED TO THE AGE DISTRIBUTION OF ALL CONTROL SUBJECTS[1]

Risk factor	With tubal sterilisation (n = 194)	Without tubal sterilisation (n = 661)	With hysterectomy (n = 171)	Without hysterectomy (n = 684)
Post-school education	41.4	49.8	47.5	48.3
Ever smoked	48.1	37.1	34.3	39.0
Parity ≥2	94.9	74.3	86.0	76.5
Heavy periods	34.8	31.1	51.7	26.1
Painful periods	61.0	48.5	63.2	46.1
Ever used oral contraceptives	68.2	63.0	63.8	64.7
Past history of pelvic infection	8.3	6.0	8.5	6.1
Ever used talc in perineal region	41.1	41.1	38.9	40.3

[1]Values are percentages.

Risk remained low 25 years or more after tubal sterilisation, when there was a 57% reduction in risk of ovarian cancer (Table II).

Hysterectomy

There were 116 cases, and 178 of 860 initially enlisted controls who reported undergoing hysterectomy with conservation of at least one ovary prior to the date of index diagnosis. Subsequent checks of available medical records revealed that bilateral oophorectomy had been performed in 5 controls, thereafter excluded from all analyses; and in a validation study (Green *et al.*, 1997), it was shown that 2 cases and 2 controls had not had a previous hysterectomy, leaving 114 cases (14%) and 171 controls (20%) for study. Controls with a previous hysterectomy were more likely to have had more children or heavy, painful periods than those without (Table I). Estimated risk of ovarian cancer among women after hysterectomy was reduced compared with women without such a history (RR 0.64, 95% CI 0.48–0.85), with maximum effect reached 15 or more years after surgery (Table II).

Surgical tubal occlusion

Among women who had had occlusion of the fallopian tubes through either or both of these surgical procedures, there was, predictably, a 37% reduction in risk of ovarian cancer compared with women who had had neither procedure (RR 0.63, 95% CI 0.49–0.79). There was little material variation in the results among the main histological sub-types of ovarian cancer or between borderline and frankly malignant tumours. After surgical tubal occlusion, the risk of developing a serous tumour, the largest histological sub-group, was reduced by 46% (RR 0.54, 95% CI 0.42–0.70), and the sub-group showing the greatest reduction in risk was that of women who had primary peritoneal tumours (RR 0.26, 95% CI 0.07–0.87).

Pelvic infection before surgery was not related to risk of epithelial ovarian cancer, and neither was duration of use of vaginal sprays or of contraceptive foams related to risk. Ever-douching for contraceptive purposes was associated with a non-significant 60% increase in risk of ovarian cancer. A modest association was seen between ovarian cancer and use of talc in the perineal region (RR 1.3, 95% CI 1.1–1.6). There was no additional effect of longer duration of talc use nor was there any relation to reported age when talc was first used in the perineal region. No associations with duration of partner's use of condoms (which may have had talc lubricants) or with duration of use of a diaphragm (which may have been stored in talc) were evident. Compared with women who had neither used talc nor had surgical sterilisation, risk was highest among talc users without surgery (RR 1.3, 95% CI 1.0–1.7) and lowest among women with a history of tubal sterilisation or hysterectomy who had not applied talc to the perineum (RR 0.6, 95% CI 0.50–0.84).

Habitual heavy periods and painful periods were each weakly associated with ovarian cancer (RR 1.2, 95% CI 0.93–1.4 and RR 1.1, 95% CI 0.86–1.4, respectively), and risk of epithelial ovarian cancer among women with either heavy or painful periods was raised to a similar level (RR 1.2, 95% CI 1.0–1.5) overall and for the main histological sub-groups. Women who reported heavy periods showed a 20% larger reduction in risk of ovarian cancer after hysterectomy (RR 0.54) than women who had light or normal menstrual loss (RR 0.74), though the reduction in risk after tubal sterilisation was similar whether or not women reported heavy periods. Women who had experienced painful periods had a lower risk of ovarian cancer after tubal sterilisation or after hysterectomy compared with women who reported pain-free periods (Table III).

DISCUSSION

Ovarian cancer was found to be significantly reduced by 39% after tubal sterilisation and by 36% after hysterectomy. Women who had these procedures tended to have had more children than other women and, thus, were already at lower risk of ovarian cancer, but the low risk persisted after adjustment for parity and other factors, which is consistent with previous findings (Booth *et*

TABLE II – DISTRIBUTION OF CASES AND CONTROLS ACCORDING TO TIME BETWEEN TUBAL STERILISATION AND HYSTERECTOMY AND DATE OF DIAGNOSIS AMONG CASES, AND RISK OF OVARIAN CANCER ADJUSTED FOR AGE, EDUCATION, BODY MASS INDEX, PARITY, DURATION OF ORAL-CONTRACEPTIVE USE, SMOKING AND FAMILY HISTORY OF OVARIAN CANCER

Time since surgery (years)	Tubal sterilisation					Hysterectomy				
	Cases		Controls		Relative risk (95% confidence interval)	Cases		Controls		Relative risk (95% confidence interval)
	Number	(%)	Number	(%)		Number	(%)	Number	(%)	
No surgery	720	(87)	661	(77)	1.0	708	(86)	684	(80)	1.0
Ever surgery	104	(13)	194	(23)	0.61 (0.46–0.85)	114	(14)	171	(20)	0.64 (0.48–0.85)
0–4	9	(1)	25	(3)	0.42 (0.19–0.96)	15	(2)	18	(2)	1.5 (0.73–3.3)
5–9	14	(2)	28	(3)	0.56 (0.27–1.1)	18	(2)	23	(3)	0.89 (0.45–1.7)
10–14	29	(4)	48	(6)	0.72 (0.43–1.2)	22	(3)	33	(4)	0.67 (0.37–1.2)
15–19	36	(4)	47	(6)	0.98 (0.60–1.6)	19	(2)	37	(4)	0.52 (0.28–0.94)
20–24	8	(1)	28	(3)	0.26 (0.11–0.62)	17	(2)	29	(3)	0.54 (0.28–1.1)
25+	8	(1)	18	(2)	0.43 (0.18–1.0)	25	(3)	31	(4)	0.49 (0.28–0.89)

TABLE III – TUBAL STERILISATION, HYSTERECTOMY AND RISK OF OVARIAN CANCER IN RELATION TO MENSTRUAL HISTORY: RELATIVE RISKS (95% CONFIDENCE INTERVALS) ADJUSTED FOR OTHER RISK FACTORS ARE SHOWN

	Tubal sterilisation	Hysterectomy
Heavy periods		
Yes	0.63 (0.38–1.1)	0.54 (0.35–0.84)
No	0.60 (0.41–0.86)	0.74 (0.50–1.1)
Painful periods		
Yes	0.55 (0.36–0.83)	0.61 (0.42–0.89)
No	0.69 (0.45–1.1)	0.69 (0.44–1.1)

al., 1989; Hankinson *et al.*, 1993; Irwin *et al.*, 1991; Mori *et al.*, 1992; Whittemore *et al.*, 1992). It is unlikely that the protective effect of hysterectomy was explained by inclusion of controls with bilateral oophorectomy since most hysterectomies among controls were validated against medical reports (Green *et al.*, 1997). Risk was low 25 years or more after surgery, discounting previous suggestions (Weiss and Harlow, 1986) that the reduced risk is due to pre-operative screening for malignancy. However, women who had bilateral oophorectomy as well as hysterectomy for pelvic endometriosis would not have been represented among controls, possibly lowering their risk of endometrioid ovarian cancer (Russell, 1994).

Another explanation of the protective effect of tubal surgery is that interruption of trophic utero-ovarian circulation results in fewer ovulations (Hankinson *et al.*, 1993; Whittemore *et al.*, 1992) or hormonal imbalance (Cattanach, 1985). The degree to which the utero-ovarian circulation is compromised by tubal sterilisation varies with the surgical technique, with diathermy of the fallopian tubes expected to interfere with the ovarian circulation more than the application of clips or rings, for example. However, the present data indicate that sterilisation techniques which minimally disturb the ovarian circulation were associated with very low risks of ovarian cancer. Furthermore, neither ovulatory frequency (Rivera *et al.*, 1989) nor hormonal activity (Wu *et al.*, 1992) showed systematic changes after tubal sterilisation. Indeed, gonadal atrophy is associated with enhanced pituitary gonadotrophin production (Oliver, 1990) and may enhance carcinogenesis. Another speculation (Cramer and Xu, 1995) is that the protective effect of tubal occlusion could be explained by a reduction in uterine growth factors reaching the ovaries through the compromised utero-ovarian circulation, but this seems unlikely when removal of the uterus, the source of the growth factors, is not as protective as tubal sterilisation (Cramer and Xu, 1995; Hankinson *et al.*, 1993). Neither is the suggestion that tubal occlusion may block the ascent of carcinogenic infectious agents (Wahlberg, 1994) supported here, nor in studies of oncogenic human papilloma virus (HPV) and ovarian cancer, only one of which (Kaufmann *et al.*, 1987) has detected HPV-6 DNA, in 10 of 12 ovarian cancers.

Our study systematically combined information from women with either tubal sterilisation or hysterectomy, to investigate the effect of tubal closure on risk of ovarian cancer. Potential exposure of the peritoneal epithelium to various agents *via* patent fallopian tubes is of concern because ovarian surface epithelial cells are particularly susceptible to malignant transformation. Not only are these cells prone to molecular genetic errors because of repetitive post-ovulation proliferation but also they behave as generative stem cells, unlike most epithelia, whereby a single mutation can be passed on to exponentially expanding progeny (Godwin *et al.*, 1993). Exposure to vaginal sprays or foams (Silver, 1994) was not associated with risk of ovarian cancer, though use may have been poorly recalled by older women. Talc from condoms (Kasper and Chandler, 1995) or diaphragms may be another peritoneal contaminant, but duration of exposure was not associated with ovarian malignancy in these data. However, use of talc in the perineal region was associated with a significant (30%) increase in risk of ovarian cancer. Again, recall of use of talc among older women may not have been accurate, tending to reduce estimated RRs; moreover, the actual quantity of talc used was unknown. Despite the limitations, these results add support to the body of evidence implicating talc as a factor in the pathogenesis of peritoneal epithelial neoplasia (Cramer *et al.*, 1982; Chen *et al.*, 1992; Longo and Young, 1979; Rosenblatt *et al.*, 1992; Whittemore *et al.*, 1988). Notably, women who had never been regularly exposed to talc in the perineal region and had surgical tubal closure experienced the lowest risk of ovarian cancer, in contrast to those women with patent tubes who were regularly exposed to perineal talc, in agreement with Whittemore *et al.* (1988). Women's usage of talc in the perineal region appears widespread—up to 40% among women in the United States (Whittemore *et al.*, 1988) and Australia alike (Purdie *et al.*, 1995)—so that even an apparently small increase in RR of ovarian cancer associated with perineal talc use would pose a sizable health risk to the population. Talc fibres have been found in normal and malignant ovaries (Henderson *et al.*, 1979). Talc is closely related to and (until recently) variably contaminated by asbestos (Longo and Young, 1979) and may have similar effects on pleural and peritoneal epithelia. Occupational exposures to talc (Kleinfeld *et al.*, 1967), asbestos (Acheson *et al.*, 1982) and rock salt (Tarchi *et al.*, 1994) are significantly associated with ovarian cancer mortality.

Some pelvic contaminants do not appear to have been studied in this context before. Retrograde passage of endometrium is believed to occur in most women with patent fallopian tubes (Halme *et al.*, 1984). We hypothesised that women who report habitual heavy or painful periods experience retrograde menstruation to a greater degree than other women and that this explains the association between heavy or painful periods and ovarian cancer (which is not explained by oral-contraceptive use). We tested this theory by seeking a differential effect of tubal surgery among women according to severity of retrograde menses and found that women who had heavy periods before hysterectomy tended to have a lower risk of ovarian cancer after surgery than women who had average or light periods. This effect was not seen for tubal sterilisation, perhaps because menorrhagia often occurs after tubal sterilisation.

After tubal occlusion, women who reported painful periods also had a lower risk of ovarian cancer than those who had surgery but did not have painful periods. This general tendency may be due merely to chance; alternatively, the differential effect may be real, suggesting that retrograde passage of endometrial fluid is involved. Normal endometrium produces an array of cytokines and growth factors which can stimulate proto-oncogenes and DNA synthesis (Smith, 1991); thus, endometrium in the peritoneal cavity could enhance epithelial tumour development and progression.

Finally, it was hypothesised that if peritoneal irritants do play a causal role in the development of malignancy of the whole peritoneal surface (Woodruff, 1979) and not only that portion overlying the ovaries, then the risk of peritoneal cancers in particular should be substantially reduced after tubal occlusion. This is because the causal mechanism generally proposed for ovarian cancer—namely, the repetitive trauma and repair of the ovarian epithelium (Fathalla, 1971)—would not be implicated for primary peritoneal tumours, leaving exposure to irritants as one of the few likely causes; indeed, a 76% reduction in risk of peritoneal tumours was observed after tubal occlusion. In view of this particular finding and the evidence presented here and elsewhere that pelvic contaminants such as talc are associated with ovarian cancer, we conclude that closure of the fallopian tubes by surgery prevents chronic contact between these agents and ovarian epithelium. It seems likely that peritoneal irritants act as co-carcinogens by increasing the accumulated number of mutational events in ovarian surface epithelial cells.

ACKNOWLEDGEMENTS

Funding for this study was provided by the Australian National Health and Medical Research Council and the Queensland Cancer Fund. We are grateful to Dr. L. Salamonsen for advice regarding uterine influences on the ovary.

REFERENCES

ACHESON, E.D., GARDNER, M.J., PIPPARD, E.C. and GRIME, L.P., Mortality of two groups of women who manufactured gas masks from chrysotile and crocidolite asbestos: a 40-year follow-up. *Brit. J. Indust. Med.*, **39**, 344–348 (1982).

BOOTH, M., BERAL, V. and SMITH, P., Risk factors for ovarian cancer: a case-control study. *Brit. J. Cancer*, **60**, 592–598 (1989).

CATTANACH, J., Oestrogen deficiency after tubal ligation. *Lancet*, **1**, 847–849 (1985).

CHEN, Y., WU, P.C., LANG, J.H., GE, W.J., HARTGE, P. and BRINTON, L.A., Risk factors for epithelial ovarian cancer in Beijing, China. *Int. J. Epidemiol.*, **21**, 23–29 (1992).

CRAMER, D.W., WELCH, W.R., SCULLY, R.E. and WOJCIECHOWSKI, C.A., Ovarian cancer and talc. A case-control study. *Cancer*, **50**, 372–376 (1982).

CRAMER, D.W. and XU, H., Epidemiologic evidence for uterine growth factors in the pathogenesis of ovarian cancer. *Ann. Epidemiol.*, **5**, 310–314 (1995).

FATHALLA, M.F., Incessant ovulation—a factor in ovarian neoplasia? *Lancet*, **2**, 163 (1971).

GODWIN, A.K., TESTA, J.R. and HAMILTON, T.C., The biology of ovarian cancer development. *Cancer*, **71** (Suppl.), 530–536 (1993).

GRAHAM, J. and GRAHAM, R., Ovarian cancer and asbestos. *Environ. Res.*, **1**, 115–128 (1967).

GREEN, A., BAIN, C., SISKIND, V., PURDIE, D., GREEN, L., DICK, M.-L. and THE SURVEY OF WOMEN'S HEALTH STUDY GROUP, Validity of self-reported hysterectomy and tubal sterilization. *Aust. N.Z. J. Publ. Health* (In press) (1997).

HALME, J., HAMMOND, M.G., HULKA, J.F., RAJ, S.G. and TALBERT, L.M., Retrograde menstruation in healthy women and in patients with endometriosis. *Obstet. Gynecol.*, **64**, 151–154 (1984).

HANKINSON, S.E., HUNTER, D.J., COLDITZ, G.A., WILLETT, W.C., STAMPFER, M.J., ROSNER, B., HENNEKENS, C.H. and SPEIZER, F.E., Tubal ligation, hysterectomy, and risk of ovarian cancer. *J. Amer. Med. Ass.*, **270**, 2813–2818 (1993).

HARTGE, P., SCHIFFMAN, M.H., HOOVER, R., MCGOWAN, L., LESHER, L. and NORRIS, H.J., A case-control study of epithelial ovarian cancer. *Amer. J. Obstet. Gynecol.*, **161**, 10–16 (1989).

HENDERSON, W.J., HAMILTON, T.C. and GRIFFITHS, K., Talc in normal and malignant ovarian tissue. *Lancet*, **1**, 499 (1979).

IRWIN, K.L., WEISS, N.S., LEE, N.C. and PETERSON, H.B., Tubal sterilization, hysterectomy, and the subsequent occurrence of epithelial ovarian cancer. *Amer. J. Epidemiol.*, **134**, 362–369 (1991).

KASPER, C.S. and CHANDLER, P.J., Possible morbidity in women from talc on condoms. *J. Amer. med. Ass.*, **273**, 846–847 (1995).

KAUFMAN, R.H., BORNSTEIN, J., GORDON, A.G., ADAM, E., KAPLAN, A.L. and ADLER-STORTHZ, K., Detection of human papilloma virus DNA in advanced epithelial ovarian carcinoma. *Gynecol. Oncol.*, **27**, 340–349 (1987).

KLEINFELD, M., MESSITE, J., KOOYMAN, O. and ZAKI, M.H., Mortality among talc miners and millers in New York State. *Arch. Environ. Health.*, **14**, 663–667 (1967).

LONGO, D.L. and YOUNG, R.C., Cosmetic talc and ovarian cancer. *Lancet*, **2**, 349–351 (1979).

MORI, M., NISHIMURA, H. and FUKUDA, K., Association of tubal sterilization and induced abortion with ovarian cancer. *J. Epidemiol.*, **2**, 111–118 (1992).

OLIVER, R.T.D., Atrophy, hormones, genes and viruses in aetiology of germ cell tumours. *Cancer Surveys*, **9**, 263–268 (1990).

PURDIE, D., GREEN, A., BAIN, C., SISKIND, V., WARD, B., HACKER, N., QUINN, M., WRIGHT, G., RUSSELL, P., SUSIL, B. and SURVEY OF WOMEN'S HEALTH STUDY GROUP, Reproductive and other factors and risk of epithelial ovarian cancer: an Australian case-control study. *Int. J. Cancer*, **62**, 678–684 (1995).

RISCH, H.A., MARRETT, L.D. and HOWE, G.R., Parity, contraception, infertility and the risk of epithelial ovarian cancer. *Amer. J. Epidemiol.*, **140**, 585–597 (1994).

RIVERA, R., GAITAN, J.R., RUIZ, R., HURLEY, D.P., ARENAS, M., FLORES, C. and HERNANDEZ, A.B., Menstrual patterns and progesterone circulating levels following different procedures of tubal occlusion. *Contraception*, **40**, 157–169 (1989).

ROSENBLATT, K., SZKLO, M. and ROSENHEIN, N.B., Mineral fiber exposure and the development of ovarian cancer. *Gynecol. Oncol.*, **45**, 20–25 (1992).

RUSSELL, P., Surface epithelial stromal tumors of the ovary. *In:* R.J. Kurman (ed.), *Blaustein's pathology of the genital tract*, Springer-Verlag, New York (1994).

SHU, X.O., BRINTON, L.A., GAO, Y.T. and YAUN, J.M., Population based case-control study of ovarian cancer in Shanghai. *Cancer Res.*, **49**, 3670–3674 (1989).

SILVER, A.-L., Tubal ligation, hysterectomy and risk of ovarian cancer. *J. amer. med. Ass.*, **271**, 1235 (1994).

SMITH, S.K., The endometrium and endometriosis. *In:* E.J. Thomas and J.A. Rock (eds.), *Modern approaches to endometriosis*, Kluwer, Dordrecht (1991).

TARCHI, M., ORSI, D., COMBA, P., DE SANTIS, M., PIRASTU, R., BATTISTA, G. and VALIANI, A., Cohort mortality study of rock salt workers in Italy. *Amer. J. indust. Med.*, **25**, 251–256 (1994).

WAHLBERG, C., Tubal ligation, hysterectomy and risk of ovarian cancer. *J. amer. med. Ass.*, **271**, 1236 (1994).

WEISS, N.S. and HARLOW, B.L., Why does hysterectomy without bilateral oophorectomy influence the subsequence incidence of ovarian cancer? *Amer. J. Epidemiol.*, **124**, 856–858 (1986).

WHITTEMORE, A.S., HARRIS, R., INTYRE, J. and THE COLLABORATIVE OVARIAN CANCER GROUP, Characteristics relating to ovarian cancer risk: collaborative analysis of 12 US case-control studies II. Invasive epithelial ovarian cancers in white women. *Amer. J. Epidemiol.*, **136**, 1184–1203 (1992).

WHITTEMORE, A.S., WU, M.L., PAFFENBARGER, R.S., SARLES, D.L., KAMPERT, J.B., GROSSER, S., JUNG, D.L., BALLON, S. and HENDRICKSON, M., Personal and environmental characteristics related to epithelial ovarian cancer. II. Exposures to talcum powder, tobacco, alcohol and coffee. *Amer. J. Epidemiol.*, **128**, 1228–1240 (1988).

WOODRUFF, J.D., The pathogenesis of ovarian neoplasia. *Johns Hopkins med. J.*, **144**, 117–120 (1979).

WU, E., BILIAN, X., WEIQIAN, Y., HUI, L. and WU, B., Hormonal profile of the menstrual cycle in Chinese women after tubal sterilization. *Contraception*, **45**, 583–593 (1992).