

AMENORRHEA ASSOCIATED WITH BILATERAL  
POLYCYSTIC OVARIES\*

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ACCORDING to leading authoritative works on gynecology, the bilateral polycystic ovary is most commonly found in association with *uterine bleeding* (Fig. 1). This association has been recognized by the medical profession and is not infrequent in occurrence. Endometrial hyperplasia, multiple follicle cysts with granulosa cell lining, and a notable absence of corpora lutea in the ovary are the significant pathologic findings in such cases. The bleeding in these patients is readily explained by the fact that the increase in number of follicles lined by granulosa cells produces an excess of secretion of estrogenic hormone.

According to the same authoritative works, little or no mention is made of bilateral polycystic ovaries accompanied by *amenorrhea*, and inasmuch as we have encountered a series of cases exemplifying the latter conditions, we desire to present the results of our study of them.

Cyst formation in the follicular apparatus of the ovary is very common and is regarded to some extent as a physiologic process. When these structures are visible to the naked eye, they are regarded as cysts; when not, they are called follicles. When this process becomes excessive, persistent or progressive, the ovary becomes enlarged, tense, tender and painful, and produces what has been termed "cystic degen-

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eration of the ovary," and is usually bilateral. The exact cause of this formation is still in doubt; formerly, it was regarded as the result of inflammatory change due to either local infection or that from some distant focus. More recent observations and experiments point to an **endocrine causal relationship of the polycystic changes in the ovaries.** Furthermore, there are usually no adhesions or other gross or microscopic evidences of inflammation in the ovaries found in these cases. In the series of patients which we observed with bilateral polycystic ovaries and amenorrhea, the ovaries were found to be from two to four times the normal size and while they often maintained their original shape, they were sometimes distinctly globular. In one case, they were flat and soft, the so-called "oyster ovaries." The ovarian cortex was found to be hypertrophied in all of the cases and the tunica thickened, tough, and fibrotic.

The cysts were follicle cysts, near the surface, and almost entirely confined to the cortex, and they contained clear fluid. There were

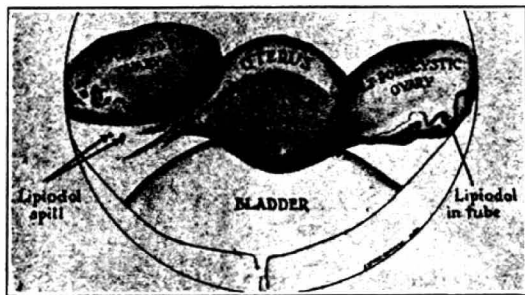


Fig. 1.

from twenty to one hundred cysts in each ovary, varying in size from 1 mm. to about 1.5 cm., but rarely larger. The color of the ovary was oyster gray with bluish areas where the cysts were superficial and appeared on the surface as sago-like bodies. On section, the variation in size of the cysts and the clear fluid contents were revealed. Corpora lutea were sometimes absent and when found, they were very small and deeply placed.

The uteri in these patients were either normal in size or smaller and firmer than normal. The remaining changes observed were those involving the secondary sex characteristics. The breasts presented no characteristic changes except in cases of long-standing amenorrhea when they were small, firm, and pale.

In some patients, there was observed a distinct tendency toward masculinizing changes. A typical rhomboid hairy escutcheon, hair on the face, arms, and legs, and coarse skin was noted. No voice changes have been observed by us. The external genitals in most

patients were normal, but in some, the labia minora and clitoris were markedly hypertrophied. Libido is apparently not affected by the changes noted in the ovaries.

#### CASE REPORTS

**CASE 1.**—M. G., aged twenty-two, married one and one-half years, gravida 0, was first seen Oct. 3, 1928. Her chief complaints were sterility and amenorrhea. Menses began at age of thirteen, irregular, two to seven months, five-day duration, moderate, no pain. She was treated with estrogenic preparations, intramuscularly; she then menstruated irregularly every six or eight weeks; small doses of thyroid extract and calcium were given.

November, 1929: Menstruated about every seven weeks. Examination revealed moderate obesity and slight struma. Bimanual examination: Uterus was 2° retroverted, normal size; right ovary palpable and cystic. January, 1930: Transabdominal pneumoperitoneum (Fig. 2), revealed bilateral cystic ovaries, each ovary appearing as large as the uterine fundus. Operation: May 2, 1930, laparotomy. Uterus was small and both ovaries were polycystic and enlarged, the right more so than the

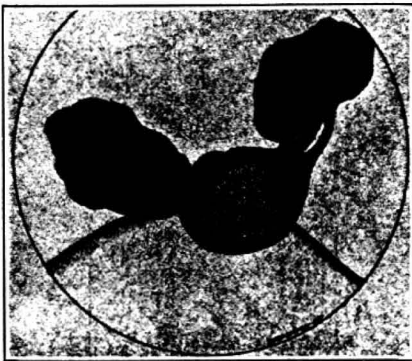


Fig. 2.



Fig. 3.

left. The left also contained a small fibroma. Wedge-resection of both ovaries. Un-  
eventful recovery; discharged from the hospital on the twelfth postoperative day.

Forty-eight hours after operation, slight uterine bleeding occurred, and normal menstrual periods occurred monthly thereafter. Patient became pregnant in October, 1930, and again in February, 1933; both pregnancies were carried to full term and delivered normally. Menstruation since confinement is entirely normal, every twenty-eight days. August, 1934: Follow-up examination showed the uterus and both ovaries to be normal.

*Pathologic Report.*—Gross: Sections from both ovaries showed numerous cystic cavities varying from 1 mm. to 1 cm. in size. Ovarian tunic was thickened and fibrous. Microscopic: Thick tunic, many cysts varying in size, lined by theca cells; one normally developing graafian follicle; corpus albicans; old corpus luteum; tortuous and dilated blood vessels.

**CASE 2.**—B. K., aged twenty-nine, married five years, gravida 0, was admitted to the hospital Aug. 10, 1931. Her chief complaints were sterility and amenorrhea. Menses began at the age of fifteen, were irregular for several months; no menses for eight years prior to first examination. Menstruated twice last year (under our observation) after treatment with estrogenic hormone, intramuscularly. Phys-

ical examination: Rigid type; tight coarse skin, hairy face, arms, and legs; masculine escutcheon. Transabdominal pneumoperitoneum; bilateral cystic ovaries almost as large as uterine fundus (Fig. 3). Operation: Wedge-resection of two-thirds to three-fourths of each ovary. Uneventful recovery. Discharged from hospital on thirteenth postoperative day.

Patient has menstruated regularly every twenty-eight days since operation. Follow-up examination in May, 1933: uterus and both ovaries normal; secondary sex characters evidence little improvement; no pregnancy to date.\*

*Pathologic Report.*—Gross: Thick tunic, numerous cystic cavities up to 1 cm. in diameter near surface of ovary (Fig. 4). Microscopic: Tunic thick and fibrous; numerous cysts varying in size, lined by hypertrophied theca layer. Granulosa cells were scarce. Small (old) corpora albicantia. No corpora lutea.

CASE 3.—L. C., aged twenty-one, married two years, gravida 0, was first seen April 24, 1929. Her chief complaints were amenorrhea and sterility. Menses began at the age of thirteen, were always irregular, one- to nine-month intervals, usually six months, lasting for five or six days, scant; no pain. Treatment was

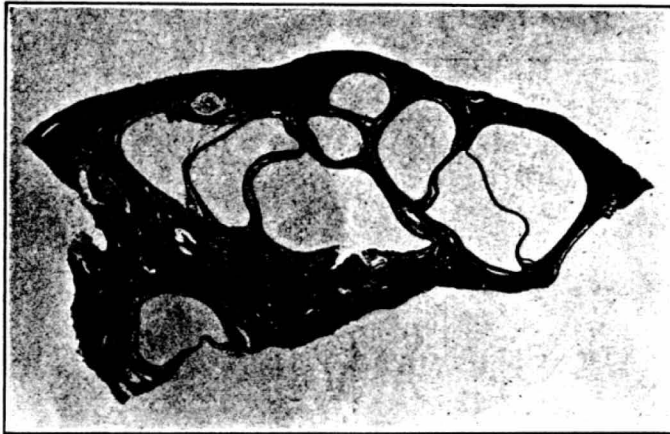


Fig. 4.—Photomicrograph (6 diameters) of section of wedge removed from ovary (Case 2).

given over a period of four years with estrogenic hormone preparations, intramuscularly, and thyroid extract by mouth. In December, 1929, patient had x-ray stimulation of ovaries with no results. In October, 1931, she became pregnant, and was delivered of a normal child at term, August, 1932. Following this, she had four normal periods at regular intervals followed by amenorrhea of one year and nine months. During this time, she was treated with estrogenic hormone preparations without benefit. Examination revealed a short, well-proportioned young woman; breasts normal, masculine escutcheon, long labia minora and hypertrophied clitoris. Bimanual examination showed normal sized uterus, both ovaries enlarged, globular and tender.

July 6, 1933: Transabdominal pneumoperitoneum and intrauterine lipiodol instillation showed both ovaries enlarged and elongated; tubes patent. Uterine contour was normal (Fig. 5). Oct. 14, 1933: Operation: Bilateral wedge-resection of about three-fourths of both ovaries, each of which was 5 by 7 cm. in diameter; the capsule was very thick and leathery. Uneventful postoperative course; discharged from hospital on twelfth day. Patient menstruated forty-eight hours after opera-

\*This patient is now (Jan. 30, 1935) three months pregnant.

tion and has had regular monthly periods for the past year. Check-up examination in September, 1934, showed the uterus and both ovaries normal to palpation.

**Pathologic Report.**—Gross: Thick tunica; numerous cysts up to 1 cm. in diameter. Microscopic: Moderately thick tunica; numerous cysts, some lined with granulosa cells, others with theca cells; some corpora albicantia; no corpora lutea; tortuous, large and thickened blood vessels.

CASE 4.—H. W., aged twenty-three, married three years, gravida 0, was first examined Jan. 3, 1933. Her chief complaints were sterility and amenorrhea, Menses began at the age of fifteen, were irregular, one to six months, usually three to four months; three- to four-day duration; profuse with clots and cramps. Last menstruation occurred six months previous to admission. No contraception for two years. Treated with estrogenic hormone intramuscularly and orally. Examination: Patient was large, obese with feminine escutcheon and large flabby breasts. Uterus normal; palpable left ovary was enlarged and cystic. Feb. 15, 1933: Transuterine pneumoperitoneum and lipiodol instillation showed the uterus to be normal in size; both ovaries were enlarged and cystic; fallopian tubes were patent (Fig. 6). Mar. 11, 1933: Operation: Bilateral wedge-resection of ovaries which were so large that

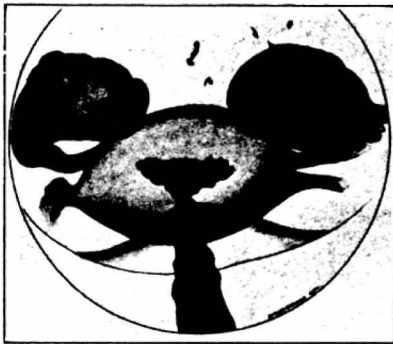


Fig. 5.

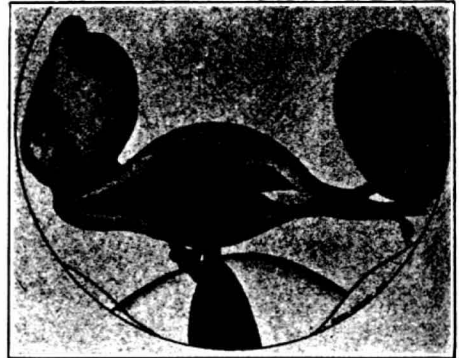


Fig. 6.

more than three-fourths of each was removed, leaving the hilus approximately the size of a normal ovary.

The patient made an uneventful recovery and was discharged on the tenth post-operative day. She menstruated on the sixth day and regularly every twenty-eight days thereafter for the past year and one-half. Bimanual examination in March, 1934, revealed a normal genital status.

**Pathologic Report.**—Gross: Each section showed several cysts up to 1.5 cm. in diameter. Microscopic: The ovary appeared normal; tunica moderately thickened and below were multiple small cysts; some lined with granulosa cells, others with theca cells. Normal cystic follicles; small corpora albicantia; cluster of granulosa cells evidently the edge of a normal follicle. No corpora lutea. In one portion was a small papillary cystadenoma. Tortuous and thickened blood vessels.

CASE 5.—O. B., aged twenty-five, married one and one-half years, gravida 0, was first seen in the clinic Jan. 9, 1933. Her chief complaints were irregular menses and sterility. Menses began at the age of fifteen, two- to three-month intervals, painful, duration three days. Last menstruation Dec. 29, 1932. Examination: Male escutcheon, hairy thighs, breasts normal. Bimanual: Cystic swelling of right ovary palpable, but not left. Uterus was small. Transuterine pneumoperitoneum and lipiodol instillation: Both ovaries cystic; right larger than left; tubes patent to gas

and filled with lipiodol (Fig. 7). Operation: Wedge-resection of one-half to two-thirds of both ovaries which were polycystic; the uterus was found to be small, firm, and slightly bicornuate.

Uneventful postoperative course; patient was discharged on the tenth day. Menstruation occurred on the fourth postoperative day, and regularly each month thereafter. Follow-up examination in September, 1934; uterus and ovaries found normal on palpation.

*Pathologic Report.*—Gross: Thick tunic; numerous cysts varying in size up to 1.5 cm. Hemorrhagic stroma. Microscopic: Moderately thickened tunic; recent corpus luteum with hemorrhagic corpus luteum cyst; many cysts lined by theca cells. Large corpus albicans; edematous vascular stroma with hemorrhage.

CASE 6.—E. A., aged thirty-three, married fifteen years, gravida ii, was admitted to the hospital Oct. 23, 1933. Her chief complaints were irregular menses for nine years, abnormal hairy growth for three years, and pain in groin for three years. Menses began at the age of twelve, regular until ten years ago, since then, five- to nine-month intervals, becoming longer. Menses were scant, lasting three or four days with no pain. Hairy growth on face, back, arms, and legs for past three years,

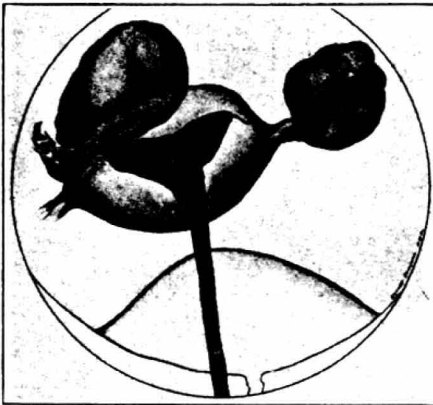


Fig. 7.

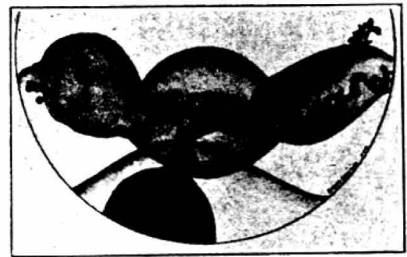


Fig. 8.

becoming more noticeable. Pain in both lower quadrants for three years, with lower abdominal pain accompanying the menstrual molimina even in the absence of bleeding. Gained 15 pounds in past year; weight, 175. Examination: short, obese, male escutcheon, hair on body and face; pendulous breasts. Uterus normal in size; both ovaries enlarged, cystic, tender. Transuterine pneumoperitoneum and lipiodol instillation: Both ovaries were enlarged, uterus was normal, and fallopian tubes were patent (Fig. 8). Operation: Bilateral wedge-resection of about one-half of each ovary, which contained multiple cortical cysts.

Uneventful recovery, discharged on thirteenth postoperative day. Uterine bleeding occurred on fifth postoperative day and menstruation recurred monthly thereafter (eleven months). Follow-up examination in June, 1934: No evidence of reformation of cysts, genital status normal.

*Pathologic Report.*—Gross: Thick tunic; numerous cystic cavities varying in size up to 1.5 cm. Microscopic: Tunic thickened in some sections and normal in others. Normal follicle with maturing ovum near surface. Large theca cyst with corpus albicans; recent corpus luteum.

CASE 7.—M. B., aged twenty, single, was admitted to the hospital Aug. 29, 1933. Her chief complaints were amenorrhea and pain in both lower quadrants for one

year. Menses began at fourteen years of age, always irregular, six weeks to four months, usually two months, seven-day duration, moderate, occasional clots, no dysmenorrhea. Physical examination revealed a tall, thin girl, with muddy complexion; facial acne; scant breast development. Rectal examination showed the uterus to be erect, and of normal size. The left ovary was cystic and from 7 to 8 cm. in length. The right ovary was cystic and 5 cm. long. Transabdominal pneumoperitoneum on Aug. 30, 1933. Bilateral polycystic ovaries, each as large as the normal uterine fundus (Fig. 9). Operation: Wedge-resection of the cystic portion of each ovary. Patient made an uneventful recovery and was discharged from the hospital on the ninth postoperative day. Menstruation has been regular since operation, and pain has been relieved. Patient was married a few months after operation and has remained in good health. She has moved to a distant city and reported in October, 1934, that she was in good health and that menstruation had recurred monthly.

*Pathologic Report.*—Gross: Sections of ovaries showed numerous cysts; and hemorrhagic and edematous stroma. Microscopic: Moderately thickened tunic; large corpus luteum cyst; numerous cysts lined by theca cells; follicle cysts with granulosa cell lining. Corpora albicantia; dilated blood vessels and very vascular stroma.

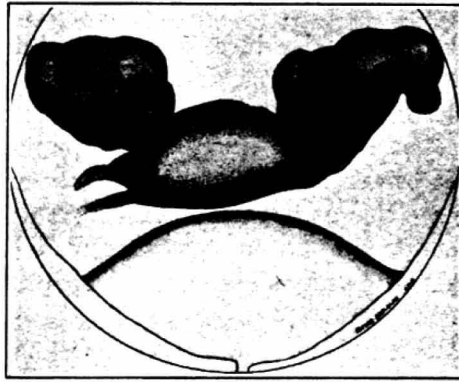


Fig. 9.

#### DIAGNOSIS AND TREATMENT

The diagnosis of polycystic ovaries is made only after careful and repeated examinations. The history of irregular menses with or without pain gives little clue to the ovarian condition and a bimanual or rectal examination may not always reveal the presence of polycystic ovaries. Due to the fact that the ovaries often show transient enlargements incident to physiologic changes, one must not arrive at hasty judgments. Furthermore, in cases of flat "oyster ovaries," it is sometimes difficult to palpate the pathologic enlargement. Conflicting opinions are not infrequent concerning the presence of these swellings.

The diagnosis is greatly enhanced in cases of ovarian swellings by the use of pneumoroentgenography, as one of us has previously described. We have been able to demonstrate the bilateral ovarian enlargements by this method when palpatory findings were doubtful or

disputed. The shadow of the normal ovary usually appears on the film to be about one-fourth of the size of that of the uterine corpus. When the ovary is polycystic, it appears from three-fourths to as large as the uterine shadow. This method of diagnosis has been of especial value when there was a difference of opinion concerning the presence of ovarian pathology. The film evidence is convincing as may be seen in the accompanying illustrations. After using pneumoroentgenographic diagnosis for more than ten years, we feel that we are qualified to endorse it as a most valuable aid in gynecology, and especially so in recognizing relatively small ovarian swellings which may escape detection on bimanual examination.

The treatment of amenorrhea and sterility in the group of patients under consideration was at first conservative, using endocrine preparations; eventually the treatment became surgical. In some of the earlier cases, injections of various endocrine preparations were made in an effort to adjust the menstrual cycle. Estrogenic hormone preparations which were reputed to be more or less potent were administered intramuscularly. Uterine bleeding occurred as a result of this treatment in some instances, but it is impossible to say whether this was true menstruation or anovular bleeding. At any rate, no lasting restoration of function followed these treatments and no pregnancies occurred. The use of anterior pituitary-like substances was avoided in order that a cystic change in the ovaries might not be thereby provoked, for, as Zondek has shown, hyperhormonal amenorrhea with overstimulation of the graafian follicles can be produced by the injection of prolan.

In the patients referred to in this series, we have resected from one-half to three-fourths of each ovary by wedge-resection, thereby removing the cortex containing the cysts, and have sutured the hilus with the finest catgut. The immediate results have been entirely satisfactory. All of the patients recovered uneventfully, and were discharged from the hospital from the ninth to the thirteenth postoperative days. Uterine bleeding occurred on the third to the fifth postoperative day and menstruation occurred monthly thereafter in every case. Our first patient, operated upon four years ago, has given birth to two children since operation.

#### DISCUSSION

The ovarian change in bilateral cystic ovaries is most probably a *result* of some hormonal stimulation and very likely relates to the anterior lobe of the pituitary gland. Geist reported fifty cases in which "antuitrin-S" was injected in large doses a few days prior to operation for fibroids. At operation, the ovaries showed definite changes. While the follicles did not grow in size, they were greatly increased in number. Geist described the additional changes in the ovary which



varied in intensity in direct relationship to the amount of hormone injected. He quotes the work of Mandelstamm and Tschackowsky who likewise produced polycystic ovaries in women by the use of anterior pituitary-like substances.

Oddly enough, the surgical treatment directed to the ovary in our series adjusted the endocrine balance to the extent of restoring normal menstruation and the reproductive function. Theoretically, one would expect that if the cystic portion of the ovary were removed without also removing the abnormal stimulus which produced the ovarian change, the same factors would still be operative, resulting in reformation of the polycystic change. Thus far, this has not been our experience although we have observed our patients over a period of from one to four years since operation.

Whenever one attempts to correlate the function or dysfunction with the structure of any of the endocrine glands, one is apt to encounter grave difficulties, due to the recognized instability of the normal anatomy of all glands of internal secretion. The association of amenorrhea with polycystic ovaries in our series is no exception to this statement. The pathologist is unable to conclude from a study of the sections taken from the ovaries in our patients that amenorrhea was a symptom. He can demonstrate no anatomic structure or characteristic change in the ovary which enables him to describe the clinical picture. The only consistent pathologic finding is the presence of follicle cysts lined by theca cells (Table I). The fact remains, however, that when we remove the cystic portion of the ovaries which to all appearances are the same as those observed in patients with uterine bleeding, normal function is restored to the sex apparatus.

It is unlikely that polycystic ovaries are congenital for the condition develops as a rule after the patient has menstruated more or less regularly for a period of years. The amenorrhea is usually secondary. It is also unlikely, for reasons stated above, that the multiple cyst formation is explained on the basis of inflammatory change. That hormones play a rôle in the polycystic change in the ovaries is extremely plausible in the light of our present-day conception of sex physiology. Whether it results from an excessive production of anterior pituitary sex hormone or not is debatable.

It is reasonable to assume that a *mechanical* factor operates actually to produce the most significant symptoms, namely: amenorrhea and sterility. The overproduction of cystic follicles which crowd the ovarian cortex but which do not rupture on the surface of the ovary, together with the presence of a thickened tunic, prevents the immature follicles from ripening and reaching the surface. It is possible that some of these follicles develop, and being impeded in their pathway to the surface of the ovary, may rupture into the cysts. We have ob-

TABLE I. BILATERAL POLYCYSTIC OVARIES WITH AMENORRHEA. HISTOPATHOLOGIC FINDINGS

	TUNICA	STROMA	BLOOD VESSELS	NORMAL FOLLICLES	FOLLICLE CYSTS		CORPORA LUTEA	CORPORA ALBICANTIA	TUMOR
					THECA	GRANULOSA			
1	Thick		Tortuous Distended	Few	Many		Recent	Many, old	Early papillary cystadenoma
2	Thick				Many			Few, old, small	
3	Thick		Tortuous Thick		Many	Few		Few, small	
4	Normal to moderately thick		Tortuous Distended	One in section	Many			Many, small	
5	Moderately thick	Edematous Vascular	Hyperplasia		Many	Few	Recent with c.l. cyst	Large, recent	
6	Normal to moderately thick			Few	Many	Few	One, recent	Many	
7	Moderately thick	Vascular	Dilated		Many		c.l. cyst	Many	

served, in one of our sections, a normal maturing follicle just below and adjacent to a thin-walled theca cyst, so situated that if the follicle ruptured at all, its contained ovum would be discharged into the cyst cavity. This may account for the finding of small corpora lutea and albicantia even in the absence of menstruation. Ordinarily no corpora lutea would be formed unless the graafian follicles reached the surface of the ovary and ruptured. In further substantiation of the mechanical theory, we observed that by removing the cystic cortex which formed the barrier, physiologic function was restored. Apparently the incisional scar in the ovary is of no significance.

#### SUMMARY AND CONCLUSIONS

1. A series of seven cases is herewith reported in which amenorrhea was associated with the presence of bilateral polycystic ovaries.

2. Bilateral polycystic ovaries are most likely the result of hormonal influences and not the result of inflammatory change.

3. The diagnosis of ovarian pathology is greatly facilitated by the use of pneumoroentgenography.

4. The treatment of the amenorrhea with estrogenic hormone in the patients referred to proved unsatisfactory.

5. Surgical treatment, consisting of wedge-resection of the cystic cortex of the ovaries, was successful in completely restoring physiologic function. Menstruation in every instance became normal and remained so during the period of observation. Pregnancy followed in two patients.

6. It is our belief that a mechanical crowding of the cortex by cysts interferes with the progress of the normal graafian follicles to the surface of the ovary. This mechanical factor may account for the symptoms of amenorrhea and sterility.

7. Recurrence of the polycystic change in the ovary was not found in the follow-up examinations in any of the patients in this series.

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