Occurrence of Estrogenic Hormone in Ovarian Cysts*†

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(Received for publication June 4, 1941)

Relatively little is known concerning the genesis of ovarian tumors and the etiologic relationship of the benign to the malignant forms. The various endocrine components of the ovary and the many hormonal influences which affect its development suggest that hormones may play a role in the production of ovarian tumors. Excessive amounts of gonadotropic hormone in both the human and in the laboratory animal may stimulate changes in the ovary, which although not neoplastic, nevertheless may be pathologic in nature. Similar conditions such as "cystic ovaries," and follicle and corpus luteum cysts, occur spontaneously in the human. That hormones play a part in some types of ovarian tumors is shown with certain rare tumors by clinical manifestations, excretion of unusual amounts of hormone, and occurrence of large amounts of hormone in the tumor tissues and fluids.

For many years the consideration of the effect of hormones on the production and development of tumors has been the subject of extensive studies both in the clinical and experimental fields. These studies have been concerned with hormone imbalance at physiologic levels, e.g., castration, pregnancy, etc., and at excessive levels by the administration of hormones. The recent studies on the relation of sex hormones to the production of benign and malignant tumors make it timely to consider any possible relation of estrogenic hormones to ovarian tumors.

Since estrogenic hormone occurs naturally in normal ovarian tissue (2, 3) it is of interest to investigate the occurrence of this hormone in ovarian tumors, especially the commonly occurring types. Excluding the previous report of the authors (1) more than 100 ovarian cyst fluids (3-5, 7-17) have been tested for estrogenic hormone. Some of the reports have been incidental to other studies but others have attempted to correlate the hormone finding with the histology of the tumor. Unfortunately most of the reports lack data either on the number of tumors examined, their size, the amount of fluid tested, the method of assay or the histology of the tumor. With the exception of an early report (4) on 3 unclassified ovarian cysts the fluids have been tested only in amounts which were convenient without extraction. Although these small amounts were usually sufficient to detect the presence of hormone in follicle and corpus luteum cysts (3, 5, 7, 9, 10, 12-15, 17) they were not adequate to establish the absence of the hormone in other types of cysts. With the amounts of fluid tested estrogenic hormone was found in 5 serous cysts (7, 9, 10) and 1 pseudomucinous cyst (12). The hormone was not found in fluids of 3 malignant ovarian cysts (9, 13). Similarly, parovarian (6, 7, 9, 13) and other extra-ovarian cysts (12, 13) did not contain the hormone.

This study is a continuation of a previous report (1) on the occurrence of estrogenic hormone in human ovarian tumors. It was hoped that a correlation of the hormone findings with the histology of the tumor might throw some light on the role of hormones in these tumors. This report deals only with the commonly occurring ovarian tumors. Tumors associated with pregnancy and the puerperium have been excluded from this report because of the large amounts of estrogenic hormone in the maternal circulation during pregnancy and the possible effects of the pregnancy hormones upon the development of the tumor. Because of the multiplicity of histologic components of the ovary and of the tumor an attempt has been made to simplify the problem by confining the study to the cystic tumors in which each cyst may be considered as a histologic entity with specific cellular lining. Extraction of the fluids has permitted large amounts of fluid to be tested.

Methods

Clinical data.—These data include only the cystic ovarian tumors and exclude all rare tumors. Except for dermoids which are often solid or semisolid, the series is fairly complete. The ovarian cysts associated with pregnancy and the puerperium have been placed in a separate group because of different hormonal conditions and these results will be reported later. The clinical material has been obtained from the University of Chicago Clinics and the Chicago Lying-in Hospital and entirely from white women. For completeness the data previously reported are included in this report.

General.—The ovarian cysts were received immediately after removal and the fluids aspirated immediately to prevent any possible diffusion of hormone from adjoining ovarian structures. A representative specimen of tissue was selected from the cyst wall, care being taken to avoid adjacent structures which might

* This investigation has been supported by the Douglas Smith Foundation of the University of Chicago, and was aided by a grant from the National Advisory Cancer Council.

† Read in part at the 34th Annual Meeting, American Association for Cancer Research, Inc., Chicago, Illinois, April 16, 1941.

confuse the histologic picture. When more than one cyst was present, each was considered individually.

Histology.—Tissues were fixed in formalin, cut at 5 to 6 microns and stained with hematoxylin and eosin.

Hormone assay.—Fluids and extracts were tested for estrogenic hormone by the vaginal smear method of biological assay using doubly ovariectomized adult albino rats. Aqueous preparations were injected three times subcutaneously in eight hours and oil preparations once. Smears were read at 48, 54, 72 hours. Because the amounts of material available for testing were usually very limited, a strictly quantitative assay was impossible. However, graded doses were used wherever possible. A "rat unit" has been arbitrarily defined as the smallest amount of fluid tested which gave a positive estrous response.

Extracts.—When extraction was desired the following method was employed: Two volumes of 95 per cent alcohol were added to 1 volume of fluid and the mixture was allowed to stand. The precipitate was removed by centrifugation and the supernatant fluid filtered through a Jena filter. The precipitate was washed twice with 95 per cent alcohol and once with anhydrous ether. The combined supernatant fluid and washings were acidified to Congo red with HCl, and evaporated dropwise under reduced pressure on a water bath. The residue was triturated 4 times with 25 cc. portions of anhydrous ether and the extract was filtered through a Jena filter. The ether solution was added dropwise to a measured amount of olive oil and the ether removed. A separate extraction was made for each amount tested. Extractions were made in triplicate when fluid was available.

Control studies.—For control studies fluids from nonovarian cystic adnexal tumors and ascitic fluids have been assayed for estrogenic hormone. These tumors consist of parovarian cysts, cystic fibroids, etc.

Classification and Incidence

In general, classifications of ovarian tumors are unsatisfactory. For the purpose of this investigation a simple classification based upon morphologic findings has been used without attempts at further refinement. The classification and the summary of the data are shown in Table I. Ovarian cysts have been classified either as benign or malignant. The benign tumors have been subdivided into 1. single type tumors in which only one type of cyst was found, although sometimes these cysts were multilocular in nature; 2. multiple type tumors in which more than one type of cyst was present; 3. bilateral cysts. The single type group is comprised of follicle and corpus luteum cysts, representing pseudoneoplasms, and simple serous, papillary serous, pseudomucinous, dermoid and a miscellaneous group, consisting of cysts devoid of epithelial lining, degenerate forms and otherwise unclassified types. The series is essentially complete except for dermoids which are often solid or semisolid and have not always been tested for hormone.

The series consists of 193 cases of ovarian cysts; 172 were benign and 21 malignant. Excluding the dermoids the series consists of 168 benign ovarian cysts of which 134 or 79.8 per cent were single type. In the benign group 17 or 10.1 per cent of the patients gave histories of previous operations for ovarian cysts or other ovarian disease and are classed as "recurrent" cysts; 15 or 8.9 per cent had multiple tumors; 19 or 11.3 per cent had bilateral involvements; 3 of which were also multiple in type. Of the 21 cases of ovarian carcinoma there was one case of bilateral tumors. In the single type group the incidence of various types of cysts excluding dermoids was: follicle 11.9 per cent, corpus luteum 11.9 per cent, simple serous 35.8 per cent, papillary serous 11.2 per cent, pseudomucinous 21.6 per cent, miscellaneous 7.5 per cent.

Table I: Classification and Summary—Cystic Adnexal Tumors

	Cases		Tumors		Fluids	
	No.	Total	No.	Total	No.	Total
Benign ovarian cysts		172		189		294
Single type	138		138		211	
*Follicle	16		16		18	
*Corpus luteum	16		16		17	
Simple serous	48		48		68	
Papillary serous	15		15		32	
Pseudomucinous	29		29		61	
Dermoid	4		4		5	
Miscellaneous	10		10		10	
Multiple type	15		15		41	
Bilateral	19		36		42	
Malignant ovarian cysts		21		23		55
Benign nonovarian cysts		26		27		28
Embryonic rests	13		14		15	
Miscellaneous	8		8		8	
Endometriosis	5		5		5	
Totals		219		239		377
Ascitic fluids (assoc. with tumors)		26				36

* Pseudoneoplasms.

Twenty-seven cystic adnexal tumors were included for control studies. They include 13 tumors arising from embryonic rests (6 parovarian, 2 bilateral parovarian, 3 wolffian, 1 hydatid of Morgagni, 1 Gartner's duct), fluid from 5 cases of endometriosis, 3 cystic fibroids, 4 hydrosalpinx, 1 Bartholin cyst. Thirty-six ascitic fluids were also examined.

Age Incidence

Since the ovary is characterized by a very rapid succession of tissue and hormonal changes over the

long period during which it is functionally active, it is of interest to consider the occurrence of ovarian cysts during various decades of life. Fig. 1 shows the age incidence for 155 benign and 19 malignant ovarian cysts of this series. The data include all the benign cysts except those of patients having a history of a previous cystectomy or oophorectomy and in which the present tumor is considered as the second occurrence of a tumor. The 3 decades, 15 to 45 years of age, have been considered to represent the period of the greatest functional activity of the ovary. Seventy-three per cent of the benign tumors were removed during this period and 26 per cent after this age. In the malignant tumor group, 58 per cent were removed after 45 years of age. The group of malignant tumors is very small. Although the number of cysts in each group of the single type cysts is too small to be signifi-

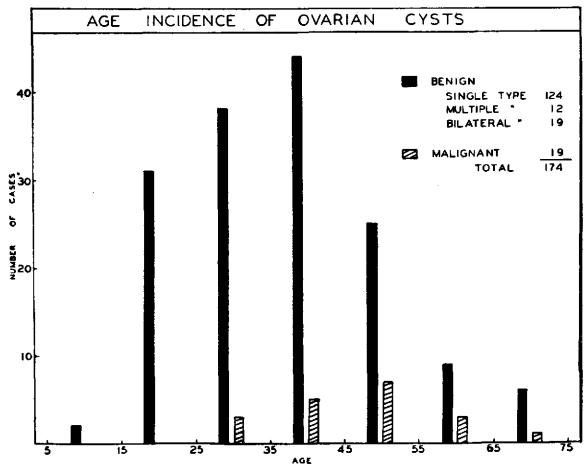

Fig. 1

cant, there seems to be a tendency for different types of cysts to occur at different ages.

Occurrence of Estrogenic Hormone in Single Type Ovarian Cysts at Various Ages

In order to avoid confusion because of the presence of different types of cysts in the same tumor or patient only single type cysts have been analyzed for estrogenic hormone during the various age periods. In the group shown in Fig. 2-A representing 124 cases 35 per cent of the cysts between ages 15 to 45 show estrogenic hormone. These data include both follicle and corpus luteum cysts in which hormone could be expected to occur. If these cysts are excluded so that only the true neoplasms, 96 cases, are included the data appear as shown in Fig. 2-B. In the age period 15 to 45 years, 21 per cent show estrogenic hormone. Thirty-six per cent of all the positive cysts were found in the patients over 45 years of age, at a period when the ovary is presumably quiescent. In the two decades after 55, 5 of 10 cysts showed hormone.

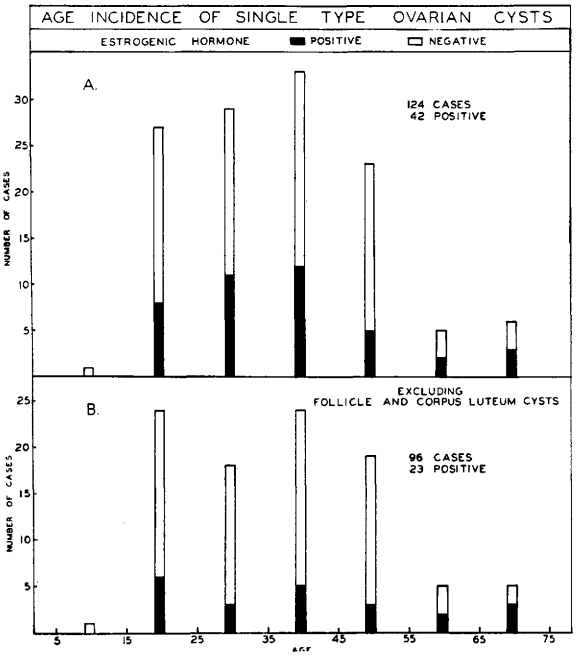

Fig. 2

Occurrence of Estrogenic Hormone in Single Type Ovarian Cysts

The data in single type cysts represented in Fig. 2-A have been analyzed according to the type of cysts

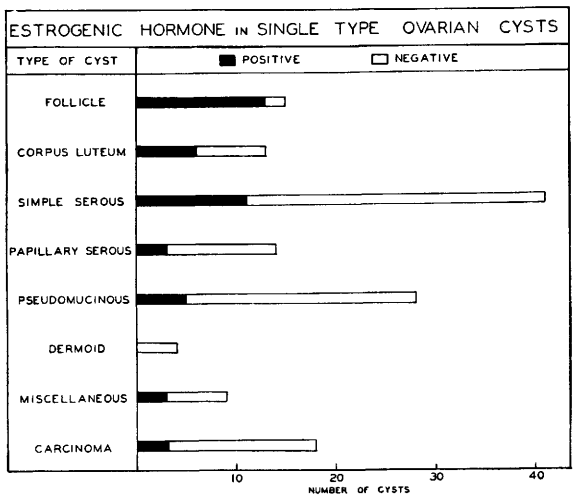

Fig. 3

which show estrogenic hormone. This analysis appears in Fig. 3 and shows the percentage of cysts with positive fluids as follows: follicle 86.7 per cent, corpus luteum 46.2 per cent, simple serous 26.8 per cent, papillary serous 21.4 per cent, pseudomucinous 17.9 per cent, dermoids none, miscellaneous 33.3 per cent.

Estrogenic Hormone in Fluids of Cystic Adnexal Tumors

General.—Assays for estrogenic hormone have been made on 377 fluids from 239 cystic adnexal tumors and 36 fluids associated with tumors, usually malignant. These data appear in Table II. The ovarian cyst fluids have been classified according to the type of lining of the cyst. The combined data for single and multiple type, and bilateral tumors and the "recurrent" ovarian cysts comprise 294 fluids from 189 benign tumors, and 55 fluids from 23 malignant tumors.

The amount of fluid tested depended upon the quantity of fluid available and upon the type of cyst. The amount of fluid obtained has been used as a measure of the size of the cyst; the actual size of the cyst or tumor is sometimes much greater than this especially when "cystic ovaries" or corpus luteum cysts are concerned. When the type of cyst was uncertain and the amount of fluid was too limited for testing graded doses, usually ½ to ⅓ the total material was injected so that a negative response indicated less than 2 to 3 rat units per cyst. Fluids were not tested at higher levels than 200 cc. per dose because it was thought that body fluids and tissues in general might contain a comparable amount of hormone. When characteristically negative fluids were tested at low levels it usually indicated small amounts of material.

The percentage of positive fluids for the different types was: follicle, 61.8; corpus luteum, 48.4; simple serous, 24.1; papillary serous, 12.2; pseudomucinous, 12.0; dermoids, none; miscellaneous, 38.5; malignant, 5.5 (Table II).

Relation of Occurrence of Estrogenic Hormone to the Amount of Fluid Tested

The amount of fluid tested depended not only upon the type of cyst but also upon the amount of fluid available. The amounts actually tested are shown on a greatly compressed scale in Fig. 4. Each dot and each circle represents the final assay value for a different fluid. The positive fluids are shown by dots at the values of the smallest amounts of fluid tested which gave positive responses, the circles indicate the largest amounts of fluid tested which still gave negative responses. Amounts of fluid tested ranged from 0.03 cc. to 200 cc. Fluids of different types showed positive responses in characteristic ranges but not all fluids of any type contain hormone. The amount of fluid required to give a positive response ranged from 0.03 cc. in some follicle fluids to more than 200 cc. in some pseudomucinous fluids. Because the amounts of fluid were often small, certain fluids could not be tested in a range where positive tests might be anticipated.

Table II: Occurrence of Estrogenic Hormone in Ovarian Cyst Fluids

	Single type			All other types: Multiple		Bilateral		Recurrent		Total			Total		
Type of cyst	No. of fluids	No. positive	Per cent positive	No. of fluids	No. positive	No. of fluids	No. positive	No. of fluids	No. positive	No. of fluids	No. positive	Per cent positive	No. of fluids	No. positive	Per cent positive
Follicle	17	13	76.5	5	2	7	3	5	3	17	8	47.1	34	21	61.8
Corpus luteum	13	6	46.2	2	2	10	3	6	4	18	9	50.0	31	15	48.4
Simple serous	58	12	20.7	6	0	8	3	11	5	25	8	32.0	83	20	24.1
Papillary serous	30	3	10.0	6	1	3	0	2	1	11	2	18.2	41	5	12.2
Pseudomucinous	60	5	8.3	7	2	12	0	4	3	23	5	21.7	83	10	12.0
Dermoid	5	0	0	1	0	2	0	1	0	4	0	0	9	0	0
Miscellaneous	9	3	33.3	3	1	0	0	1	1	4	2	50.0	13	5	38.5
Total	192	42	21.9	30	8	42	9	30	17	102	34	33.3	294	76	25.9
Carcinoma	38	3	7.9	0	0	9	0	8	0	17	0	0	55	3	5.5

Concentration of Estrogenic Hormone in Ovarian Cyst Fluids

When estrogenic hormone is found in ovarian cyst fluids the concentration seems to be characteristic for different types of fluid. Fig. 5 shows the concentration per cc. expressed on a greatly compressed scale. For the positive fluids dots represent rat units per cc. and for the negative fluids circles indicate the presence of less than that number of rat units. Follicle fluids range from 0.07 to 33 rat units per cc., corpus luteum from 0.12 to 2, simple serous 0.005 to 0.2, papillary serous

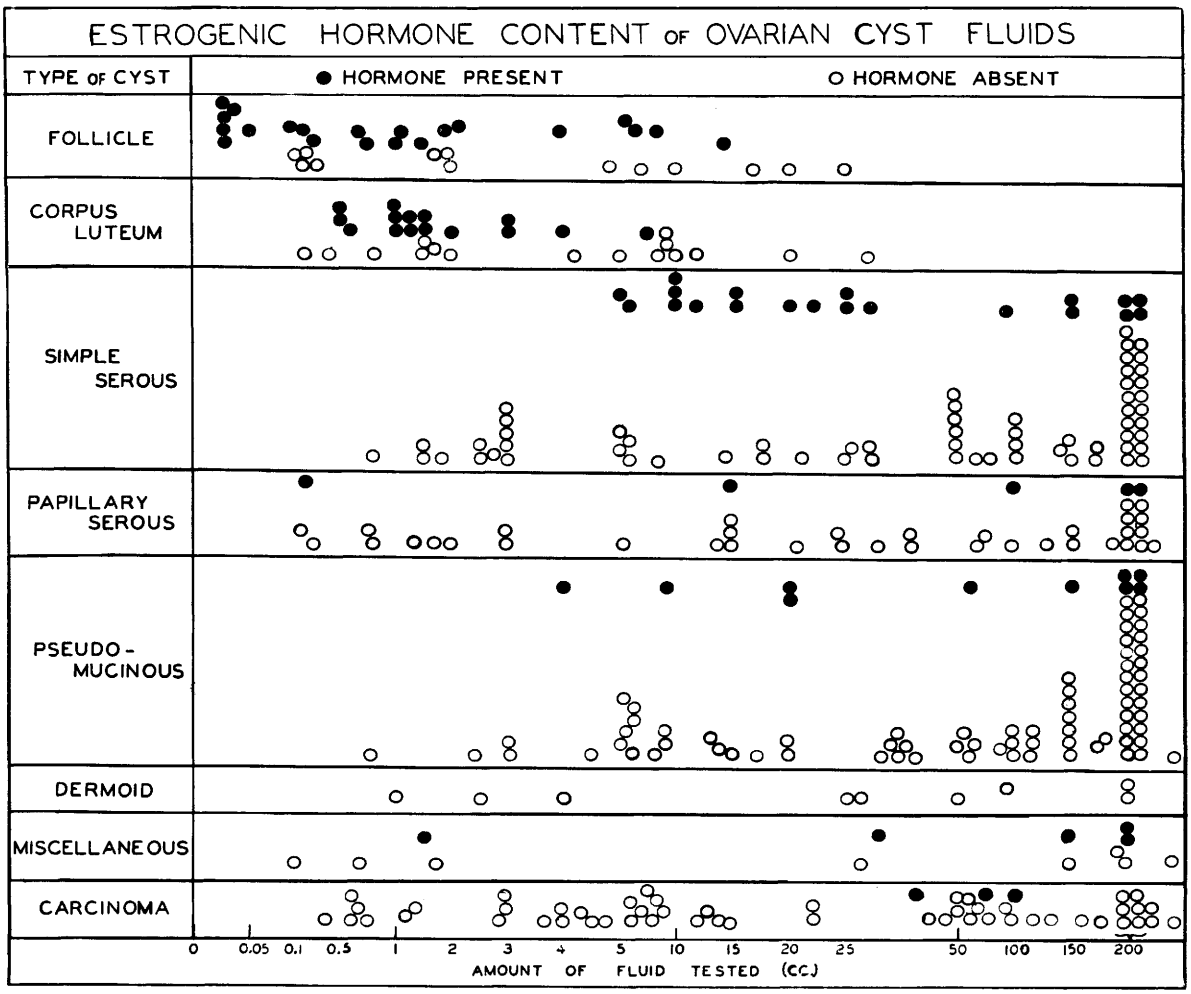

FIG. 4

and pseudomucinous showed scattered values in the same range but were characteristically negative, dermoids were negative, 3 malignant cysts showed 0.01 to 0.03 rat units per cc.

THE TOTAL AMOUNT OF ESTROGENIC HORMONE IN OVARIAN CYSTS

As previously shown (1) the size of the cyst probably is not a determining factor in regard to the presence or absence of estrogenic hormone. The amount of fluid obtained has been used as a measure of the size of the cyst. Cyst fluids ranged in amount up to 20 liters. Hormone was found in large as well as in small cysts. Apparently its absence in large cysts is not a result of dilution as the cyst increases in size. The absence of hormone in small cysts indicates that diffusion into the cyst from ovarian structures and storage are probably not important factors.

In single type cysts the total amount of estrogenic hormone per cyst, expressed in rat units, was 1.3 to 215 for follicle, 1.7 to 96 for corpus luteum, 1.4 to 225 for simple serous, 7.5 to 200 for papillary serous, 1.1 to 16 for pseudomucinous cysts. The total amount of hormone found in the cysts was not characteristic for any type of cyst, but seemed to depend not only upon the amount of hormone per cc. of fluid but also upon the size of the cyst.

ESTROGENIC HORMONE IN FLUIDS OF SINGLE TYPE CYSTS

The occurrence of estrogenic hormone in fluids of single type cysts differs from that of the entire group of fluids. This difference is due to a different distribution of positive fluids in the multiple and bilateral groups and in recurrent cysts derived from patients with histories of previous ovarian disease. The group

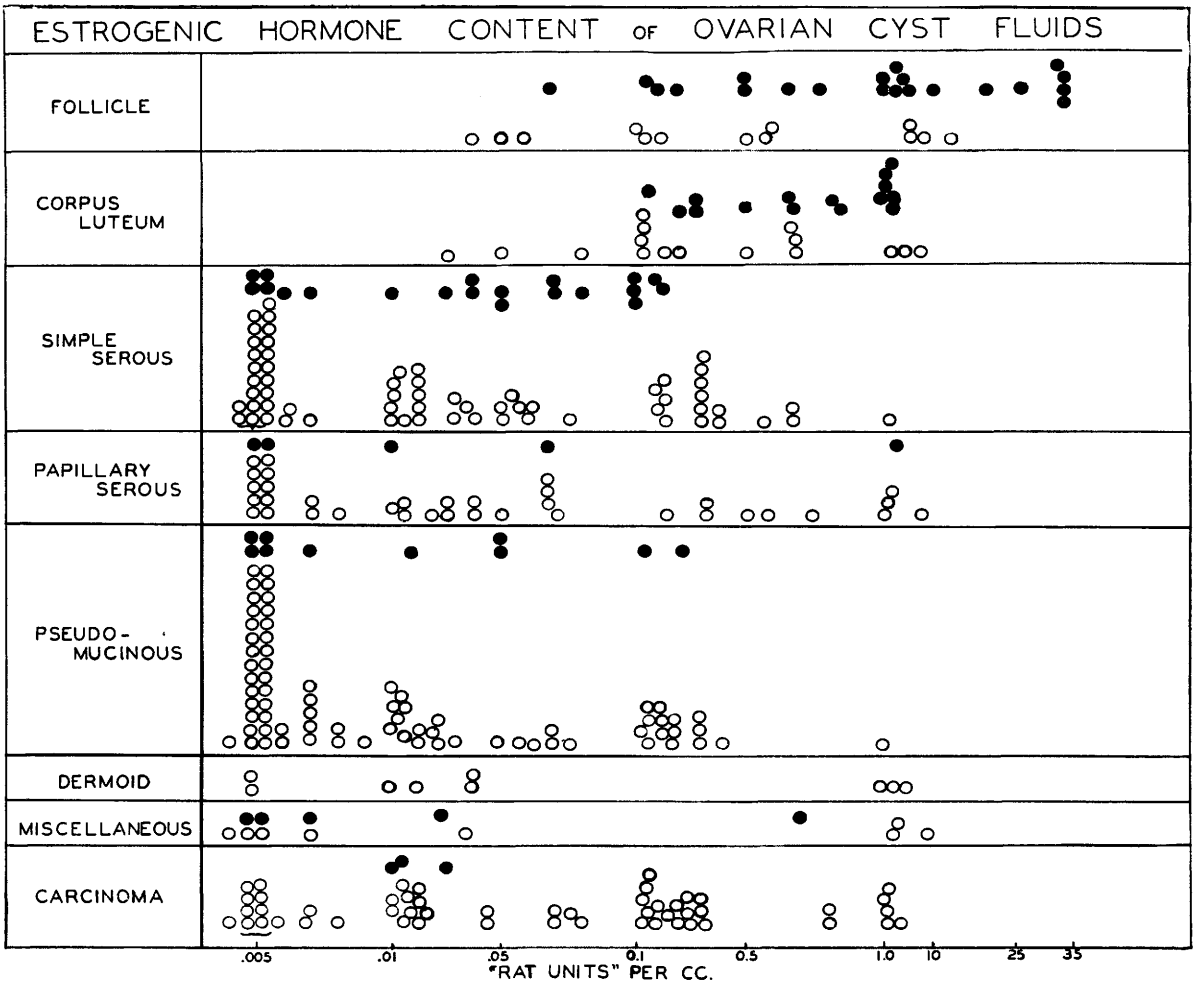

FIG. 5

of cases is the same as that in Fig. 3 but represents the total number of fluids instead of tumors. The data appear in Table II and Fig. 6. The percentages of positive fluids are: follicle 76.5 per cent; corpus luteum 46.2 per cent; simple serous 20.7 per cent; papillary serous 10.0 per cent; pseudomucinous 8.3 per cent; dermoid none; miscellaneous 33.3 per cent. The differences in the two groups are shown, for example, in the incidence of 76.5 per cent positive follicle fluids in single type fluids in contrast to 47.1 per cent in other groups combined and 8.3 per cent positive single type pseudomucinous fluids with 21.7 per cent in the other groups. These differences will be discussed later.

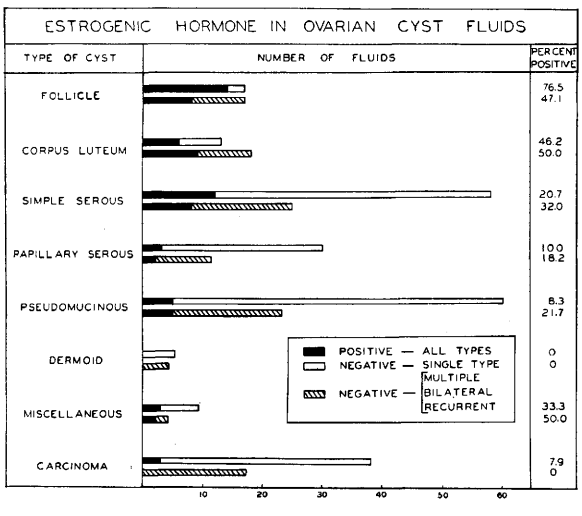

FIG. 6

MULTIPLE TYPE OVARIAN CYSTS

The multiple type group of ovarian cysts includes those tumors which contain more than one type of cyst. Fifteen tumors of this type have been examined

and the data appear in Table II and III. Three other tumors of this type also appear in the group of bilateral tumors (Table IV). Multiple type tumors are various combinations of cystic structures, both neoplastic and pseudoneoplastic. Three of the patients gave histories of previous ovarian disease. Two of these cysts and three others involved primarily the follicle or corpus luteum. Pseudomucinous cysts also occurred commonly in these tumors and were the chief cyst in 3 tumors and the minor cyst in 2. Simple serous cysts were the major cyst in 2 and minor in 3. Papillary serous cysts occurred as major in 3 and minor in 2. Five dermoid cysts were found in this group. Dermoid, pseudomucinous and follicle cysts have been found in one tumor. Apparently cysts can grow adjacently without diffusion of hormone from one cyst fluid to the other. Two of the 3 cysts which were primarily pseudomucinous in type showed hormone and 1 of these was a "recurrent" cyst. One of the 3 papillary serous contained hormone.

Bilateral Ovarian Cysts

The group of bilateral ovarian cysts includes 19 cases in which both ovaries showed cysts or ovarian disease and were removed simultaneously. When tumors or ovaries have been removed at some previous time the present tumors have been classed in a "recurrent" group and are shown in Table V. Of the 19 cases in this group, 3 were multiple type tumors. Of the 16 cases of single type cysts, 6 showed the same type of cyst on the two sides—1 follicle, 1 lutein, 1 simple serous, 1 papillary serous, 2 pseudomucinous; 2 of the bilateral multiple type showed bilateral dermoids and the other bilateral cysts with combined simple serous and corpus luteum cysts. Another showed a follicle cyst on one side and 2 corpus luteum cysts in the other ovary. Seven patients showed follicle or corpus luteum cysts on one side and serous, pseudomucinous, or dermoid on the other. Two were combined pseudomucinous and simple serous. Ten of the 16 cases showed either follicle or corpus luteum cysts in one ovary. The occurrence of bilateral tumors of different types (other than follicle or corpus luteum cysts) is of interest. The positive fluids were found among the follicle and corpus luteum cysts with the exception of 2 cases of bilateral simple serous cysts in which 3 of 4 cysts contained estrogenic hormone.

Recurrent Ovarian Cysts

This group includes 17 patients with histories of previous ovarian cystectomies or oophorectomies performed at other institutions. The data appear in Tables II and V. Three of the tumors were also multiple type. In the remaining 14 cysts the incidence was: 1 follicle, 3 corpus luteum, 7 simple serous, 1 papillary serous, 1 pseudomucinous, 1 with no epithelial lining. The large percentage of positive fluids from the true neoplasms is to be noted. Excluding the follicle and corpus luteum cysts, 10 of the 19 (53 per cent) fluids of this group contained estrogenic hormone in contrast to 14.2 per cent in the same group of single type cysts. One patient in the general series with a large simple serous cyst with fluid which contained estrogenic hormone developed a malignant tumor a year later. There are three cases of recurrent tumors in the group of malignant ovarian tumors.

Malignant Ovarian Cysts

There are twenty cases of unilateral and one of bilateral malignant ovarian cysts in this series. Three patients had been operated upon previously; one for a cyst and two for ovarian carcinoma. These three tumors were probably of a papillary serous type and were negative or contained less than 1.1, 1.5, 4.6 r. u. per cyst. Only 3 of the 55 fluids tested were positive for estrogenic hormone, 2 of these were from papillary serous cysts. Considering the types of fluid examined the amounts tested were often too small to permit anticipation of finding the hormone. Of the two papillary serous cysts one contained 0.03 r. u. per cc. and 63 r. u. per cyst and the other 0.01 r. u. per cc. and 3.5 r. u. per cyst. The third cyst contained 0.013 r. u. per cc. and 24 r. u. per cyst. The per cent in which hormone was found corresponds with that of the benign series. It may be noted that not all parts of the same tumor present evidence of malignancy or the same degree of malignancy.

Nonovarian Cystic Adnexal Tumors

Twenty-seven nonovarian cysts have been tested for estrogenic hormone in order to determine its occurrence in extra-ovarian fluids. Fourteen of these were cysts of embryonic origin and included 6 cases of unilateral parovarian cysts, 2 bilateral parovarian, 3 wolffian, 1 hydatid of Morgagni, 1 Gartner's duct. With one exception, all of these fluids were negative; the positive fluid was from a parovarian cyst and contained 0.02 r. u. per cc. and 10.6 r. u. for the entire cyst. Fluids were negative at 200 cc. in 4 cases. Fluids from 4 cases of hydrosalpinx, 3 cystic fibroids and 1 Bartholin cyst were all negative. Five fluids associated with endometriosis were also negative.

Ascitic Fluids

Ascitic fluid from 26 patients with tumors has been tested for estrogenic hormone. Twenty of the 36 fluids were tested at 200 cc.; usually extractions and tests were made in triplicate. All of the 36 fluids were negative.

TABLE III: ESTROGENIC HORMONE IN MULTIPLE TYPE OVARIAN CYSTS

Number	Age	Type	Amount of fluid in cc.	Amount tested (cc.)		Estrogenic hormone, R.U. per cc.		Previous operation for ovarian disease
				Positive	Negative	Present	Less than	
11 A	32	Corpus luteum	12	...	5	...	0.2	Cystectomy
C		Follicle	10	1.0	...	1.0	...	.....
B		Follicle	1.5	1.3	...	0.77	...	.....
281 A	40	Follicle	14.5	0.75	...	1.3	...	None
C		Papillary serous	1.5	...	0.8	...	1.3	.....
B		No epith. lining	0.8	...	0.7	...	1.4	.....
154	28	Corpus luteum (old)	38	...	30	...	0.03	Cystectomy
A		Simple serous	7	...	3	...	0.33	.....
190 B	27	Corpus luteum	23	1.0	...	1.0	...	None
A		No epith. lining	13	1.5	...	0.67	...	.....
C		No epith. lining	0.12	...	0.12	...	8.3	.....
296 A	34	Corpus luteum	90	7.5	...	0.13	...	None
C		Follicle	0.3	...	0.2	...	5.0	.....
D		Follicle	0.25	...	0.2	...	5.0	.....
B		Simple serous	2	...	1.8	...	0.56	.....
143	39	Simple serous	145	...	50	...	0.02	None
A		Aspirated †	3.5 *	...	2	...	0.5	.....
152	35	Simple serous	607	...	200	...	0.005	None
A		Aspirated †	0.6 *	0.05	...	20	...	.....
110	44	Papillary serous	1,235	...	200	...	0.005	None
A		Papillary serous	218	...	100	...	0.01	.....
B		Follicle	2	...	2	...	0.5	.....
118	57	Papillary serous	10,260	200	...	0.005	...	None
A		Pseudomucinous	96	...	90	...	0.012	.....
B		Pseudomucinous	32	...	30	...	0.033	.....
151	43	Papillary serous	1,850	...	200	...	0.005	None
A		Pseudomucinous	440	...	200	...	0.005	.....
54	63	Pseudomucinous	480 ‡	...	100	...	0.01	None
A		Aspirated †	28	...	10	...	0.1	.....
101	29	Pseudomucinous	1,660	20	...	0.05	...	Oophorectomy
A		Pseudomucinous	25	20	...	0.05	...	.....
B		Pseudomucinous	9.5	9	...	0.11	...	.....
D		Follicle	39	...	20	...	0.05	.....
E		Follicle	46	...	25	...	0.04	.....
C		Dermoid	28.6	...	28	...	0.036	.....
158	40	Pseudomucinous	3,200	200	...	0.005	...	None
A		Pseudomucinous	23	...	20	...	0.05	.....
B		Pseudomucinous	75	60	...	0.017	...	.....
C		Papillary serous	17	...	15	...	0.067	.....
139 D	19	Dermoid §	..	...	...	...	...	None
139		Simple serous	202	...	100	...	0.01	.....
A		Simple serous	31	...	29	...	0.034	.....
B		Simple serous	16	...	14	...	0.071	.....
C		Aspirated †	52	...	45	...	0.022	.....
234 A	28	Dermoid	148	...	50	...	0.02	None
B		Follicle	2.8	0.04	...	25	...	.....

* Composite.
† Aspirated and no histology.
‡ Incomplete specimen.
§ Not tested.
See Table IV.

TABLE IV: ESTROGENIC HORMONE IN BILATERAL OVARIAN CYSTS

Cyst No. 1				Estrogenic hormone				Cyst No. 2			Estrogenic hormone			
				Amount tested (cc.)		R.U. per cc.					Amount tested (cc.)		R.U. per cc.	
Number	Age	Type	Amount of fluid in cc.	Positive	Negative	Present	Less than	Number	Type	Amount of fluid in cc.	Positive	Negative	Present	Less than
67	31	Follicle	19	...	7	...	0.14	68 A	Follicle	12.5	4	...	0.25	....
								68 B	Follicle *	0.47	...	0.2	...	5.0
10 A	27	Corpus luteum	9	4	...	0.25	....	10 B	Corpus luteum	4	...	1.5	...	0.67
247 A	38	Papillary serous	222	...	190	...	0.005	248	Papillary serous	77	...	65	...	0.015
B		Papillary serous	0.6	...	0.3	...	3.3	...	.....	...	...	...	...	....
268	37	Simple serous	165	25	...	0.04	....	269	Simple serous	101.5	90	...	0.01	....
74	62	Pseudomucinous	3,800 †	...	200	...	0.005	75	Pseudomucinous	90 †	...	50	...	0.02
208	21	Pseudomucinous	175	...	150	...	0.007	209 A	Pseudomucinous	7	...	6	...	0.17
								C	Pseudomucinous	142	...	120	...	0.008
								D	Pseudomucinous	43	...	35	...	0.028
236	48	Simple serous	1,703	...	200	...	0.005	237	Follicle	2	...	1.7	...	0.59
166 A	39	Corpus luteum	27	1.5	...	0.67	....	165	Follicle	5.8	0.03	...	33.3	....
B		Corpus luteum	20	...	8.8	...	0.11	...	.....	...	...	...	...	....
45	26	Pseudomucinous	5,360	...	200	...	0.005	46	Follicle	26	2.1	...	0.5	....
72	14	Pseudomucinous	192	...	115	...	0.009	71	Follicle	35	...	10	...	0.1
297	43	Pseudomucinous	212	...	180	...	0.006	298	Follicle	2.2	...	1.6	...	0.6
141	22	Pseudomucinous	2,260	...	200	...	0.005	142	Follicle *	8	0.05	...	20	....
30	48	Pseudomucinous	3,350	...	150	...	0.007	31	Simple serous	210	...	140	...	0.007
39	58	Simple serous	2,200	...	200	...	0.005	40	Pseudomucinous	2,000	...	150	...	0.007
229	44	Dermoid	218	...	200	...	0.005	230	Corpus luteum	3.5	...	2	...	0.5
303	23	Simple serous	120	...	80	...	0.013	304	Corpus luteum	10	3	...	0.33	....
260 A	33	Dermoid	109.5	...	95	...	0.01	261	Dermoid ‡	...	...	...	...	....
B		Corpus luteum	0.3	...	0.2	...	5	...	.....	...	...	...	...	....
270	26	Simple serous	9.0	...	5.0	...	0.2	272 B	Simple serous	31	22	...	0.05	....
B		Corpus luteum	1.0	...	0.4	...	2.5	A	Corpus luteum	12	...	9.25	...	0.11
282	31	Dermoid ‡	...	...	...	...	....	...	.....	...	...	...	...	....
A		Corpus luteum	6.6	...	4.05	...	0.25	...	Dermoid ‡	...	...	...	...	.

* No histology. † Incomplete specimen. ‡ Not tested.

TABLE V: ESTROGENIC HORMONE IN RECURRENT OVARIAN CYSTS

Number	Age	Single type	Amount of fluid in cc.	Amount tested in cc.		Estrogenic hormone R.U. per cc.		Previous operation for ovarian disease
				Positive	Negative	Present	Less than	
96	36	Follicle	7.6	2.0	...	0.5	...	Oophorectomy
245 A	41	Corpus luteum	13.5	3.0	...	0.33	...	Oophorectomy
B		Corpus luteum	13.0	0.6	...	1.67	...	.....
262	25	Corpus luteum	69	1.2	...	0.83	...	Ooph., resection
289	40	Corpus luteum	30	1.0	...	1.0	...	Oophorectomy
18	49	Simple serous	37	...	18.0	....	0.06	Oophorectomy
66 A	39	Simple serous	260	15	...	0.07	...	Oophorectomy
B		Simple serous	120	15	...	0.07	...	.....
98	34	Simple serous	3,990	200	...	0.005	...	Oophorectomy
130	56	Simple serous	52	...	20.0	....	0.05	Oophorectomy
A		Simple serous	14	...	3.0	....	0.33	.....
B		Simple serous	8	...	3.0	....	0.33	.....
146	40	Simple serous	955	...	200	....	0.005	Oophorectomy
156	24	Simple serous	815	150	...	0.007	...	Oophorectomy
184	36	Simple serous	362	150	...	0.007	...	Cystectomy
134	46	Papillary serous	89	15	...	0.067	...	Oophorectomy
A		Papillary serous	44	...	25	....	0.04	.....
138	67	Pseudomucinous	9,000	...	200	....	0.005	Cystectomy
256	37	No epith. lining	234	200	...	0.005	...	Resection
		Multiple type						
11 A	32	Corpus luteum	12	...	5	....	0.2	Cystectomy
B		Follicle	1.5	1.3	...	0.77	...	.....
C		Follicle	10	1.0	...	1.0	...	.....
101	29	Pseudomucinous	1,660	20	...	0.05	...	Oophorectomy
A		Pseudomucinous	25	20	...	0.05	...	.....
B		Pseudomucinous	9.5	9	...	0.11	...	.....
C		Dermoid	28.6	...	28	....	0.036	.....
D		Follicle	39	...	20	....	0.05	.....
E		Follicle	46	...	25	....	0.04	.....
154	28	Corpus luteum (old)	38	...	30	....	0.03	Cystectomy, oophorectomy
A		Simple serous	7	...	3	....	0.33	.....

SUMMARY

In an attempt to correlate the occurrence of estrogenic hormone in cystic ovarian tumors with the morphology of the tumor 212 ovarian cysts have been examined. Of these 189 were benign and 23 were malignant. As a control study 27 cystic nonovarian genital tumors and 36 ascitic fluids associated with tumors have been studied.

Seventy-three per cent of the benign ovarian cysts were removed between the ages of 15 to 45 years, during the period of the greatest functional activity of the ovary. Fifty-eight per cent of the malignant ovarian cysts were removed after 45 years of age. Estrogenic hormone was found in 35 per cent of the benign cysts in the age group 15 to 45 years. If those cysts arising from known ovarian structures (follicle and corpus luteum) are excluded, 23 per cent of the cysts contain hormone. In this group of neoplastic cysts 28 per cent of the cysts from patients over 45 years of age contain hormone. This comprises 36 per cent of all the positive cysts in this group.

The percentage of different types of single type cysts containing estrogenic hormone were: follicle, 86.7; corpus luteum, 46.2; simple serous, 26.8; papillary serous, 21.4; pseudomucinous, 17.9; dermoids, none; miscellaneous, 33.3. Considering all the fluids of these cysts, which include multilocular cysts, the following percentages of positive fluids were obtained: follicle, 76.5; corpus luteum, 46.2; simple serous, 20.7; papillary serous, 10.0; pseudomucinous, 8.3; dermoids, none, miscellaneous, 33.3. Fluids from multiple type and bilateral cysts and cysts from patients with histories of previous ovarian disease (recurrent group) showed a different percentage incidence of positive fluids, as follows: follicle, 47.1; corpus luteum, 50.0; simple serous, 32.0; papillary serous, 18.2; pseudomucinous,

21.7; dermoid, none; miscellaneous, 50.0. These differences result from (a) fewer positive follicle fluids in all the groups but especially in the multiple and bilateral groups; (b) a larger number of positive simple serous fluids in the bilateral and recurrent groups; (c) a higher per cent of positive pseudomucinous fluids in the multiple and recurrent groups. Excluding follicle and corpus luteum fluids, 10 of 17 of the positive fluids in the special group are found in the recurrent group and 3 of 17 in the bilateral group.

When estrogenic hormone was present in ovarian cyst fluids the amount found varied with the type of cyst. The concentration per cc. of fluid, expressed in rat units, was as follows: follicle, 0.07 to 33; corpus luteum, 0.12 to 2; simple serous, 0.005 to 0.2; papillary serous and pseudomucinous showed only a few positive fluids in scattered range; dermoids were negative.

In single type cysts the total amount of estrogenic hormone per cyst depended upon the concentration of the hormone and the amount of cyst fluid. The total amounts, in rat units, for various types of fluids were: follicle, 1.3 to 215; corpus luteum, 1.7 to 96; simple serous, 1.4 to 225; papillary serous, 7.5 to 200; pseudomucinous, 1.1 to 16.

Twenty-three malignant ovarian cysts have been studied. Only 3 of the 55 fluids tested contained estrogenic hormone. One contained 0.03 rat units per cc. and a total of 63 rat units, another 0.01 rat units per cc. and a total of 3.5 rat units and the third 0.013 rat units per cc. and 24 rat units per cyst.

Fourteen cysts arising from embryonic rests were tested and with the exception of one parovarian cyst all were negative for estrogenic hormone. Fluids from 4 specimens of hydrosalpinx, 5 from endometriosis, 3 cystic fibroids, 1 Bartholin cyst, and 36 ascitic fluids were also negative for hormone.

We wish to express our appreciation to Dr. Lucia J. Dunham for her assistance in the morphologic studies and to the other members of the staff for their cooperation in supplying the clinical material for this investigation.

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