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A Ten Year Study of Ovarian Tumors

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Summary. A study of 213 ovarian tumors was undertaken with respect to the published assumption that there may be a relationship between presence of crystals of silicate in the ovarian tissue and neoplastic transformation. The histological review gave the opportunity to classify these tumors according to the recommendations of the World Health Organization.

The frequency of histological types, age distribution and the site of involvement were determined. These data were compared to those in the literature. Our findings confirm the high incidence of serous tumors and bilaterality reported by others as well as the high risk of ovarian cancer in women in their fifties. A comparative study of the age distribution of cystadenomas was made. It suggests that cystadenomas might be considered as a precursor to the cystadenocarcinomas because of their appearance at younger age.

A deliberate search for silicate crystals in periovarian adhesions and in tumor tissue showed a minimal incidence of crystalline material. This does not support a direct relationship between silicate crystals and ovarian tumors. However, it is suggested that neoplastic changes may occur in the ovarian surface as a result of adhesions engendered by deposition of silicate crystals.

Introduction

The review of all ovarian neoplasms at the University Hospital, San Diego, from 1964 through 1973 was prompted by the recent suggestion that a causal relationship may exist between the presence of silicate crystals, in particular talc, and the development of ovarian malignancy (Henderson *et al.*, 1971). The direct nature of this association is not understood at present. For this reason a detailed search for crystals was undertaken in the material on file at this hospital. There were 213 cases of ovarian tumors diagnosed histologically in the Surgical Pathology Laboratory which were reviewed. An attempt was made to analyze the material with special reference to predisposing factors. They were grouped according to the International Histological Classification of ovarian tumors proposed by the World Health Organization (Serov *et al.*, 1973).

Materials and Methods

Two hundred and thirteen ovarian tumors, removed from 204 patients, were accessioned during this ten year period. All slides available were reviewed and relabelled according to the International Histological Classification of ovarian tumors. A problem was encountered particularly in the classification of borderline tumors since at times not enough sections were

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Table 1. Frequency of ovarian tumors with respect to histological type. The slides of 213 cases were reviewed and the histological diagnoses made with respect to the histological typing of ovarian tumors recommended by the World Health Organization

Histological diagnoses	No. of cases			% of all cases		
Common epithelial tumors	120			56.3		
Serous tumors		88			41.3	
Cystadenomas and papillary cystadenomas			31			19.7
Adenofibromas and cystadenofibromas			11			21.6
Adenocarcinomas and cystadenocarcinomas			46			
Mucinous tumors		27			12.6	
Cystadenomas			11			5.1
Adenocarcinomas and cystadenocarcinomas			16			7.5
Endometrioid carcinomas		4			1.8	
Brenner tumor		1			.5	
Sex cord stromal tumors	16			7.3		
Granulosa cell tumors		2			1	
Tumors in the thecoma-fibroma group		14			6.3	
Thecomas			6			2.8
Fibromas			8			3.5
Germ cell tumors	54			25.3		
Dysgerminomas		4			1.8	
Teratomas		50			23.5	
Immature			2			1
Mature			48			22.5
Secondary metastatic tumors	23			10.8		
Krukenberg's tumor		6			2.8	
Lymphoma		2			1	
Leiomyosarcoma		1			.5	
Others		14			6.5	
	213	213		100	100	

available for proper designation of these intermediate grades. A systematic search was made for adhesions on the surface of the ovaries or tumors and, employing Nicol's prisms, a detailed search at 400× magnification for birefringent crystals was undertaken in all sections, particularly in adhesions but also in the tumor tissue. Additional blocks were cut when appropriate and available, and in some cases the autopsy material was also reviewed.

Findings

1. Distribution of Histologic Types

The various histologic types encountered in this study are listed in Table 1. As will be seen, the "common epithelial tumors" were the most frequent neoplasms of the ovary. The commonest lesion was of the serous type, including cystadenoma and cystadenocarcinoma. 41.3% of the tumors were of this histologic phenotype,

and half of these were malignant. These tumors had the usual histologic pattern; most malignant ones were cystic, papillary, and well differentiated. Very uncommonly, totally undifferentiated tumors were found among this group. In a few of these tumors a small mucinous component was present as well. This component was not deemed sufficiently extensive to include these tumors in the mucinous group. If a category for sero-mucinous tumor existed, they should have been placed in this subcategory. Mucinous tumors represented 12.6% of the total tumors and were the second most common of the epithelial variety. These tumors were also considered to be of "epithelial origin" even though in the past the suggestion has been made that they may derive from germ cell tumors (Masson, 1956). A deliberate search for other components was made and when none was found the tumor was included in the mucinous variety. Specific stains for argentaffin cells or determination of enzymes from fresh tissue was not undertaken. Moreover, there is doubt from other studies that this would have been helpful in elucidating the true origin of mucinous tumors (Linder and Posner, 1970).

Only four endometrioid carcinomas, representing 1.8% of the total, were encountered in this group. This number may be smaller than in other series because we deliberately excluded those patients in whom recently a uterus had been removed for carcinoma of the endometrium.

The sex cord stromal tumors form the smallest group in this series. A particularly striking feature is the rarity of granulosa cell tumors, only two having been diagnosed; one was considered malignant, the other benign. An attempt was made to distinguish between fibroma and thecoma and while the diagnosis appeared very clear in some cases, in others it must be admitted that the assignment is arbitrary and we believe a clear-cut decision cannot always be reached.

The second most frequent overall group are germ cell tumors due to the great frequency of cystic teratomas ("dermoid cysts") in this category. Germ cell tumors comprised 25.3% of the entire series. Only two immature teratomas were encountered and there were only four cases of dysgerminoma. One of these is remarkable in that the large tumor mass had diffusely infiltrated the left fallopian tube (Fig. 1). The gross appearance and histologic features of the mature teratomas were represented most commonly by the classical dermoid cysts. These were composed of a mixture of mature tissues of neuroectodermal origin. In only two cases was a significant component of thyroid tissue present, warranting the diagnosis of struma ovarii.

Secondary tumors of the ovary comprise 10.8% of the entire material. Six of these twenty-three cases had the histologic pattern of the Krukenberg tumor containing large numbers of mucin-filled signet ring cells and accompanied by stromal proliferation of ovarian tissue. Fourteen others had the histologic quality of common carcinomas and three cases of metastatic sarcoma were present. The metastatic carcinomas arose from the breast in eleven cases, from the colon in six cases, and in three cases from the endometrium.

2. Age Distribution

The youngest patient in our group is a fifteen year old patient with serous cystadenocarcinoma, the oldest, an 86 year old woman with a fibroma. No childhood tumors were encountered in this hospital. The distribution of patient's ages

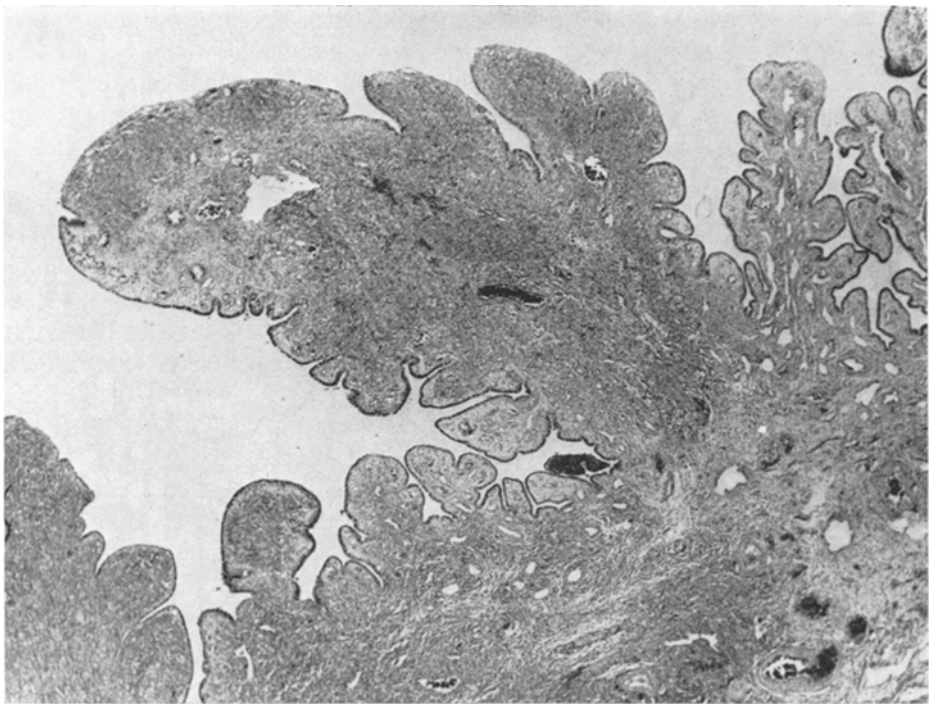

Fig. 1. Fallopian tube of patient with dysgerminoma showing the unusual infiltration of tumor cells into the mucosa, lifting the epithelium off the connective tissue. (H & E ×10)

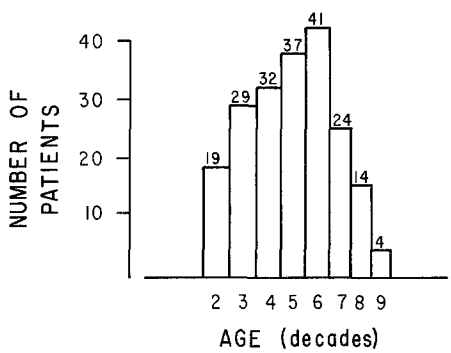

Fig. 2. Bar graph illustrating the age distribution of 200 patients with ovarian tumors at time of diagnosis

is graphically depicted in Fig. 2. As will be seen the peak incidence of tumors occurs in patients between the ages of 40 and 70, women in their fifties being the most frequently affected. The decline in frequency after age 70 may reflect the decline in the population and may not be indicative of a natural decrease in the incidence of tumor at that age. A more detailed breakdown of the distribution of

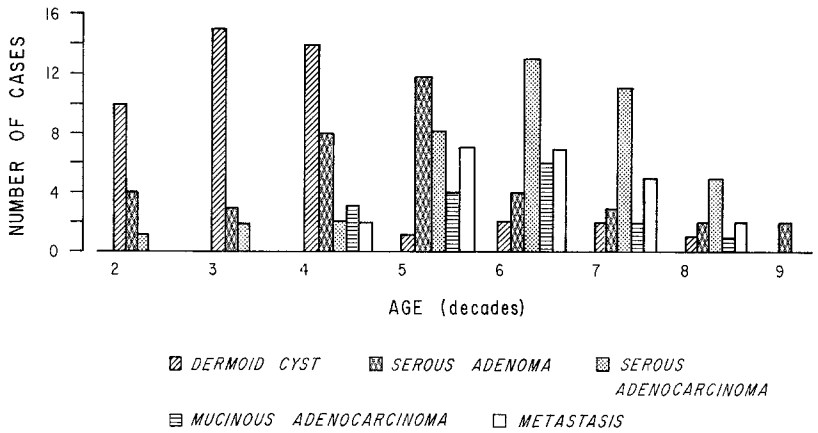

Fig. 3. Bar graph illustrating the age distribution of the most frequent tumors in this series

various tumors at different ages is shown in Fig. 3. It is apparent from this bar graph that there are striking differences of certain types of tumors at different age groups. Thus, dermoid cyst, a benign ovarian tumor, is most frequent among young women and becomes uncommon after the age of 40. Thirty-nine of forty-five women in whom the age was recorded and who were operated on for cystic teratoma were at an age between 11 and 40 years, comprising 90% of all cases of dermoid cysts. Conversely, the serous cystadenocarcinoma is much more common in patients beyond 40 years of age even though our youngest patient at 15 suffered from this disease. Thirty-seven of our forty-one cystadenocarcinomas with known age were from patients over 40, comprising 90% of these tumors. The peak incidence is observed in the sixth decade. Serous cystadenoma and adenofibroma were found in patients of all ages, while a peak for this tumor occurs in the fifth decade. Although mucinous adenocarcinoma was considerably less frequent than serous cystadenocarcinoma, its age distribution has much the same shape as the serous variety. A considerable number of metastatic tumors was encountered in this series and, as might be expected, they occurred primarily after age 40. Twenty-one of the twenty-three tumors (91%) were found in patients after 40.

3. Distribution of Benign and Malignant Tumors

This series of 213 tumors contains 107 benign and 93 malignant tumors in patients with recorded ages. The distribution of the ages at which these tumors were diagnosed is graphically represented in Fig. 4. As will be seen, ovarian tumors are most commonly benign in patients under 40 years of age, 64 of 107 benign tumors being observed in these patients, i.e. 60% of all benign tumors. In contrast, 77 of 91 malignant tumors were encountered in patients older than 40 years of age, implying that 82% of all malignant tumors were removed from women who were at least 40 years of age. These figures are nearly identical when one removes from this group the metastatic tumors and considers the malignant potential of ovarian tissues per se.

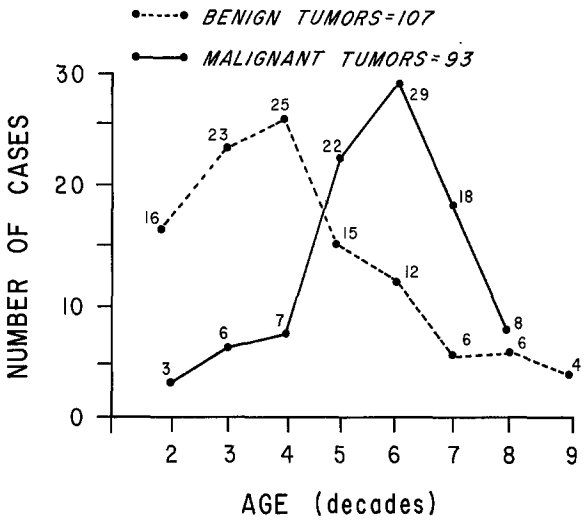

Fig. 4. Graphic representation of age distribution in 107 benign and 93 malignant ovarian tumors

Table 2. Site of involvement of our cases

Site of involvement	Benign tumors		Malignant tumors	
	Number of patients	%	Number of patients	%
Left ovary	50	50	24	30
Right ovary	39	39	24	30
Bilateral	12	11	32	40
Total	101	100	80	100

4. Bilaterality

The site of involvement of ovaries is tabulated in Table 2 for both benign and malignant tumors. The site of involvement was accurately recorded in 181 of ovarian tumors studied, 24% of which were found to be bilateral. Among the benign bilateral tumors 7 were serous cystadenomas or adenofibromas, 3 mature teratomas, 1 thecoma and 1 fibroma. Of thirty-two malignant tumors with bilateral occurrence, serous cystadenocarcinoma was found in eighteen cases, mucinous adenocarcinoma in 7 cases, metastatic carcinoma in 6 cases and 1 case of dysgerminoma.

5. Adhesions and Crystals

Adhesions were found in 52 of 152 cases in which ovarian tissue was recognized within or adjacent to the tumor mass. The diagnosis of those ovarian tumors associated with adhesions is listed in Table 3. It may be seen that adhesions were associated with approximately three fourths of the cases with common epithelium tumors which are commonly considered to have derived from coelomic epithelium

Table 3. Ovarian tumors associated with ovarian adhesions

Histological diagnosis	Number of cases		%
Common epithelial tumors	36		73.5
Serous cystadenomas adenofibromas		17	
Serous cystadenocarcinomas		14	
Mucinous cystadenomas		2	
Mucinous cystadenocarcinomas		3	
Sex cord stromal tumors	2		4
Thecoma		1	
Granular cell tumor		1	
Germ cell tumor	10		20.5
Mature teratoma		10	
Secondary tumor	1		2
Malignant lymphoma		1	
	49	49	100

(Hertig and Gore, 1961). Definite silicate crystals were found in the ovarian adhesions of only 5 patients, 3 of whom suffered from serous tumors while 2 had dermoid cysts. In 2 other cases, a serous adenocarcinoma and an immature teratoma, birefringent suture material was found in the tumor tissue and in one adenocarcinoma starch particles were observed. The relative paucity of crystalline material in our cases may reflect the fact that normal ovarian tissue was not recognized in 61 cases. In these it was impossible then to identify ovarian adhesions, and crystals were not noted in the tumors themselves as was the case prominently in one ovarian tumor at autopsy (Fig. 5). The relative paucity of crystalline material is also somewhat in disagreement with our rather frequent finding of such material in other gynecologic operative specimens, particularly from cases of pelvic inflammatory disease. A representative example of large amounts of crystalline material encountered in one patient with mucinous cystadenocarcinoma is shown in Fig. 5. The histologic interpretation of this crystalline material is consistent with talcum or other complex silicates. It rules out suture material.

Discussion

Comparative Study of Frequency of Ovarian Tumors

The distribution of tumors identified in our consecutive series is compared with the large series reported by previous authors (Kent and McKay, 1960; Bennington *et al.*, 1968; Santesson and Kottmeier, 1968; Philippe *et al.*, 1971). We categorized their data according to a unified nomenclature as presented in Table 4. In agreement with these other studies, among our benign tumors the serous cystadenoma is a commonly encountered tumor. Our figure of 35.9% falls between the percentages given by these other reports. Similarly, the rarity of Brenner tumors in our study (0.8%) approximates that of other authors, and the thecoma—fibroma group shows general agreement. Our finding a 41% incidence among the

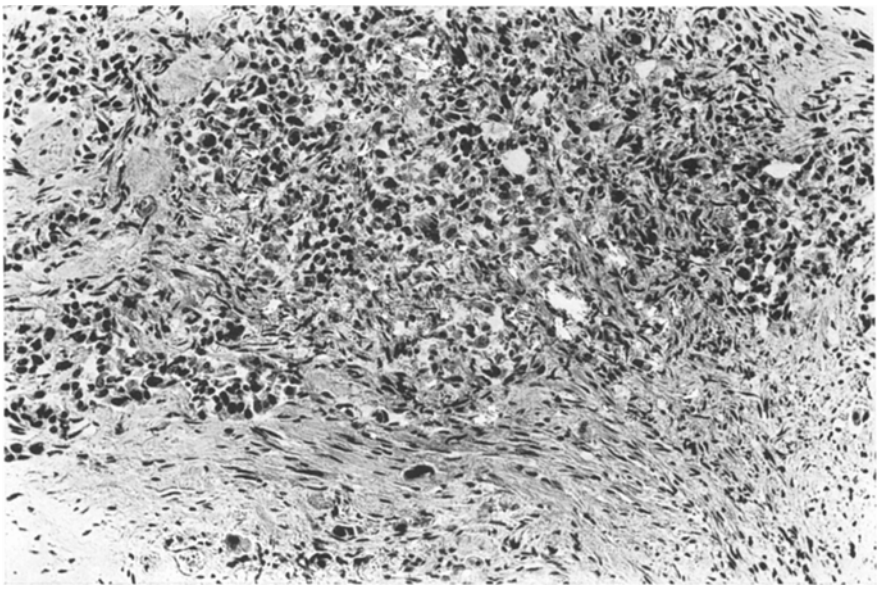

Fig. 5. Section of mucinous cystadenocarcinoma at autopsy. With partially crossed Nicol's prisms large numbers of birefringent crystals (white) are present amongst dark tumor cells. (H & E ×160)

benign tumors of mature teratoma deviates from the findings of other authors. Generally, in series of ovarian tumors the serous cystadenomas slightly out number mature teratomas. Conversely, mucinous cystadenoma comprises only 9.4% in our series which is considerably below the frequency reported by others.

With respect to malignant tumors our distribution agrees closely with that of previous reports. Serous cystadenocarcinoma is the most frequently found tumor, making up 47.7% of our cancers, lying midway between the 39.2% reported by Santesson and Kottmeier (1968) and 51% by Bennington *et al.* (1968). Mucinous cystadenocarcinoma is less common in our hands than metastatic carcinoma and thus slightly lower than in reports from the literature. The percentages for metastatic carcinoma given by Santesson and Kottmeier (1968) are 6.4% and by Bennington *et al.* (1968) 23% of all ovarian cancers. In our findings, 21.8% of all malignant tumors were metastatic, similar to the figure reported by Bennington *et al.* (1968). We also found similar types of primary tumors from which metastases arose (Bennington *et al.*, 1968: 13 breast, 4 GI tract, 3 endometrium, 3 cervix and 3 urinary tract cancers). Everyone agrees that malignant germ cell tumors, represented in our series by 6.1%, are the least frequent cancers of all. A special point for consideration should be the variation in incidence of endometrioid carcinomas from our series. We had 4.1% endometrioid carcinomas while Phillippe *et al.* (1971) listed 3.1% and Santesson and Kottmeier (1968) 21% of their malignant tumors. Presumably, these differences reflect the difficulties of classification. More precise criteria for the histologic typing of this category of ovarian tumor would seem desirable since it is apparent that endometrioid carcinoma of the

Table 4. Comparative study of the frequency of ovarian tumors

% of bening tumors (117 cases)

Authors	All cases	Serous cyst-adenoma adeno-fibroma	Mucinous cyst-adenoma	Brenner tumor	Mature teratomas	Fibromas	Thecomas
Bennington[a] *et al.*	549	51	12.4	1.3	30	5.6	
Kent and MacKay[a]	2181	18.6	19.2	1.2	20	39.9	2.5
Santesson and Kottmeier	1361	NR	NR	NR	NR	NR	NR
Phillipe[a] *et al.*	2570	31	28.4	0.7	29	7.6	2.1
Personal report	213	35.9	9.4	0.8	41	6.8	5.1

% of malignant tumors (96 cases)

Authors	All cases	Serous cyst-adeno-carcinomas	Mucinous cyst-adeno-carcinomas	Endo-metrioid carcinoma	Dys-germinoma	Immature teratoma	Secondary carcinomas
Bennington[a] *et al.*	549	51	10	4.7	5.5		23
Kent and MacKay[a]	2181	61.3	16.3	3.7	0.1		NR
Santesson and Kottmeier	1361	39.2	10	21	5.7		6.4
Phillipe[a] *et al.*	2570	40.8	29.6	3.1	1.1		10.6
Personal report	213	47.7	16.6	4.1	4.1	2	21.8

NR = Not reported.

[a] Tumors recategorized and % calculated from the data reported by these authors.

ovary has a better prognosis than other adenocarcinomas. It has been suggested that one should consider as endometrioid carcinoma not only those carcinomas that developed from definitely preexisting endometriosis but also all primary ovarian carcinomas that have the appearance of endometrioid cancer. Possibly for this reason the reported incidence of 21% by Santesson and Kottmeier (1968) is higher than that of other investigators.

Age Distribution

Janowski and Paramanandhan (1973) reported that ovarian tumors may be encountered from the 30 week fetus to the 92 year old woman. Kent and McKay (1960) reported that the majority of ovarian cancers occur between the ages of 40 and 79 and that with the exception of the 2nd and 9th decades the serous adeno-carcinoma predominated in frequency. Bennington *et al.* (1968) found that the benign teratoma is the most frequent tumor in the age interval 0–19, while serous tumors are more frequent thereafter.

We have endeavored to graph the age distribution of our ovarian tumors (Fig. 3). From this representation it will be seen that the most frequent tumor of

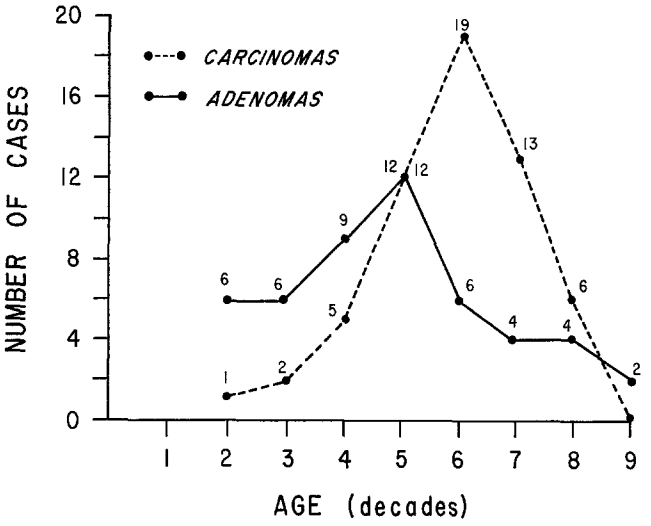

Fig. 6. Graphic representation of age distribution of benign and malignant serous cystomas

the ovary in patients under 40 was the dermoid cyst, while the serous cystadenoma was the most frequent tumor in women in their forties. After the age of 50, serous cystadenocarcinoma clearly predominated.

Bilaterality

In their study of ovarian tumors Buka *et al.* (1968) reported that 29.5% of ovarian cancers involved the left ovary, 27.5% the right and 43% are bilateral at the time of first operation. Our findings generally agree with these figures and it is important to note that 40% of all ovarian cancers were bilateral at the time of their discovery. This finding, well known to surgeons, who when faced with an ovarian cancer follow the rule of performing bilateral salpingo-oophorectomy and total hysterectomy, regardless of the age of the patient and whether these organs appear grossly normal. If for any reason more conservative approaches are employed at surgery extremely careful follow-up seems mandatory.

Cystadenoma and Cystadenocarcinoma

It is generally agreed now that early treatment of preneoplastic lesions such as dysplasia and carcinoma *in situ* has improved the salvage rate of certain types of malignancies, particularly carcinoma of the cervix. In ovarian neoplasms one is rarely so fortunate as to be able to identify and cure a preneoplastic lesion. Indeed the precarcinomatous nature of cystadenoma and cystadenofibroma has not been proven. However, when one considers the age distribution between these two classes of lesions (Fig. 6) one observes that the adenomatous variety of the epithelial tumors has a younger age distribution than the carcinomatous type. By analogy from the data published for carcinoma of the cervix a case can be made that indeed the cystadenofibroma and cystadenoma may be considered as precursor lesions to the fully developed adenocarcinomatous variant. Should this be

proven correct more aggressive therapy of this lesion when identified should be considered.

Common epithelial tumors of the ovary are frequently considered to be derived by infolding of the ovarian peritoneal surface, occlusion of the infolded epithelium, proliferation and papillary formation as a result of the included state of the epithelium. The metaplastic capacity of the epithelium may then mimic any type of epithelium originating from the coelomic cavity, squamous, serous, mucinous, endometrial or endocervical in type (Hertig and Gore, 1958). If this assumption is true, and all evidence favors the derivation of these tumors from the peritoneal covering the presence of periovarian adhesions may very well engender the formation of inclusion cysts. The proliferation of epithelium may then hasten the process that more frequently takes place spontaneously with advancing age. Periovarian adhesions commonly arise following pelvic inflammatory disease and also appear to be frequent following various abdominal surgeries. The presence of crystals of talc type often released from surgeons gloves in the past, has been clearly demonstrated as an inciting event of adhesion formation in the peritoneal cavity (Litchman *et al.*, 1946). This coincides with the finding of crystalline material occasionally within the adhesions in this series. With increasing time after the operation the amount of crystalline material presumably decreases because of the gradual solubility of crystalline silicates (Krisch, 1960), in analogy with the deposits in pulmonary silicosis. Silicates have also been demonstrated by us to have reached the peritoneal cavity from douching with detergents that contain silicate crystals; in fact diffuse sterile peritonitis has been so identified in this hospital. Presumably they gain access through the fallopian tubes and are irritating to the peritoneal surface so as to engender exudation and adhesion formation. The relationship, therefore, between the deposition of crystalline material and ovarian cancer noted electronmicroscopically by Henderson *et al.* (1971) may be an indirect one. Crystals may induce adhesions which, by enveloping the ovaries, cause inclusion cysts whose ultimate fate may be the development of cystadenomas and cystadenocarcinomas. However, that there is a direct response by epithelial cells to silicates, transforming these cells to malignant types, is speculative and not as yet directly supported by laboratory experimentation. Reeves *et al.* (1971) have observed the development of mesotheliomas in animals exposed to the intraperitoneal injection of certain types of asbestos within 12 to 17 months. Some types of crystals in the lung lead to carcinogenic development (Doll, 1955). Keal (1960) followed by Enticknap and Smither (1970), showed an association between peritoneal tumors and intraabdominal asbestos dusting in experimental animals. Moreover, recently the possible association of asbestos exposure and cancer of the gastro-intestinal tract has been suggested by Hammond *et al.* (1965). Finally, from Japanese populations a higher incidence of cancer of the stomach has been related hypothetically by Merliss (1971) to the talcum dusting of rice consumed in their diet and its possible contamination with asbestos. Henderson *et al.* (1971), who found talc particles localized deep within tumor tissues of the ovary and cervix by electronmicroscopy (1–2 μ) suggest that talc is a possible predisposing factor in carcinomatous changes of the ovary and cervix. The latter report formed the working hypothesis for this investigation; however, the minimal incidence of admittedly larger crystalline material detected by our study leads us to deny the direct relationship between silicate and the development of ovarian cancers. On

the other hand, the possibility that neoplastic changes may occur on the ovarian surface as a result of adhesions engendered by the deposition of silicate crystals should be considered. It is premature to refute the hypothesis on these grounds, since the crystalline material may be so small that it is beyond the limits of the optical microscope. Moreover, the slight but definite solubility of some of this material may have precluded its detection at the time when the ovarian tumor was first identified.

References

Bennington, J. L., Ferguson, B. R., Haber, S. L.- Incidence and relative frequency of benign and malignant ovarian neoplasms. Obstet. and Gynec. **32**, 627–632 (1968)

Buka, N. J., MacFarlane, K. T.: Malignant tumors of the ovary. Amer. J. Obstet. Gynec. **90**, 383–393 (1964)

Doll, R.: Mortality from lung cancer in asbestos workers. Brit. J. industr. Med. **12**, 81–86 (1955)

Enticknap, J. B., Smither, J.: Peritoneal tumors in asbestos. Brit. J. industr. Med. **21**, 20–31 (1970)

Hammond, E. C., Serikoff, I. J., Churg, J.: Neoplasm among insulation workers in the U.S. with special reference to intra-abdominal neoplasia. Ann. N.Y. Acad. Sci. **132**, 519–525 (1965)

Henderson, W. J., Joslin, C. A. F., Turnbull, A. C., Griffiths, K.: Talc and carcinoma of the ovary and cervix. J. Obstet. Gynaec. Brit. Clth **78**, 266–272 (1971)

Hertig, A. T., Gore, H. M.: Ovarian cystomas of germinal epithelial origin. Rocky Mtn med. J. **55**, 47–50 (1958)

Hertig, A. T., Gore, H. M.: Atlas of tumor pathology, sect. ix, vol. 33. Tumors of the female sex organs, part 2. Tumors of the vulva, vagina and uterus. Washington, D.C.: Armed Forces Inst. of Pathology 1961

Janowski, N. A., Paramanandhan, T. L.: Ovarian tumors. Stuttgart: Georg Thieme Publishers 1973

Keal, E. E.: Asbestos and abdominal neoplasms. Lancet **1960II**, 1211–1216

Kent, J. W., McKay, D. G.: Primary cancer of the ovary. Amer. J. Obstet. Gynec. **80**, 430–438 (1960)

Krisch, K.: Biochemische Untersuchungen zum Silikoseproblem. Studien zur Permeabilität von oligomerer Kieselsäure in Rattenleberschnitten. Hoppe-Seylers Z. physiol. Chem. **320**, 258–271 (1960)

Linder, D., Posner, J.: Further evidence for post-meiotic origin of teratoma in the human female. Ann. hum. Genet. **34**, 21–30 (1970)

Litchman, A. L., McDonald, J. R., Dixon, C. F., Mann, F. C.: Talc granuloma. Surg. Gynec. Obstet. **83**, 531–546 (1946)

Masson, P.: Tumeurs humaines, 2nd ed., p. 532. Paris: Librairie Maloine S.A. 1956

Merliss, R. R.: Talc-treated rice and Japanese stomach cancer. Science **170**, 1141–1142 (1971)

Philippe, E., deMot, E., Muller, G., Foussereau, S., Boog, G., Gandar, R.: Teratomes benins kystiques de l'ovaire-étude anatomo-clinique de 481 cas. Gynéc. et Obstét. **70**, 513–528 (1971)

Reeves, A. L., Puro, H. E., Smith, R. G., Vorwald, A. J.: Experimental asbestos carcinogenesis. Environ. Res. **4**, 496–511 (1971)

Santesson, L., Kottmeier, H. L.: General classification of ovarian tumors. In: Ovarian cancer, UICC, vol. II. Berlin-Heidelberg-New York: Springer 1968

Serov, S. F., Scully, R. E., Hobin, L. H.: Histological typing of ovarian tumors. Geneva: WHO 1973

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