

# GYNECOLOGY

---

## GENERAL PRINCIPLES

**Clinical Significance of Paraurethral Ducts and Glands.** John W. Huffman<sup>3</sup> (Northwestern Univ.) states that there are numerous ducts and epithelium-lined pockets with widespread branching of tubular channels and glands which surround the female urethra, mostly laterally and posteriorly, commonly limited to the distal half of the urethra, the terminal branches of which frequently extend cephalad for a considerable distance parallel to the urethral canal and may reach to within a few millimeters of the bladder. These paraurethral ducts terminate in branched tubular glands lined for the most part by columnar epithelium and containing occasional nests of mucus-secreting cells. Few large paraurethral ducts open into the proximal urethra; its mucosa, however, contains crypts and lacunae lined with columnar epithelium.

With the patient in the lithotomy position and the vulvar labia well separated, light digital pressure near the urethral meatus will cause the urethral labia to fall apart, exposing the orifices of the outermost paraurethral ducts (Fig. 50). Gentle pressure on the anterior vaginal wall beneath the outer third of the urethra may reveal inflammatory induration or thickening along the posterolateral ducts, pathognomonic of previous neisserian infection. Most lesions of the urethro-vaginal septum of a paraurethral origin can be detected during routine vaginal examination in the lithotomy position or in the Sims position with a Sims speculum to expose the anterior vaginal wall. Pressure along the urethra may express purulent material from the ducts somewhat as prostatic secretion is obtained in the male. Tumefactions are easily palpable, and a gush of seropurulent material from the meatus is strongly suggestive of urethral diverticulum.

---

(3) A. M. A. Arch. Surg. 62:615-626, May, 1951.

Infection of the paraurethral ducts invariably accompanies acute gonorrheal urethritis and may persist as an undiscovered source of reinfection during the later stages of the disease. These ducts and glands act as a nidus for chronic nonspecific urethritis and may harbor *Trichomonas vaginalis*. Examination of the material aspirated from the ducts may reveal trichomonads. Small suburethral abscesses, formed from periurethral glands, may rupture into the urethra, form-



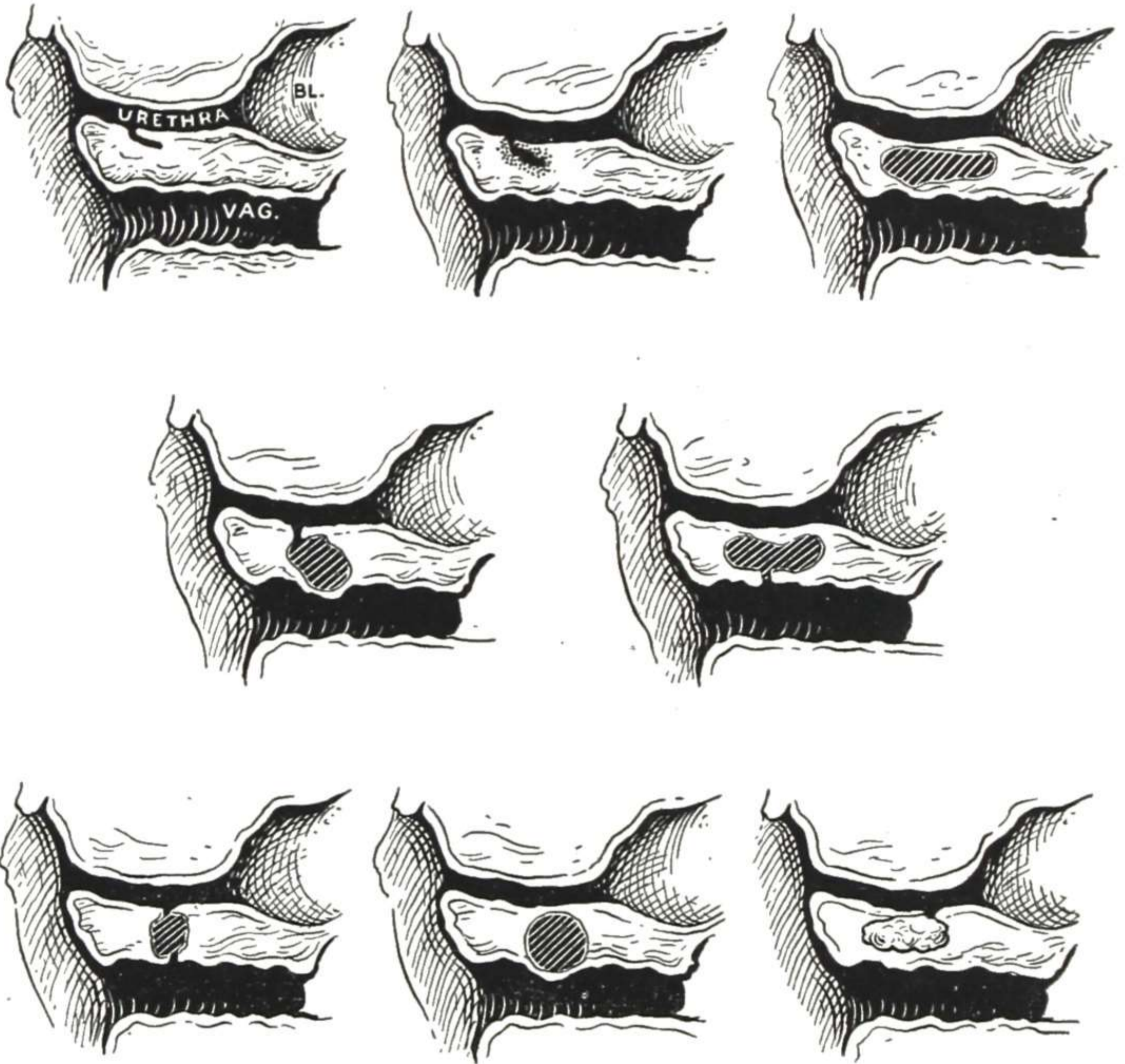
Fig. 50.—Pitlike depressions just within meatus indicate openings of larger paraurethral ducts. (Courtesy of Huffman, J. W.: *A. M. A. Arch. Surg.* 62:615-626, May, 1951.)

ing diverticuli. Cystic dilatation of the ducts is common and can be felt vaginally.

Adenomas and adenocarcinomas of the female urethra, both rare, originate in the paraurethral glands. Urethral caruncles do not develop from the paraurethral glands. Histologically, adenocarcinoma of the female urethra resembles prostatic carcinoma.

Acquired urethral diverticula arise from retention cysts of the paraurethral ducts which, as the result of suppuration or trauma, usually obstetric, rupture into the urethral lumen.

Congenital defects form few diverticula, and obstetric trauma alone would produce a urethrocele rather than a true diverticulum. A paraurethral duct abscess rupturing both into



- Fig. 51 (top left).—Normal paraurethral duct.  
 Fig. 52 (top center).—Infected duct.  
 Fig. 53 (top right).—Suburethral abscess (infected duct or duct abscess).  
 Fig. 54 (center left).—Urethral diverticulum (infected duct or paraurethral abscess ruptured into urethral).  
 Fig. 55 (center right).—Vaginal sinus (infected duct or abscess ruptured into vagina).  
 Fig. 56 (bottom left).—Urethrovaginal fistula (infected duct or abscess ruptured into both urethra and vagina, trauma to duct).  
 Fig. 57 (bottom center).—Anterior vaginal wall cysts (paraurethral duct cyst in urethrovaginal septum).  
 Fig. 58 (bottom right).—Urethral tumors of duct and gland origin.  
 (Courtesy of Huffman, J. W.: *A. M. A. Arch. Surg.* 62:615-626, May, 1951.)

the urethra and into the vagina may create a urethrovaginal fistulous tract (Figs. 51-58).

**Squamous Epithelium and Squamocolumnar Junction of Cervix during Pregnancy** were studied by D. N. Danforth<sup>4</sup>.

(4) *Am. J. Obst. & Gynec.* 60:985-999, November, 1950.

(Northwestern Univ.). Included in these observations were cervixes from 22 pregnant and 46 nonpregnant women; all specimens were obtained by complete hysterectomy for reasons other than cervical disease. For comparison of histologic findings in these two groups the thickness of the squamous

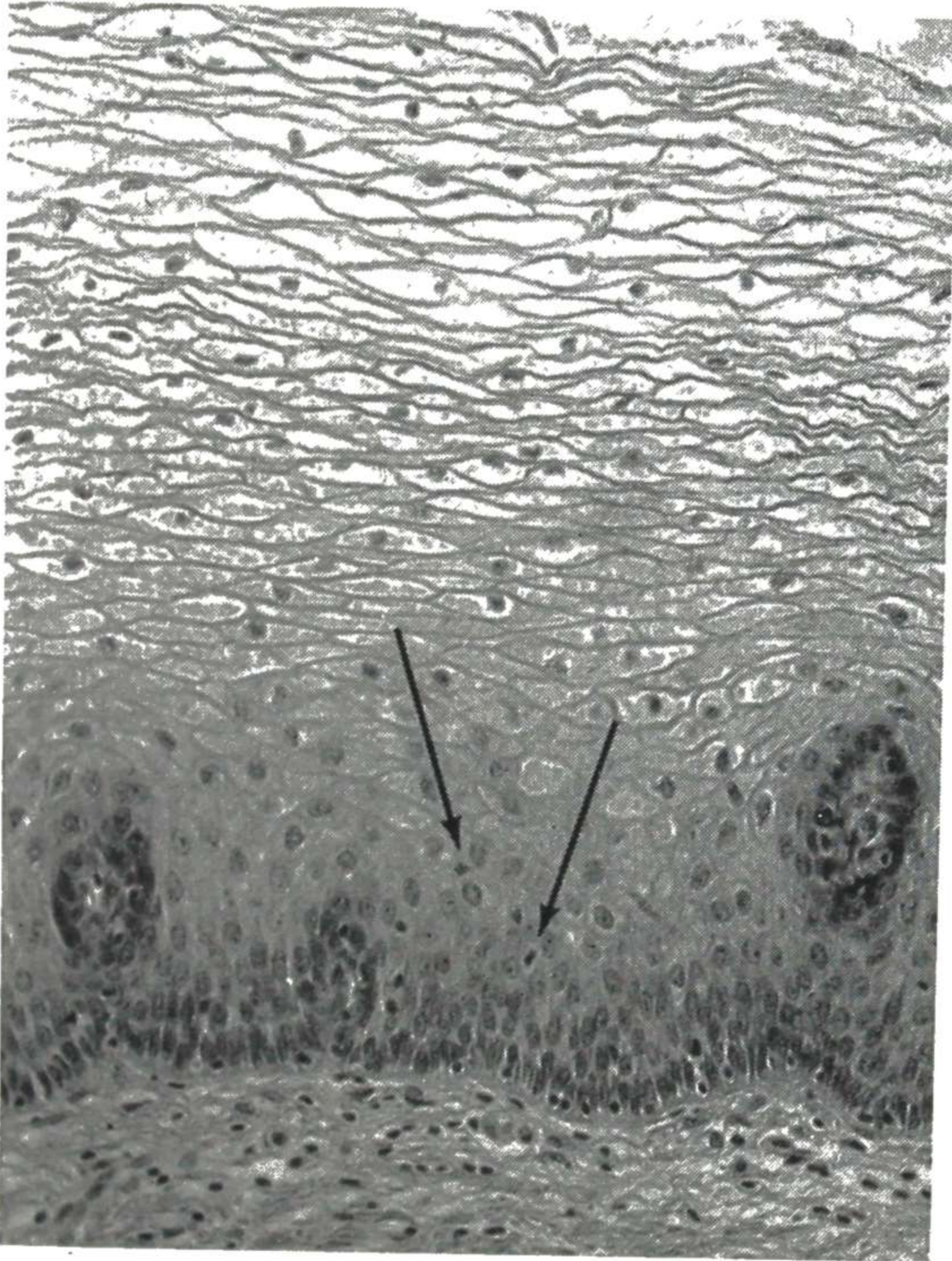


Fig. 59.—Squamous epithelium, showing two mitotic figures high in basal zone. Hematoxylin-eosin; reduced from  $\times 840$ . (Courtesy of Danforth, D. N.: *Am. J. Obst. & Gynec.* 60:985-999, November, 1950.)

epithelium was divided into three zones: basal, corresponding to the lower third; the midzone, or glycogen-containing portion, corresponding to the middle third, and superficial, comprising the upper third.

There was no evidence of malignancy, either invasive or intraepithelial, in any cervix studied. In the pregnant group particularly, deviations from normal tended to occur within



Fig. 60 (top).—Squamocolumnar junction, showing squamous metaplasia of columnar epithelium, with flattening of basal layer of cells of squamous epithelium. Mucicarmine;  $\times 350$ .

Fig. 61 (bottom).—Squamous metaplasia near squamocolumnar junction, showing considerable variation in nuclear size but good uniformity in staining reaction. Hematoxylin-eosin;  $\times 1,602$ .

(Courtesy of Danforth, D. N.: *Am. J. Obst. & Gynec.* 60:985-999, November, 1950.)

a radius of 5-6 mm. of the external os; the peripheral portions of the cervix generally conformed more strictly to the accepted normal.

No changes appeared in the pregnant group which could not be found also in the nonpregnant. However, slight to moderate irregularity in size, shape and staining quality of the basal zone nuclei was noted three times as often in the pregnant as in the nonpregnant group; mitotic figures were five times as frequent in the pregnant group and tended to appear higher in the basal zone (Fig. 59). Epithelial buds, or downgrowths into the underlying stroma, were twice as frequent in the pregnant group; multiple nucleoli and coarsely granular chromatin clumps were rare in the nonpregnant and frequent in the pregnant group; active nuclei in significant numbers were present in the midzone six times as frequently in the pregnant group; squamous metaplasia and subepithelial inflammatory reaction at the squamocolumnar junction were more than twice as frequent in the pregnant group (Figs. 60 and 61).

The hyperactive deviations noted in pregnancy, considered usually reversible, call for a conservative attitude toward equivocal or borderline cervical cancer. Regression of such suggestive lesions seems at least as possible as progression to frank malignancy and more probable in the pregnant than in the nonpregnant cervix.

[One statement in this important study should be emphasized, namely, that since the deviations observed in pregnancy are hyperactive ones considered to be for the most part reversible, one's attitude toward equivocal or borderline cervical cancer during pregnancy should be particularly conservative. I repeat this statement because some uteri have been removed after cervical cancer was diagnosed in pregnancy but no carcinoma was found when the cervix was examined postoperatively.—Ed.]

**A pH Study of Human Cervical Secretions** was made by Mary Alice B. Breckenridge, D. P. Pederson and W. T. Pommerenke<sup>5</sup> (Univ. of Rochester). Subjects were young, healthy women with normal pelvic structures and menstrual cycles. Sample collection was begun shortly after menstruation stopped and was continued as long as sufficient mucus was available. The pH of the last portion of mucus withdrawn was immediately determined by Beckman glass electrode or by hydrion indicator paper, pH range 4-9.

Cervical mucus was predominantly alkaline in all phases

(5). *Fertil. & Steril.* 1:427-434, September, 1950.

of the intermenstrual cycle, as determined through 63 cycles. Three types of pH cycles were encountered: (1) small fluctuations in the alkaline range in 59 per cent; (2) occasional acid samples in a predominantly alkaline cycle in 17 per cent; (3) wide fluctuations throughout the cycle in 24 per cent. There was no consistent variation referable to amount of secretion or phase of menstrual cycle. Mucus collected near the cervical os had a lower pH in all phases of the cycle than that farther up the cervical canal. The intracervical pH, measured through 10 cycles by a specially designed instrument, fell within a narrow, low alkaline range of 7.0-7.5 in 83 per cent of determinations. A second mucus specimen was collected from subjects in the ovulatory phase several hours after initial evacuation of the cervical canal. In 7 of 10 instances, pH was higher in the second than at first aspiration. This fact may explain certain cases of infertility in apparently normal women.

**Observations on Symptomatology and Treatment of Cervical Erosion.** Jean R. W. Ross<sup>6</sup> analyzed 128 of 870 cases of cervical erosion treated with electric thermocautery and followed 6-24 months. Complications after cauterization in the entire group are reviewed. Most common symptoms were leukorrhoea, backache in the lumbosacral region, abdominal pain and dysuria; others included menorrhagia, pruritus vulvae, dysmenorrhoea, dyspareunia, cervical hemorrhage, sterility and a sense of pelvic weakness simulating prolapse. Many patients also complained of general fatigue and listlessness.

Treatment by cervical cauterization in the outpatient department, without anesthesia or preliminary dilatation, was usually satisfactory. There were cures in 99.2 per cent of the 128 cases, 109 six weeks after the first treatment, 17 after two treatments and one after the third, with only six recurrences (4.7 per cent) in the follow-up period. Serious complications followed cauterization in only 0.7 per cent of the 870 cases. Although mild secondary hemorrhage from the cauterized area was common, only two patients experienced bleeding severe enough for hospitalization. There were one case of pelvic cellulitis, one of acute exacerbation of chronic salpingitis and two of atresia of the cervical canal.

(6) Brit. M. J. 2:647-650, Sept. 16, 1950.

Failure in discovery and treatment of cervical erosion, the cause of many gynecologic complaints, often results from failure to appreciate the symptoms. Common teaching that lower abdominal pain in the right or left iliac fossa is ovarian in origin is unsound; more often such pain is due to cervical erosion.

**Effect of Incubation on Sugar Concentration of Cervical Mucus.** Indications are that spermatozoa utilize sugar, largely glycogen, as nutriment. W. T. Pommerenke and Edith M. Lipphardt<sup>7</sup> (Univ. of Rochester), in attempting to show that a function of the sugars in cervical mucus might be to provide this nutriment, noted a spontaneous reduction of sugars when the mucus was incubated. To determine the extent to which spermatozoa utilize these sugars it seemed necessary to quantitate this reduction.

In nine healthy normal subjects an unlubricated speculum was introduced and mucus aspirated into glass cannulas. The quantity obtainable varies, being most abundant at the ovulatory phase and often scanty just before and after menstruation, when division of single specimens into aliquots would be impractical. This is especially true since cervical mucus is not homogeneous. Therefore entire single specimens collected not more than once in 24 hours were used. Specimens to be incubated were weighed, stored over water in closed containers for 24 hours at room temperature, then analyzed. Fresh specimens and those to be incubated were collected on alternate days when possible so that they would be as nearly alike as possible. Somogyi's modification of the Shaffer-Hartman copper reagent was used for acid hydrolysis which reduces polysaccharides, including glycogen. Products of hydrolysis plus free-reducing substances native to the mucus constitute total reducing substance expressed as milligrams per cent of glucose.

Analysis of 276 specimens from the nine subjects during 31 separate menstrual cycles disclosed a distinct fall in sugar content after incubation. Loss was 16.5 per cent in the pre-ovulatory, 31.6 per cent in the ovulatory and 20.7 per cent in the postovulatory phase. Though the reason for this fall is unknown, it may be due to enzyme action, with bacteria of the vagina and/or cervix possibly playing a role.

(7) *Fertil. & Steril.* 1:423-426, Sept.-Oct., 1950.



**Urologic Aspects of Gynecology.** According to R. W. Te Linde<sup>8</sup> (Johns Hopkins Univ.), the well trained gynecologist should be grounded in the gynecologic and obstetric aspects of urology. The generative and urologic systems are closely related anatomically, and carcinoma, tuberculosis and gonorrhea readily cross the boundary lines. Malignant tumors of the generative organs, especially cervical carcinoma, eventually involve the ureters. This involvement is of prognostic significance in that the commonest cause of death in cervical carcinoma is the resulting renal insufficiency. In 50 of 100 patients with benign pelvic conditions, there was demonstrable upper urinary tract dilatation as a result of inadequate drainage due to pressure of the pelvic tumor or displacement and kinking of the ureter from uterine prolapse. Only in uncomplicated cystocele is there no interference with ureteral drainage. Often, if the upper urinary tract were investigated in patients with fibroid, it would be found that the fibroid, although asymptomatic, is giving rise to ureteral compression and therefore should be removed. Indeed, this may be the explanation of the "myoma heart" of the earlier literature. Furthermore, the high incidence of ureteral dilatation with large fibroids and ovarian tumors indicates how often they impinge directly on the ureters. Catheterization of one or both ureters is recommended before removal of these tumors so as to reduce ureteral injury. In 26 per cent of the patients with benign tumor, actual urinary tract infection was present.

Pregnancy also causes dilatation of the ureters. Te Linde bases his belief that this is due to pressure also and is not hormonal, as some suppose, on the fact that a patient with a horseshoe kidney located at the brim of the pelvis failed to show dilatation of the ureters in a urogram at any time during pregnancy.

Damage to the urinary tract by irradiation may give rise to ulcerative cystitis characterized by dysuria and frequency, even though the patient is cured of malignancy. It sometimes leads to interference with drainage, followed by destruction of kidney function. Although evidence of postirradiation urinary tract involvement was found in 50-55 per cent of patients with cervical cancer, obstruction was of serious clinical significance in only 15-20 per cent.

(8) *Am. J. Obst. & Gynec.* 60:273-284, August, 1950.

A urethral diverticulum can be successfully treated by excision and closure of the defect; urine can be diverted through a surgical vesicovaginal fistula temporarily if necessary. Stress incontinence can usually be treated successfully by a modification of Kelly's technic, with mattress sutures to plicate the full length of the urethra; fascia can be brought together beneath the urethra for support in case of urethrocele. In a small group of cases, however, a fascial sling operation such as the Aldridge modification of the Goebell-Stoeckel operation is necessary. Vesicovaginal fistula, most commonly found at the vaginal apex after total hysterectomy, can be closed effectively by the Latzko partial colpocleisis.

Injured ureters are usually repaired by ureteroureteral anastomosis over a ureteral catheter, but if the injury is near the bladder, the ureter is usually implanted in the bladder. If the injury is not suspected until the postoperative period, postponement of further operation for six weeks is desirable if possible; an interim nephrostomy or pyelostomy may be performed if necessary. Nephrectomy represents a defeatist attitude and can usually be avoided.

[It is well known that disturbances in the urethra, bladder, ureters and kidneys may produce signs and symptoms suggesting trouble in the uterus, tubes or ovaries, and vice versa. The chief reason for frequent association of disturbances in the genital and urinary tracts is the close proximity of both the organs and their vascular, lymphatic and nerve supplies. Urinary symptoms caused solely by pathologic conditions of the generative organs are present in about 25 per cent of gynecologic patients, and about 20 per cent of patients with urologic disturbances have concomitant gynecologic symptoms or pathologic conditions.

Changes in the generative tract most often responsible for urinary tract symptoms are pregnancy, adnexal inflammation with or without masses, pelvic neoplasms, uterine displacement, childbirth lacerations and chronic cervicitis. Urinary tract disturbances which produce symptoms in the genitalia are urethritis, urethral stricture, ureteritis, ureteral stone, utereteral stricture, ectopic ureter and ectopic kidney.

There is a close relation between benign and malignant pelvic lesions and obstruction of the ureters. Long and Montgomery (*Am. J. Obst. & Gynec.* 59:552, March, 1950) found that 49.4 per cent of 379 women with extensive pelvic lesions had ureteral obstruction, the incidence of urinary tract obstruction in the various gynecologic conditions being: malignant ovarian tumors, 69.2 per cent; benign ovarian tumors, 57.8 per cent; cervical carcinoma, 53.4 per cent; pelvic inflammatory disease, 48.9 per cent; uterine fibromyoma, 47.5 per cent; cystocele and prolapse of the uterus, 37.9 per cent, and adenocarcinoma of the corpus, 31.2 per cent. Extensive changes may be present in the urinary tract without producing symptoms; hence, there should be preoperative investigation of the urinary tract in all women with extensive pelvic disease, certainly in those with suspected or definite malignant disease. The urinary tract must

be studied without fail before a radical hysterectomy is contemplated for carcinoma of the cervix.—Ed.]

**Practical Application of Psychology in Gynecic Practice** is discussed by Willard R. Cooke<sup>9</sup> (Univ. of Texas). The old-time doctor was a successful psychotherapist; he was to patients the epitome of wisdom and the unquestioned counselor. Factors destroying this doctor-patient relation have been "education of the public" in medical matters and the trend toward impersonal, assembly line dogmatism and manner. Intelligent psychotherapy is an important factor in every female patient.

Initial greeting of the patient should be friendly but not familiar; pleasant but not facetious; dignified but not stilted, and above all, natural and not affected. Simple questions such as, "What's on your mind? Now, what's it all about?" relax the patient. Letting the patient tell her own story puts her at ease and creates the impression of interest in her as an individual. Abrupt firing of questions couched in medical terms, coupled with contempt toward the patient's story, and interruption of anything but direct answers may result in antagonism and an inaccurate history. History should be completed before the pelvic examination is done. Patients appreciate recognition of their dislike of this examination.

The method of breaking bad news must be suited to the individual. The patient or a responsible relative deserves an accurate statement, preferably written, of diagnosis, treatment or operation.

Many brilliant diagnoses and successful operations are completely nullified because the physician does not convince the patient that the talebearing of other women is false and based on ignorance.

Psychotherapy has not succeeded in dysmenorrhea except in cases wholly psychic in origin. Minor menstrual disorders, unless they are symptoms of a causative lesion or bleeding is excessive, are treated effectively by psychotherapy. In primary and secondary frigidity and pregnophobia, reassurances and explanations may be effective. Psychotherapy is rarely beneficial in extreme tokophobia. Inhibition of labor, however, may be overcome by the substitution of a greater fear. Sedation and psychotherapy are effective for hyperemesis.

(9) Nebraska M. J. 35:371-376, December, 1950.

As far as female tradition and sadism are concerned, the "menopause" is more horrible than operations or childbearing. Unfortunately many physicians make the "menopause" a diagnostic carryall for any and all forms of functional disturbances and even unrelated psychoneuroses.

[In gynecology more and more attention is being paid to functional disturbances and to the psychosomatic aspects, and with good reason. In a large proportion of women their symptoms depend greatly on disturbances in the psyche. It requires a tactful and sympathetic physician to ferret out the basis of the trouble in many women, but it is remarkable how quickly women will talk freely to a physician when they believe that he is sympathetic. When the physician gives the patient sufficient time to unburden herself, he will learn a great deal which will aid not only in diagnosis but in therapy. In most cases the physician himself is psychologist and psychiatrist enough to be of great help. It is the exceptional woman who requires a physician trained in psychiatry or psychoanalysis.

Strassmann (*Am. J. Obst. & Gynec.* 60:783, October, 1950) stressed the association of the constitutional psychology and the reproductive system in women. Knowledge of background and heredity is of great importance in handling individual patients. Formerly, the family physician acquired this faculty through his daily contacts. The modern specialist is deprived of this advantage and must replace it by a good working knowledge of constitutional psychology. Analysis of every patient on a basis of physique, temperament and intelligence not only adds color to the sometimes monotonous daily practice but leads to better understanding and results.—Ed.]

**Functional Disturbances Encountered in Gynecic Practice** are discussed by Willard R. Cooke<sup>1</sup> (Univ. of Texas). Dysmenorrhea, a symptom of underlying dysfunction or disease, is manifested in four distinct types. The myometrial type, characterized by severe suprapubic pain, is caused by painful hypercontraction of muscle. The congestive type, a vague and aching pelvic or sacral pain, originates in the walls of overdistended vessels. The ovarian type is localized to the viscerosensory area of pain reflex from the ovary, situated 2-3 cm. below and mesial to McBurney's point on each side. The peritoneal type, a deep-seated acute pain, is caused by peritoneal irritation. The psychoneurotic type is manifested by exaggeration or imitation of any of the definite types or, more characteristically, by vague and bizarre localization.

Most effective treatment (85 per cent) for myometrial dysmenorrhea is suppression of ovulation by 1 mg. diethylstilbestrol daily for 20 days in each cycle starting preferably the fourth day of bleeding. Disadvantages include temporary sterility, acyclic bleeding and occasionally nausea. Dilata-

(1) *Nebraska M. J.* 35:275-282, September, 1950.

tion of the cervix is sometimes effective. In refractory cases presacral neurectomy is indicated. Any psychoneurotic element must be eliminated or reduced.

In the congestive type the underlying cause must be corrected. A physically fit woman rarely has congestive dysmenorrhea. Ovarian dysmenorrhea is cured only by division of the ovarian nerves. The peritoneal type requires oophorectomy or radiation castration; that due to endometriosis is controlled by massive ascending dosage of diethylstilbestrol.

Primary polymenorrhea is usually associated with developmental retardation, anovulation or infertility. Secondary polymenorrhea suggests anovulation, hyperestrinism or follicle cyst, with temporary sterility. It occurs mostly between 18 and 35 and responds readily to 1 gr. thyroid daily for six months. In women past 40, radiation castration may be justifiable. Determination of whether ovulation occurs in the menstrual pattern is most important.

In menorrhagia the first essential is determination of cause, whether (1) purely functional, (2) caused by disease in the uterus, adnexa or elsewhere, or (3) functional but coincidental with a nonetiologic disease. Functional menorrhagia is most common before 18, in the late twenties and thirties and after 35. The second group responds to ergotrate every three hours to a maximum dosage of 30 tablets for immediate control of bleeding, and 1 gr. thyroid daily for at least six months to correct the underlying cause. If there is no response to ergotrate, bleeding may be controlled by massive doses of diethylstilbestrol (25-100 mg. or more daily) or by testosterone given daily for not longer than three months, with maximal dosage 350 mg./month. If medical therapy fails or bleeding requires immediate control, curettage is indicated, with endometrium as completely removed as possible. Hormonal therapy must be continued after curettage. With continued resistance, hysterectomy and subcastrative irradiation must be considered. After 35, thyroid becomes decreasingly effective, and testosterone or massive dosage of diethylstilbestrol is required. In young adolescents, massive doses of progesterone may be of value.

Metrorrhagia always indicates careful search for possible malignancy. Estrus bleeding is diagnosed readily from basal temperature records.

Gynecologic dysfunctions and dysplasias may result from disturbances of the pituitary, hypothalamus, pineal, adrenal cortex or thyroid. Exploration of the gonads and adrenals in cases of hemaphroditism is a matter of judgment. Precocity, defeminization, masculinization and obesity are difficult problems. The only generalization that can be made is that definite masculinization usually indicates adrenal disturbances, ectopic adrenal tissue or masculinizing ovarian tumors.

**Clinical Specificity of Vulvar Fluorescence.** McDonald and Margolese reported that irradiation of the vulva with about 3,650 A. near ultraviolet resulted in luminescence unique to this area. Ralph C. Benson, Louis A. Strait and Clifford C. Chappell<sup>2</sup> (Univ. of California) studied vulvar fluorescence in 103 obstetric or gynecologic patients exposed to conventional and filtered ultraviolet light. Some patients were viewed over consecutive days or weeks and variations of original colors noted. A correlation between colors of vulvar fluorescence and functional status of the patient was formulated.

A relation was found between the patient's functional status and six colors: deep purple, purple, green, yellow, brown and red. Deep purple vulvar fluorescence was usually seen in pregnant women. A much less specific purple was often apparent in incomplete abortion or dysfunctional uterine bleeding during functional years. Green and yellow occurred during the puerperium and in menopausal states. Brown was seen in postmenopausal women not treated with estrogens. Vivid red was nearly always observed with even slightly extended clinical vaginal bleeding. Red was on the surface and could be wiped away, in contrast with other colors which were in the tissues. Deep purple, brown and red seemed highly specific when checked against the clinical history of pregnancy, postmenopause and clinical vaginal bleeding respectively. Also significant was absence of deep purple in abortions of uncertain status. Fading deep purple was usually followed by fetal loss. Purple, however, could not be linked with hyperestrogen or normal estrogen states or to progesterone effect. Green and yellow to brown seen in the patient not recently gravid was suggestive of hypoestrinism. Administration of estrogen and/or progesterone caused reappearance of purple in postmenopausal women.

(2) Surg., Gynec. & Obst. 92:14-21, January, 1951.

Reflection of all visible purple was eliminated by use of a specially designed filter which excluded all significant wavelengths above 3,650 A. Intensity of the six colors was reduced but they were not eliminated. Preliminary studies with a new viewing filter indicate that nonsuperficial colors do not arise from luminescence due to intrinsic hormonal properties or content of vulvar tissue. They are probably the result of general tissue luminescence modified by the physical nature and selective optical properties of vulvar tissue. Superficial vascularity and physical nature of this tissue seem important.

---

## DIAGNOSIS

**Hysterography and Hysterosalpingography: Analysis of 2,500 Cases with Special Emphasis on Technic and Safety of Procedure** was made by Richard H. Marshak, Charles S. Poole and Morris A. Goldberger<sup>3</sup> (Mount Sinai Hosp., New York City). Indications for uterosalpingography were menometrorrhagia, dysmenorrhea, sterility, fibroid uterus and postmenopausal bleeding. Contraindications were pelvic inflammatory disease with increased sedimentation rate, increased white cell count or fever; intrauterine pregnancy and purulent vaginal discharge, and serious constitutional disease. Contrast mediums used were lipiodol,<sup>®</sup> diodrast,<sup>®</sup> skiodan<sup>®</sup> acacia, hippuran,<sup>®</sup> visco-rayopaque and iodochloral. Optimal time for the procedure is one week after cessation of menstruation.

**TECHNIC.**—With the patient on an x-ray table equipped with Bucky diaphragms, bimanual examination is performed and a preliminary abdominal film taken. The patient is placed in the lithotomy position, and the cervix is exposed and painted with antiseptic. A uterine sound is introduced to determine direction and depth of the uterine cavity. The medium is then introduced slowly and gently through a cannula. In hysterography, 1 cc. dye is injected and a film taken; fractional amounts of dye up to 3-4 cc. are introduced and films taken at each injection. If obstruction is encountered, injection is discontinued. A film taken in the oblique position facilitates interpretation of filling defects in the uterine cavity and demonstrates lesions on the posterior uterine wall. The uterine cavity and tubes can be visualized in 95 per cent of sterile patients with 6 cc.

(3) Surg., Gynec. & Obst. 91:182-192, August, 1950.

dye and minimal pressure. Larger amounts of dye are necessary in the presence of an enlarged uterine cavity or large hydrosalpinx.

The technic in uterosalpingography depends on whether a water-soluble or oily medium is used. Injection of lipiodol<sup>®</sup> is discontinued when there is obstruction to flow of a dye at a pressure of 200 mm. Hg. With a water-soluble medium, pressures up to 250 mm. Hg may be used since intravascular penetration followed by embolization cannot occur. Dye must reach the peritoneal cavity because a delayed film cannot be taken due to rapid absorption.

Complications due to contrast mediums are not serious or permanent. There is pain when a water-soluble medium enters the peritoneal cavity and tubes. This can be adequately controlled with demerol.<sup>®</sup> Quickly absorbing mediums do not damage tissue and embolization does not occur. In this series there were no instances of permanent injury to the tubes or embolization due to lipiodol,<sup>®</sup> although these complications have been reported. Instances of allergic phenomena were few. Complications from the procedure itself are rare. There were two cases of hemorrhage, one of short duration which required no therapy and one which was the fault of technic and the condition present. Pelvic inflammatory disease occurred seven times, but always in patients with previous history of the disease. The uterus was accidentally perforated once. Although two patients with unsuspected pregnancies had uterosalpingograms for sterility, both delivered normal infants at term. The relatively infrequent complications and safety of the procedure are such that there should be no hesitation in its use when indicated.

[There is no doubt that hystero-graphy will reveal not only the shape and size of the uterine cavity but pathologic conditions such as polyps, submucous myomas, carcinoma and tuberculosis. In fact, some gynecologists prefer hystero-graphy to curettage in diagnosing carcinoma of the endometrium. I do not agree with this.

Marshak, Goldberger and Epstein (Radiology 55:725, November, 1950) report three cases in which curettage done because of abnormal bleeding showed no evidence of tumor within the uterine cavity. Subsequent hystero-graphs, however, revealed a submucous tumor in each case. The failure of the curettage to reveal a tumor is explainable, since the submucous fibroid occupied the entire uterine cavity and formed a false smooth wall which could not be differentiated from the normal uterine wall by the operator.—Ed.]

**Hysterosalpingography: Its Dangers and Their Prevention.** Dangers are tissue reaction to the medium, introduction or spreading of infection and embolism. James L. Royals, Carlton N. Price and Paul Titus<sup>4</sup> (St. Margaret Memorial

(4) Postgrad. Med. 8:363-367, November, 1950.



Hosp., Pittsburgh) give these precautions against complications. (1) Incidence of performance should be reduced. Hysterosalpingography should be done only on actual indications and not as often as tubal insufflation. (2) Damage to integrity of the tissues by preliminary dilatation of the cervix, curettage and undue force or pressure in introducing the opaque medium must be avoided. Smooth metal or rubber-tipped can-

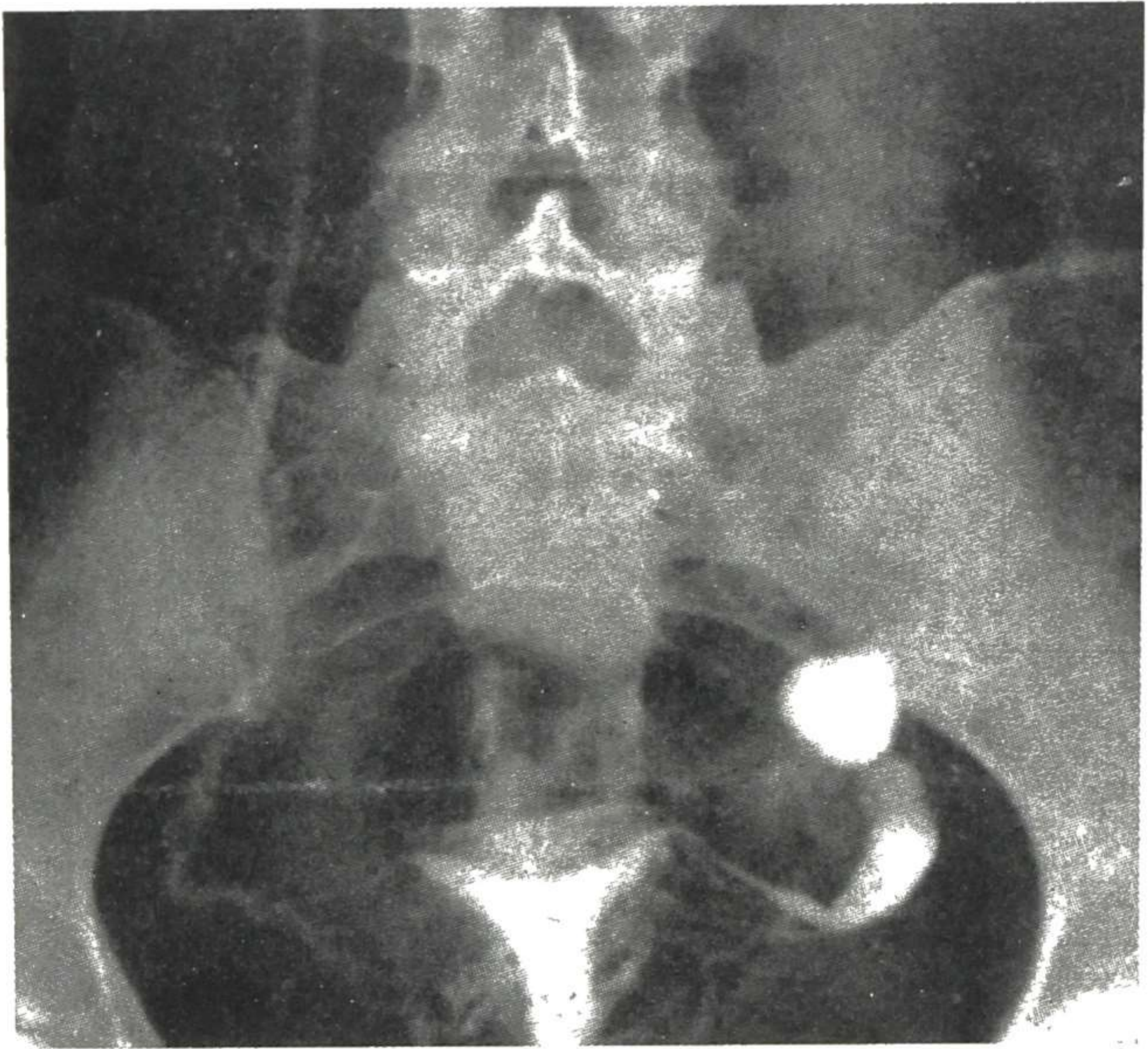


Fig. 62.—Venogram of uterus and right ovarian vein after accidental intravasation with skiodan® acacia. (Courtesy of Royals, J. L., *et al.*: *Postgrad. Med.* 8:363-367, November, 1950.)

nulas are preferable to those with screw-threaded tips. (3) The least irritating radiopaque mediums should be used and nonabsorbable oil-based mediums, which have caused severe reaction and even death, avoided.

Skiodan® acacia, a nonoily radiopaque medium with a viscosity identical with that of lipiodol® at body temperature, is the medium of choice. It is rapidly absorbed and eliminated within 72 hours. So far, mild urticaria, probably due to sensitivity to acacia, has been the outstanding ill effect. A recent x-ray, taken after the third fractional injection of skiodan®

acacia, showed veins of the entire uterus and of the right ovary (Fig. 62). Another film taken 20 minutes later revealed no skiodan® in uterus or veins and only a residue in a clubbed tube. Patient had no untoward effects except transitory urticaria.

[To the dangers of iodized oil injections into the uterus listed here I should like to add peritoneal reactions with pain, pelvic abscess, foreign body reaction, endometriosis, ectopic pregnancy, accidental vascular injection, rupture of the tube and even death. I fully agree with the authors that hysterosalpingography should be used only after a Rubin test has shown closed tubes.

Among 328 women who became pregnant after hysterosalpingography had been performed by Schultze (*Geburtsh. u. Frauenh.* 9:454, 1949), 198 were primarily sterile. Results of the pregnancies were: full term, 241; abortion, 33; ectopic, 15; no information, 39. The 5 per cent incidence of ectopic pregnancies following hysterosalpingography is very high.

Rosset (*Am. J. Obst. & Gynec.* 60:892, October, 1950) gave 25 patients the Speck phenolsulfonphthalein test and found only 14 results correctly correlated with the actual condition of the tubes. The author believes the PSP tubal patency test has limited value because of the indefinite color and points and the ability of some dilated, blocked and diseased tubes to absorb the testing material.

Alvarez Bravo (*Estud. esteril.* 1:50, January, 1950) reports on 586 sterile women, of whom 37.7 per cent had primary or secondary ovarian dysfunction. Among the latter 221 women, 87 (39.3 per cent) did not ovulate. Bravo employed four chief methods of therapy: production of cycles by ovarian steroids and by gonadotrophins; use of thyroid preparations, and pituitary irradiation. The ovarian steroids produced a high percentage of success. The gonadotrophins are dangerous and therefore should not be used. The good results obtained with thyroid require no explanation. Irradiation of the pituitary is useful but should be used only as a last resort.

Frank (*Am. J. Obst. & Gynec.* 60:645, September, 1950) studied 240 infertile couples. Pregnancy occurred in 26.1 per cent. Factors responsible for success in this series are believed to be (1) thorough study, (2) detailed instruction on utilization of the fertile period and improvement of sex habits, and (3) judicious use of thyroid extract.

Minimal procedures for the evaluation of the barren marriage are listed in *Fertility and Sterility* (2:1, January, 1951). The procedures were prepared by the Research Correlating Committee of the American Society for the Study of Sterility. They should be read by everyone interested in the subject of sterility.—Ed.]

**Uterotubal Studies Using Lipiodol.®** John C. Brougher<sup>5</sup> (Vancouver, Wash.) performed 501 hysterosalpingographies without death or serious complications. A few patients had cramps and nausea which subsided with heat and rest within 24 hours, but none had abdominal tenderness or fever. Two with chronic salpingitis had recurrence of pelvic inflammatory symptoms which required operation.

Visualization of the uterine cavity and tubes gave essen-

(5) *J. Internat. Coll. Surgeons* 14:603-607, November, 1950.

tial evidence of structural and organic defects. Tubal obstruction, uterine malformation and defects caused by tumors were demonstrated. Developmental defects such as bicornate uterus and uterus didelphys were observed, as well as salpingitis isthmica nodosum, hydrosalpinx and tuberculous pyosalpinx. Pathology of the cervix was studied. Although oil injections are of value in differential diagnosis of irritable colon, chronic appendicitis and chronic salpingitis, in diagnosis of uterine disease in obese patients and dysmenorrhea, and in tracing the cause of repeated abortions, their chief value has been in treatment of sterility. In this series percentage of pregnancies after successful opening of occluded tubes in sterile patients was 28 per cent.

**Hysterosalpingography in Study of Sterility.** Albert W. Holman<sup>6</sup> (Portland, Ore.) discusses two types of the many abnormal changes which may be diagnosed by uterotubal x-ray using the short-tipped, all metal cannula, juvenile uterus and abnormalities in the cervical canal. In an hysterosalpingogram the immature uterus is characterized by an abnormally long, conical or tubular cervix. Over-all length of the organ is often the same or longer than that of the average mature uterus, but the proportion of cervix to body varies. Length of the cervix is at least three times that of the body. Abnormalities in the cervical canal, such as obstructing weblike bands, hyperplasia of cervical mucosa and cervical strictures, are easily seen in an hysterosalpingogram.

Hysterosalpingograms of 350 women whose primary complaint was sterility revealed evidence in 86 of polyps, thickening of cervical mucosa or cervical strictures or stenoses. The fallopian tubes were diseased or absent in 75. X-ray evidence of juvenile uterus was found in 19. One patient often had two or more of these changes. Adjunctive treatment of sterility was performed when indicated and possible. Of 152 patients suitable for therapy, 93 had supplementary treatment; of these, 56 became pregnant after intrauterine injection of iodized oil. Dilation and, when indicated, curettage were performed on 36 patients with x-ray evidence of cervical obstruction. Fifteen became pregnant shortly after operation. Seventeen patients were treated for immature uterus. The 3 women treated with large doses of diethylstilbestrol became

(6) West. J. Surg. 58:523-534, October, 1950.

pregnant, whereas only 2 of the remaining 14 became pregnant without diethylstilbestrol therapy. A total of 82 women became pregnant, 53.6 per cent of those treated. This illustrates the value of hysterosalpingography in diagnosis and treatment of sterility.

[In all cases of sterility, I prefer to test the tubes first by means of the Rubin test using carbon dioxide. If I find the tubes closed after two Rubin tests, I then resort to hysterosalpingography. Occasionally one finds that tubes that seemed to be closed when the carbon dioxide gas was used are patent when iodized oil is injected into the uterus and a hystero-gram is made.

White (Brit. J. Med. 2:336, Feb. 17, 1951) emphasizes that it is not well enough recognized that the kymograph does not always depict the true state of the fallopian tubes when tubal patency is studied. Patency of the fimbrial lumens may be diagnosed when such is not the case. There seems to be no certain way of avoiding the occasional misdiagnosis of patency in some patients with terminal tubal occlusion but no distention. Shoulder pain following insufflation is not inevitable, for it is experienced by some women when nonpatency is confirmed. When hydrosalpinx does not exist there is no means of recognizing closure of the tubes. A hollow sound on insufflation and bilateral pelvic pain are suggestive, but a diagnosis can be made only from salpingograms.—Ed.]

**Some New Ideas on Tubal Kymographic Insufflation** are discussed by Louis Bonnet<sup>7</sup> (Paris). He considers those tubes stenosed which present a diminished opening, either due to internal causes (mucosal lesions) or to external causes (peritubal adhesions, torsion, bending, etc.).

Examination is begun by opening the cock of the gas intake and starting with a flow of 30 cc./minute. A pressure rise is registered (solid line on the tracing rising obliquely) until opening of the uterotubal orifices takes place. This opening pressure is generally higher when stenosis is present. With normal tubes it is from this point that the oscillations signifying rhythmic contractions of the tubes are registered. With impermeable tubes the pressure continues to rise regularly until the gas is cut off. As soon as the gas begins to pass through the uterotubal orifices, a change in direction is observed in the tracing. It becomes more oblique and forms an angle ( $\alpha$ ) with the prolongation of the first part of the tracing; the angle is greater as the stenosis is more extensive. In a certain number of cases, before the tracing changes direction, a slight fall in pressure is registered, which in the absence of escape of gas at the neck indicates that the stenosis is situated at the level of the pavilion of the tube (the gas

(7) Gynec prat. 1:317-327, 1950.

suddenly finds a new cavity to fill). On continuing the examination the new tracing curves in on itself more or less rapidly and becomes paraboloid, although it may become practically horizontal.

If the stenosis is relatively small in relation to the flow used, the tracing soon ends with a horizontal line corresponding to the "phase of equivalence." Where the opening is relatively narrow, the tracing cannot register a horizontal line within the limits of the graph. Two new maneuvers will then confirm passage of a small quantity of gas.

The gas is cut off when the pressure reaches about 200-250 mm. (250 mm. is the maximum). With complete tubal impermeability a horizontal line is registered, but here, as the gas contained in the uterotubal cavity continues to escape, a fall of pressure is registered, more rapid if the opening is wider. The initial part of this new segment of tracing forms an angle ( $\beta$ ) with the horizontal line. Before the pressure falls to the degree of opening of the uterotubal orifices the gas is again turned on, and by regulating the cock controlling the flow a certain flow (less than the initial flow) is immediately found with which the horizontal line indicating the "phase of equivalence" is registered.

To measure the caliber of tubal openings, Bonnet tests the pressure in the cylindric tube of the apparatus against the reading taken clinically, since the tube of the apparatus has a more regular diameter. Three elements of the tracing can be used for this purpose. (1) The angle  $\alpha$  is less definite because it is relatively small. (2) The angle  $\beta$  is more interesting as it diminishes with the leveling of pressure. Thus, when the clinical tracing is compared with a series registered by artificial calibrated openings, diameter can be measured in hundredths of a millimeter. (3) The "phase of equivalence" tracing is most useful since it permits measurement to a thousandth of a millimeter.

The diameter of stenosed tubes varies from 50 to 150  $\mu$ , a small opening being 50-90, medium 90-130 and large over 130. Such measurements are of great importance, e.g., to record improvement during insufflation or after diathermy.

For spasm, Bonnet used papaverine and synthetic antispasmodic agents. In only 3 of 17 patients was permeability improved, with registration of small oscillations in 1 at the

end of the examination. This indicates that in most patients the cause of stenosis is organic rather than functional. Diathermy, especially short wave, gives better results than anti-spasmodic agents.

The diameter of normal tubes was found to be 230-500  $\mu$ . This explains why an ovum 200  $\mu$  in diameter can pass through a normal tube but not through a stenosed tube.

[This experimental and clinical study is a step forward in the use of the Rubin test. After determination of the amount of stenosis by Bonnet's method it may be possible to overcome the stenosis in some cases by experimenting with antispasmodics and other therapeutic measures.—Ed.]

**Pressure-Trol, New Safety Device for Use in Uterotubal Insufflation**, evolved by Abner I. Weisman and John L. Marco<sup>8</sup> (New York City), is a simple escape valve which can be hooked into any insufflation system (Fig. 63). Maximal

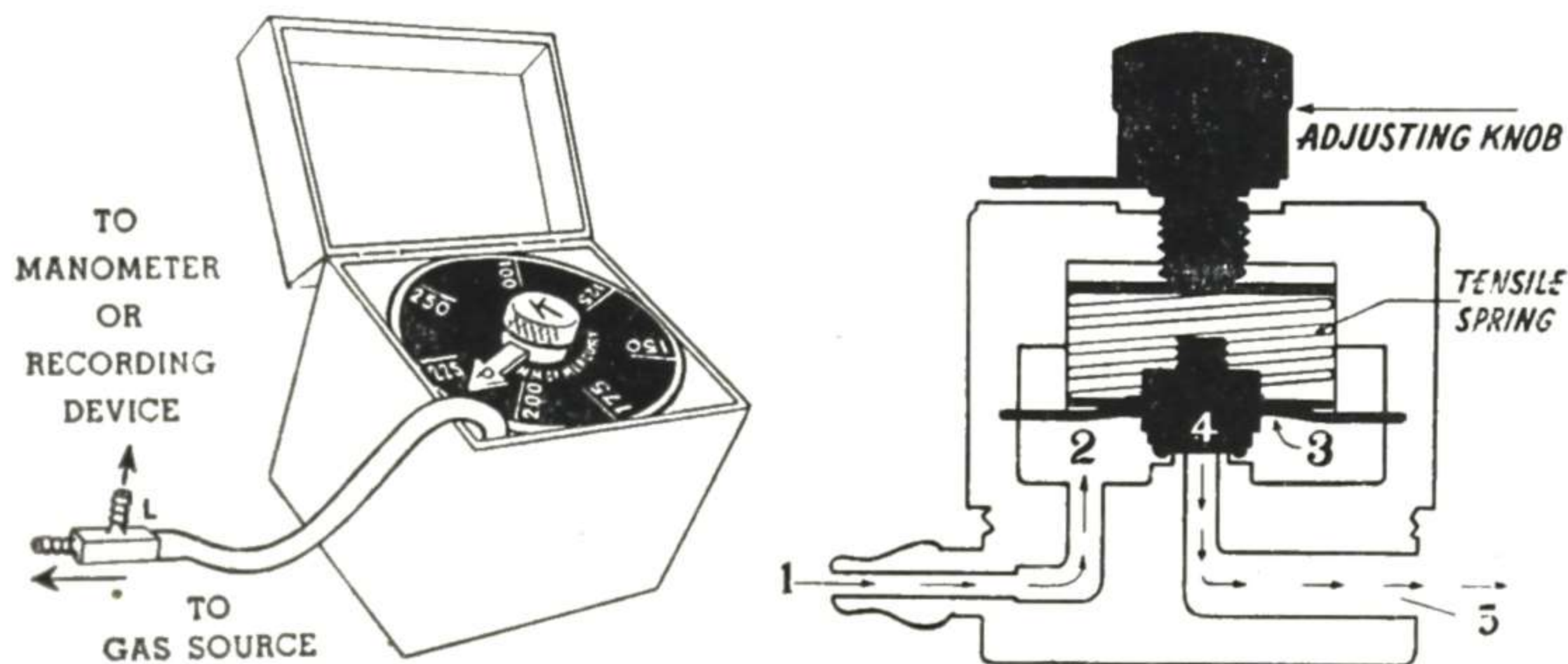


Fig. 63 (left).—Pressure-trol; actual size, approximately 3 in.

Fig. 64 (right).—Pressure-controlling device. Incoming gas, 1, builds up pressure in chamber, 2, which acts on diaphragm, 3. When pressure is more than desired level, it lifts the diaphragm, raising the rubber seat, 4, and allowing excess to escape through 5.

(Courtesy of Weisman, A. I., and Marco, J. L.: West. J. Surg. 58:428-429, August, 1950.)

pressure of gas desired in the uterus is set by dialing the pointer of the pressure control (Fig. 64). Because excess gas pressure is automatically released, a continuous flow of gas at the desired maximal pressure can be maintained as long as desired without closing and resetting valves for repeated testing. Tubal spasms are minimized because the maximal pressure can be increased slowly by finger-tip control and once the initial flow rate and pressure are set, no further manipulation is necessary. Pressures up to 250 mm. can be

(8) West. J. Surg. 58:428-429, August, 1950.

constantly maintained during insufflation of closed tubes.

[This device should prove helpful to those who perform many uterotubal insufflations.

Weisman (*Am. J. Obst. & Gynec.* 61:202, January, 1951) describes a method of estimating the potential capacity of the human uterine cavity and fallopian tubes based on fluoroscopic study of the radiopaque oil required to fill these organs in the nulliparous woman. Average capacity of the normal uterus in 739 cases was 1.7 cc. oil, while the fallopian tubes required an additional 1.0-1.5 cc. to outline the uterotubal tract completely. It is not advisable to inject excessive amounts of viscous radiopaque substance (8-12 cc.) into the uterus for ordinary hysterosalpingographic procedures. Realization that the uterine cavity of the virgin woman in its nongravid state is not a true cavity but merely a potential slitlike space should be of practical value in performing uterotubal tests. Weisman (*Radiology* 56:104, January, 1951) also describes the gynograph, an improved gynoroentgenologic apparatus for use with fluorography and radiography of the female genital tract. He has used it to perform over 2,000 uterotubal x-ray studies without a complication.—Ed.]

**Culdoscopic Observations on Tubo-ovarian Mechanism of Ovum Reception.** Albert Decker<sup>9</sup> (New York City) found that a definite mechanism of the ovary and its proper ligament and the fallopian tube at ovulation causes a change in position of the tube and ovary, facilitating reception of the ovum into the tube. Culdoscopy in the knee-chest position allowed visualization of the ovaries and tubes in each patient. Decker believes that at or near ovulation the proper ligament contracts, drawing the ovary to the uterus below the tube to a small fossa on the posterior surface of the broad ligament. This fossa is bound anterosuperiorly by the isthmus portion of the tube, laterally by the curved ampullar portion of the tube and medially by the uterus. The floor of the fossa is formed by the posterior layer of the broad ligament. In this position the fimbriae are in contact with the ovary. Possibly the tube plays a more than passive part in facilitating entrance of the ovum into the tube (Fig. 65).

Culdoscopic observations were made on a definite day of the menstrual cycle corresponding to the day of ovulation as calculated by basal temperature and by choosing the 14th day before menstruation in regularly menstruating women. Ovulation was verified by the appearance of the ovary and on occasion by recovery of an egg from the follicle by aspiration at time of observation (Fig. 66). Length of the proper ligament varied from 1.5 cm. at day of ovulation to 3.5-4.5 cm. at the 1st or last day of menstruation in the same patient.

(9) *Fertil. & Steril.* 2:253-259, May-June, 1951.

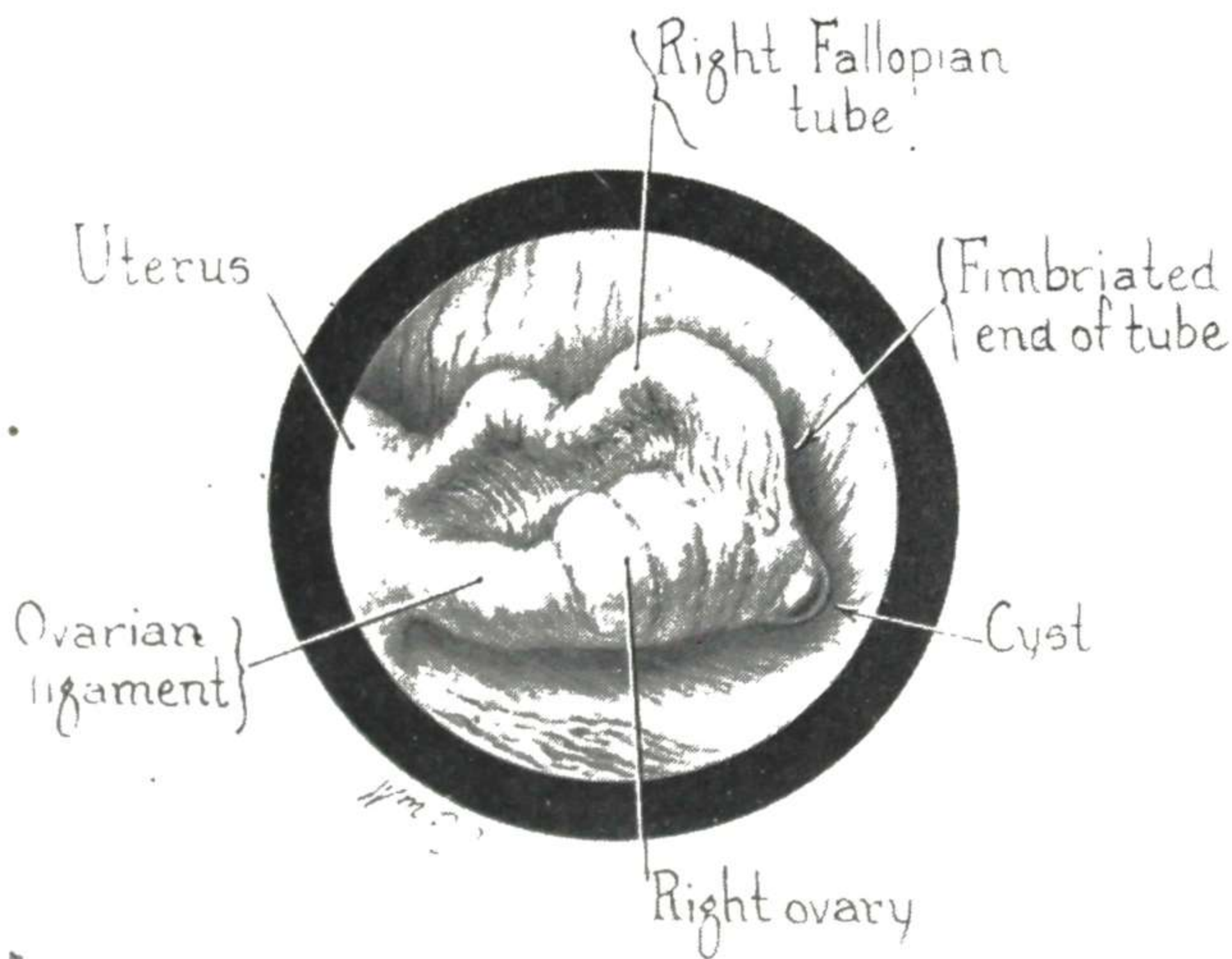
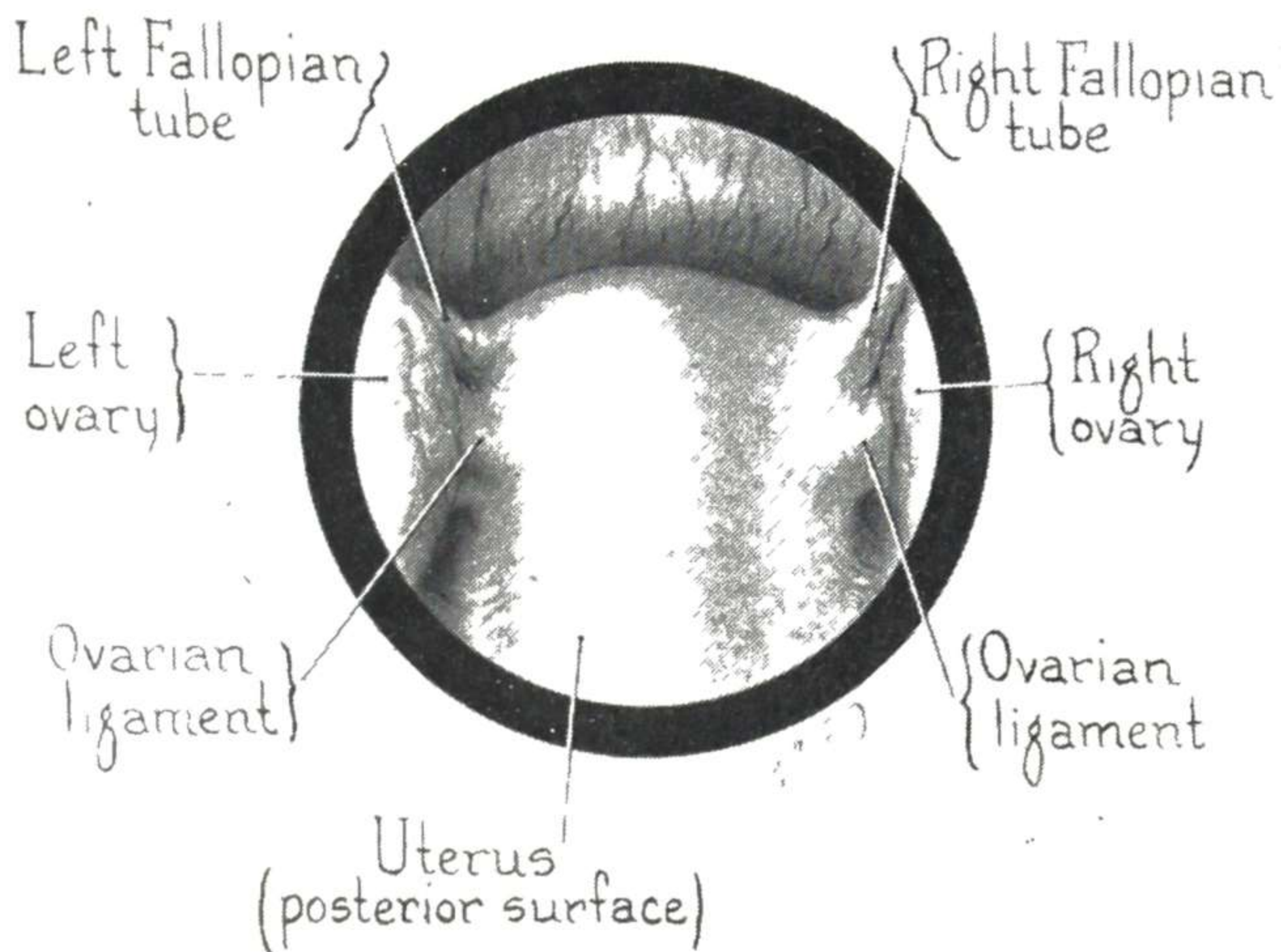


Fig. 65 (top).—Culdocoscopic view of posterior surfaces on day of ovulation.  
 Fig. 66 (bottom).—Same patient, 28th day of same cycle.  
 (Courtesy of Decker, A.: *Fertil. & Steril.* 2:253-259, May-June, 1951; from American Cystoscope Makers, Inc.)



Ovarian and tubal adhesions and pathologic conditions that interfere with the mechanism may possibly become factors that delay or prevent conception even though the tubes are patent. Immobilization of the tube and fixation of the ovary may be due to (1) previous nonspecific abdominal infection with pelvic spread, as with acute appendicitis, (2) postpartum and postabortal infection, (3) tuberculous peritonitis, and (4) endometriosis. Early and unsuspected endometriosis, especially with a history of dysmenorrhea, often causes infertility. Local resection of the little implants, which are distinctive in appearance and easily seen during culdoscopy, brings permanent relief from symptoms and probably increased fertility.

Results of surgical correction of extratubal disease, either inflammatory or endometriosis excel those obtained when tubal plastic surgery is required. Preoperative culdoscopy is of definite prognostic and diagnostic value.

[McGee and Feck (Ann. West. Med. & Surg. 5:281, April, 1951) have found culdoscopy very helpful when an accurate differential diagnosis cannot be made by the more usual methods. In their last 66 cases they used only local anesthesia for this procedure. The chief indication for culdoscopy was suspected ectopic pregnancy. In some patients classified as psychoneurotic, culdoscopy will reveal organic pelvic disease, particularly endometriosis and chronic pelvic inflammation.—Ed.]

**Bacteriology of Cervix in Cases of Infertility.** Cervical infections have long been a recognized factor in infertility. C. S. Matthews and C. L. Buxton<sup>1</sup> (Columbia Univ.) cultured endocervical secretions of 100 infertile patients to determine whether spermicidal organisms were actually growing in the cervical canal. Organisms cultured were isolated and identified and tests made with sperm suspensions in vitro.

Results showed that certain organisms, especially *Escherichia coli*, *Streptococcus viridans* and hemolytic streptococci, were highly spermicidal: *E. coli* reduced sperm motility over 30 per cent in the first half hour and produced consistent agglutination almost immediately after contact; *Str. viridans* caused complete immobility of sperm after six hours, but no agglutination. Hemolytic streptococci produced an initial temporarily increased agitation of sperm quickly followed by complete mortality. When appropriate antibacterial drugs, streptomycin or penicillin, were placed in in vitro suspensions of sperm plus spermicidal organisms, the sperm lived as long

(1) Fertil. & Steril. 2:45-52, Jan.-Feb., 1951.

as those in control suspensions. The pH variation did not affect longevity of sperm. Other spermicidal organisms were *Clostridium welchii* and *Proteus vulgaris*. Diphtheroids, bacillary streptococci, hemolytic and nonhemolytic staphylococci were entirely innocuous to sperm. A small number of patients harboring spermicidal organisms were treated with injections of the appropriate antibiotic into the cervix. Sufficiently encouraging results warrant continuation of this investigation and treatment.

---

## INFERTILITY

**Time of Ovulation: Correlation between Basal Temperature, Appearance of Endometrium and Appearance of Ovary.** C. L. Buxton and E. T. Engle<sup>2</sup> (Columbia Univ.) had 23 patients, who were scheduled for gynecologic operations, chiefly for removal of fibromyomas, make temperature records for a month or more to find if their charts showed any regularity. Of these, 18 proved acceptable for study. They were hospitalized several days before the expected temperature rise and were operated on the day their temperatures showed the characteristic rise which had been interpreted as indicative of ovulation. Analysis showed that operation was performed from a few hours to not more than 30 hours after the exact moment of temperature rise, since temperature observations were made at customary intervals.

At operation an endometrial biopsy specimen was obtained and both ovaries were carefully examined. If what appeared to be a corpus luteum was present, it was excised for microscopic examination. An attempt was then made to correlate the data thus obtained. Interpretation of the age of the corpus luteum, admittedly difficult and at best relative, was based on careful histologic data including the change of granulosa cells to a syncytial appearance in 12 hours, ingrowth of fibroblastic cells in 24 hours, invasion of this new lutein layer by capillaries in 36 hours, characteristic vascularization by the end of 48 hours and the approach of the vessels to the fibrin net of the central cavity in 72 hours.

---

(2) *Am. J. Obst. & Gynec.* 60:539-551, September, 1950.

Six patients showed no evidence of ovulation; two corpora lutea were possibly under 12 hours old; four were judged to be about 24 hours old; two, about 36 hours; two, 48 hours, and two, 72 hours. The endometriums showed much less progressive change than did the corpora lutea and no evidence of secretory change was found until the corpora lutea were at least 36 hours old. These observations suggest that, even allowing for possible technical variation of 24-36 hours, there remains a certain amount of variation in the luteal age which indicates that the ovulatory temperature rise is not entirely simultaneous with time of ovulation. Rigid use of temperature charts as ovulation indicators is apparently a mistake since there may be as much as four days variation. Patients who use temperature charts must be told that they are only approximate indicators of ovulation time.

[This report will dampen the ardor of some enthusiastic users of basal body temperatures for determination of the date of ovulation. I have most of my sterility patients use basal body temperature charts, but I have found them helpful in less than 50 per cent. Nor have I derived much information from vaginal smears in determining the date of ovulation. Like other gynecologists, I depend chiefly on the type of endometrium obtained by a biopsy curet just before menstruation for detecting ovulation. In view of the observations of Buxton and Engle, it is unwise to resort to artificial insemination only once, i.e., at the time of a temperature rise in the chart. It is preferable to inseminate three times during one week, usually during the three days before the supposed day of ovulation and the three days after this particular day.

Schäfer (*Zentralbl. Gynäk.* 71:969, 1949) determined the exact date of a fertilizing coitus in 37 cases of rape. In 17 it occurred the 1st to 10th day after commencement of menstruation (in 11 instances during menstruation); in 11 it occurred on the 11th to 20th day and in 9 on the 21st to 30th day. The author believes these findings confirm Stieve's view that function of the ovaries is governed not exclusively by hormones but also by the nervous system and that conception is possible at any time in the cycle. Schrank and Koch (*Geburtsh. u. Frauenh.* 132:200, 1950) studied 732 cases of rape in Heidelberg. In 64.1 per cent pregnancy followed. The pregnancy was interrupted in 146 (31 per cent). There were 216 women who had regular 26-30 day cycles and who apparently knew the exact time of the last menstrual period and, of course, the day of rape. A graph showed that conception occurred on all days of the cycle and that a substantial proportion occurred during the so-called "safe" period. Actually, 59.1 per cent of the conceptions took place before or after days 9-17 of the menstrual cycle, which is the interval Knaus regards as the period when almost all women who have 26-30 day cycles will conceive. In 65 cases (30.4 per cent) conception occurred after the 17th day and up to the premenstrual period. The authors, however, do not regard this deviation from the Knaus doctrine as a contradiction. They believe that extraordinary conditions in which these instances of rape took place, e.g., in concentration camps or during flight, may have interfered with the normal ovulatory processes and, moreover,

that these same circumstances may have served to confuse the women about the exact date of the last menstruation.

Stieve (Zentralbl. Gynäk. 72:897, 1950) maintains that healthy women with an average cycle of 28 days usually ovulate between day 13 and day 16 after the beginning of menstruation. However, many women can ovulate and become pregnant on other days.—Ed.]

**Etiology, Diagnosis and Surgical Treatment of Female Sterility.** Axel Westman<sup>3</sup> (Karolinska Inst.) reports 1,402 cases of female sterility with no evidence of endocrine disturbances. Sterility was primary in 959 and secondary in 443. Ninety-three per cent were followed for two years after treatment. Patients were aged 25-40 and most had been infertile over three years. In 398 patients, no abnormality of the sexual organs was found; in 663, adnexal inflammation; in 93, uterine anomalies or displacement; in 104, benign tumors or endometriosis; in 120, endometritis or cervicitis. In 24 patients the vulva and vagina were the seat of inflammation. In 529 of the 663 patients with adnexal inflammation, further studies were made. Fifty-eight had tuberculosis of the reproductive organs, usually without symptoms. In these, occlusion of the tubes was not discovered until salpingography was done.

Of 614 operations, 498 were abdominal and 116 vaginal. Separation of adhesions only was done in 78 patients; to avoid recurrence the wound was covered with free peritoneal strips. Ventrofixation was added to this procedure in 44. The presacral nerve was resected in 42 patients. Salpingostomy was done in 140; implantation of the tube into the uterus in 15 and of the ovary into the uterus in 23; cystectomy, oophorectomy or resection of the ovary in 67; enucleation of myoma in 44; exploratory laparotomy in 20, and bilateral salpingectomy in 25. Vaginal operations were evulsion and excochleation in 81 and plastic repair of the cervix or vagina in 35.

Westman uses salpingostomy so often because it offers a possible chance of success. If the tube is not too seriously damaged an artificial opening is made, but methods must be used to keep the stoma open. A plug of cholesterol oleate may be inserted in the opening at operation and the patient given fever therapy with vaccine to liquefy it. Implantation of the tube into the uterus is also aided by such a plug, for it may obviate clogging of the tube in the uterus by a blood clot.

(3) Acta obst. et gynec. scandinav. 30:186-202, 1950.

Of the 498 patients operated on abdominally, 90 became pregnant. Separation of adhesions was followed by pregnancy in 28 of the 78 patients, separation of adhesions and ventrofixation in 16 of the 44, transection of the presacral nerve in 11 of the 42, salpingostomy in only 9 of the 140, implantation of the tube in 3 of the 15 and implantation of the ovary in 4 of the 23. Of the 116 patients operated on vaginally, 26 became pregnant. There were 19 miscarriages, the incidence being about the same in both operative groups.

[This article is interesting for a number of reasons. For one, the incidence of tuberculosis in Westman's 529 cases of sterility was 11 per cent, which is high. Many of the women had no symptoms of tuberculosis. Second, among the 498 operations performed on these patients were 140 salpingostomies, an astounding number. Implantation of the tubes into the uterus was done 15 times, and implantation of the ovaries into the uterus 23 times. Now what were the results of these operations? After the 140 salpingostomies there were only nine pregnancies, or 1 in 15½ operations. After implantation of the tubes there were three pregnancies (1 in 5), and of the 23 patients who had implantation of the ovary into the uterus, 4 became pregnant (1 in 6). Is it worth while to perform so many of these operations for such meager results? I doubt it. However, I grant that there are times when a surgical operation such as salpingostomy or tubal implantation is definitely indicated, particularly in women who have tried everything and who are desperate and because some may develop mental disturbances if they have not tried everything. Westman does not state how many live babies were born in this series. Two patients died after operation, one of pulmonary embolism and the other of ileus.—Ed.]

**Tubal Surgery and Sterility.** Juan Carlos Ahumada, Raul M. Chevalier and José Maria E. Mezzadra<sup>4</sup> believe some element of tubal occlusion is present in about half of all women.

Tubal occlusion was confirmed by three hysterosalpingographic insufflations at 200 mm. pressure, performed once a month under fluoroscopic control. In some cases, the x-ray picture of rigid tubes with ragged outline and diverticula permitted diagnosis of tuberculous origin. Candidates for surgery were selected from among women under 35, married less than 10 years, with absence of original infection at the time of operation and whose husbands' semen had normal index of fertility. Operations were performed postmenstrually under general anesthesia.

In the ampullar zone, salpingolysis, salpingostomy and salpingostomatoplasty would be performed; in the isthmic zone, amputation of proximal stump or resection and end-to-end anastomosis, and in the intramural zone, resection and

(4) *Semana méd.* 58:248-260, Feb. 22, 1951.

reimplantation or total salpingectomy and transplantation of ovary. There were 10 salpingolyses, 3 resulting in pregnancy; 3 salpingostomies, without results; 3 stomatoplasties, resulting in patent tubes for two years but no pregnancy; 6 reimplantations, resulting in patent tubes in four cases and one pregnancy. In four cases of complete occlusion of the tubes, transplantation of an ovary into the uterine cavity did not interfere with menstruation but produced no pregnancies. There were no operations on the isthmic zone. The authors believe that better selection of patients and search for history of infection, especially of subclinical tuberculosis, will provide a greater number of suitable candidates for surgery for sterility.

[This is an excellent review. Since revival of interest in surgical treatment to overcome tubal sterility several improved methods of operating have been described. Perhaps results of plastic operations on the tubes will be improved. In the past, results have been poor, and hardly good enough to justify the large number of operations which have been performed on the tubes.

Perl (*J. Internat. Coll. Surgeons* 15:576, May, 1951) describes and illustrates a method of using anchored polyethylene intubation in reimplantation of the oviducts.—Ed.]

**Treatment of Sterility.** S. Leon Israel and Lennard L. Weber<sup>5</sup> (Univ. of Pennsylvania) state that systematic investigation of a barren marriage is not so formidable that it should discourage an interested family physician. In a minimal diagnostic survey the essential etiologic factors which should be sought are gross pelvic disease, male infertility, errors of cervical insemination, tubal occlusion and endocrine deficits. Incidence of various defects in 245 barren couples, from which patients with gross pelvic disease were excluded, was male infertility in 53 per cent, errors of cervical insemination in 24 per cent, tubal occlusion in 30 per cent and endocrine faults in the female in 18 per cent. Sixty-one couples had two or more of these defects.

In male infertility a careful history regarding genitourinary disturbances and sexual habits must be taken, and endocrine and nutritional defects, genital infection, compromised circulation and cryptorchidism must be ruled out. It is important to note whether coitus has taken place during the probable time of ovulation and not too often, for repeated ejaculations reduce the number of spermatozoa and increase

(5). *J. Indiana M. A.* 44:119-122, February, 1951.

the abnormal forms. Oligozoospermia was present in 39.5 per cent of the males in this series. This condition is best managed by correction of faulty habits and diet, maintenance of proper weight, correction of hypothyroidism and elimination of adnexal infection. Faults of cervical insemination were diagnosed by microscopic study of postcoital cervical and vaginal secretions. To correct this condition, injections of antibiotics, repeated dilations of a stenotic cervix and small doses of estrogen are of value. Uterotubal insufflation or salpingography will show tubal occlusion; it was a factor in 19.3 per cent of the cases studied. When partial, occlusion can be eliminated by heat, small doses of estrogen and repeated Rubin tests; when complete, surgery must be considered but it is successful in only 10 per cent of cases.

In the female, dysfunctional menstrual disorders, amenorrhea or abnormal bleeding point to disturbed endocrine function. Cyclic administration of ovarian steroids and low dosage irradiation are of value. Anovulatory menstruation is diagnosed by means of a temperature graph or endometrial biopsy; it is due to either ovarian dysfunction, which is benefited by progesterone, or pituitary failure, which is benefited by gonadotrophin. Low dosage irradiation of the pituitary gland and ovaries sometimes restores normal menstruation.

[It is interesting to review the etiologic factors in these 245 cases. In a little more than half the cases the men were at fault. In only 18 per cent of all cases was an endocrine disturbance considered responsible for the sterility. This should make doctors ponder before they fill their patients with hypodermic medication in an effort to overcome sterility. More than half the women with endocrine faults either had complete anovulatory menstruation or ovulated infrequently. The outlook for these patients is bad. I have little faith in progesterone or gonadotrophins for overcoming sterility in these patients. Low dosage irradiation of the pituitary does help, but extreme caution must be exercised in the selection of patients for this type of therapy.

Schtirbu (*Obst. y ginec. latino-am.* 7:603, 1950) used x-ray treatment of the hypophysis in 15 cases of sterility associated with oligomenorrhea or amenorrhea. Sterility had been present 2½-6 years. A normal menstrual cycle was restored in 11 and pregnancy resulted in a normal child in 5. One patient aborted. The pregnancies occurred two to four months after treatment.

Sanchez Cordero (*Estud. esteril.* 1:58, May, 1950) used roentgen therapy to the hypophysis and ovaries to overcome sterility due to primary functional disturbances, but of six patients, only one had a baby.

As Rutherford, Banks and Lamborn (*Am. J. Obst. & Gynec.* 61:443, February, 1951) point out, an extremely difficult patient to handle in sterility practice is the one who has been pregnant before and has been unable to conceive again. In 100 such cases the single greatest cause of

failure to conceive was impatience rather than mechanical impediment. The second greatest cause seemed to be tubal occlusion. More and more investigators are suggesting the routine use of curettage in all cases of spontaneous abortion even though the observer may feel that the abortion has been complete. Certainly this is an easy and safe procedure. Infection in retained products may play some part in subsequent sterility, as suggested by its frequency in the patients studied by Rutherford and his associates. There should be a wider use of sulfonamides and/or the antibiotics in any patient showing a morbid reaction, whether there be clinical symptoms or not.—Ed.]

**Sterility.** Robert J. Crossen<sup>6</sup> (Washington Univ.) reviews the literature and reports on the treatment and investigation program of the sterile couple. General and sexual history is first obtained. Especially important is the menstrual history, for this is an excellent indicator of endocrine balance. A thorough pelvic examination and smear tests of any secretion are then made. The pH of the vagina is tested and a smear and hanging drop preparation made if purulent discharge is present. Laboratory tests, including a basal metabolic test scheduled halfway between menstrual periods, should be made. If no lesion is found, the patient is given general instructions on diet and general habits. Caloric intake is reduced if the patient is overweight and increased if underweight. The habits to be investigated are occupation, rest, including sexual rest, alcohol consumption and use of tobacco. The importance of determining the time of ovulation is self evident. The patient is advised to elevate the hips on pillows during and for a half-hour after intercourse if the pelvic floor is lax and the semen does not remain in the vagina. In retrodisplacement, the knee-chest position after coitus helps to immerse the cervix in the seminal pool.

The Huhner test is then made. If the husband can be ruled out as a factor in the sterility, the Rubin test should be done. If the tubes are blocked, determination of the site of the block by injection of a radiopaque substance and by roentgenography follows. Because of the low average of success with operation, other methods of establishing tubal patency have been sought. Rubin and others suggest repeated insufflations; the therapeutic value of iodized oil in opening blocked tubes has been reported and diathermy, estrogens and antibiotics have all been used with varying success.

Crossen reviews the literature on organic lesions causing

(6) Northwest Med. 49:521-526, August, 1950.



sterility. Pronounced dyspareunia with a tight opening or vaginismus may result in nonpenetration or infrequent coitus. If the floor is so lax that the semen does not stay in the vagina long enough for insemination, perineorrhaphy should be done. Cervical infection, if superficial, should be treated with sulfonamides locally with triple sulfonamide cream and also with adequate doses by mouth. Cervical stenosis and acute angulation of the cervix, occasional causative factors, can usually be relieved by dilation. Retrodisplacement is not a frequent cause of sterility; but if the uterus is movable, trial with a pessary and correction of other lesions are indicated. Operative correction should be tried only after other causes of sterility have been ruled out and then only in cases of fixed retrodisplacement. Endometrial hyperplasia is often corrected by curettage. Treatment of tubal occlusion by conservative measures has been discussed; operative treatment consists of salpingostomy or implantation of the tube into the uterus.

**Thirty Years of Progress in Treating Infertility.** I. C. Rubin<sup>7</sup> (New York City) discusses the role of the gynecologist, internist, urologist, endocrinologist and psychiatrist in diagnosis and therapy. Significant advances include (1) Huhner's sperm test of cervical secretions; (2) stress on constitutional and endocrine characteristics of the male and (3) on the role of the thyroid gland; (4) studies on the morphologic appearance of human spermatozoa; (5) observation that the cervical secretion is most favorable to sperm penetration during the ovulation phase; (6) testicular biopsy; (7) biochemical study of seminal fluid, especially the role of hyaluronidase; (8) disclosure of unfertilized ova in uterine washings; (9) recovery of ova at hysterectomy done after anticipated ovulation date; (10) culdoscopy; (11) indirect methods of determining ovulation, such as endometrial biopsy, vaginal Papanicolaou smear, temperature recording and determination of preovulatory excretion of urinary gonadotrophin, and (12) Rubin's test for tubal patency.

Rubin traces his early experiments with oxygen and lipiodol® in uterotubal insufflation. Use of the kymograph gave a permanent record of the pressure changes, established the functional status of the tubes and allowed the test to be

(7) *Fertil. & Steril.* 1:389-406, September, 1950.

used therapeutically. Rubin's test demonstrated that one fourth to one third of all female sterility is due to complete tubal obstruction and one-fourth to some form of partial tubal obstruction. In at least a fourth of the latter cases, uterotubal insufflation is helpful. Rubin recommends rayopake® for diagnosing intrauterine lesions affecting sterility and carbon dioxide for ureterotubal insufflation.

Rubin's test has shown the importance to sterility of appendicitis, tubal abortion, myomas, implication of the tubes in the technic of myomectomy, possible production of peritubal adhesions and strictures after pelvic operations, and the importance of uterine retroflexion and retroversion. Kymographic studies have shown the muscle function of the tubes and the correlation between ovarian and tubal activity.

Estrogens have aided therapy indirectly by (1) inducing regenerative changes in the tubal epithelium through trophic influences, (2) increasing tubal contractility, thus freeing the tubes of adhesions and mucus plugs, (3) rendering the cervical mucus plug less viscid and (4) favorably influencing underdeveloped uterus and cervix. Increased ovulation and production of pregnancy have been reported after use of potent gonadotrophins. Diathermy for chronic tubo-ovarian inflammation and both x-ray and radium therapy to pituitary and ovaries have been used.

In about 10 per cent of cases no cause for sterility is found. Possible influences in these cases are (1) incompatibility of blood groups; (2) sperm-killing substances in some vaginal secretions; (3) group-specific properties in the sperm; (4) psychic tensions, and (5) the role of sympathetic and parasympathetic systems.

**Role of Latent Genital Tuberculosis in Pathogenesis of Female Sterility: with Special Reference to Its Detection by Cultures of Uterine Secretions.** Among 1,550 sterile women (560 primary and 990 secondary cases) I. Halbrecht<sup>8</sup> (Maternity Hosp., Hadera, Israel) found 71 (4.58 per cent) with latent genital tuberculosis. The only diagnostic methods of practical value were endometrial biopsy, cultures of menstrual and intermenstrual discharges specific for *Mycobacterium tuberculosis* and hysterosalpingography. Diagnosis was made 62 times by endometrial biopsy and 9 by culture. Endometrial

(8) *Fertil. & Steril.* 2:267-273, May-June, 1951.

biopsy had several disadvantages. Despite precautions, severe peritonitis developed in three women immediately after biopsy and cleared up only after prolonged treatment. Negative results were not always reliable. In five cases the first biopsy was negative, but the second or third showed tuberculosis. Biopsy was valueless in cases of tuberculosis of the tubes without accompanying endometrial tuberculosis. Although tuberculosis of the endometrium is never encountered without accompanying tuberculosis of the tubes, the reverse is not true.

In 28 of 530 cultures of menstrual discharges and in 6 of 130 intermenstrual cultures, *M. tuberculosis* was present. Latent genital tuberculosis was found in 9 other cases in which results of endometrial biopsy were negative; in 12 additional cases, cultures confirmed the positive findings of endometrial tuberculosis made by biopsy. Halbrecht prefers culture of menstrual and intermenstrual discharges to endometrial biopsy as a diagnostic method because cultures can be repeated indefinitely and tuberculosis of the tubes may also be detected. Mucus and endometrial shreds mixed with blood expressed from the cervix may be collected daily and cultures made during the entire period of menstrual flow. In 400 cases, hysterosalpingography was at best only indirectly helpful in diagnosing endosalpingitic tuberculosis. Anatomic changes brought about in the uterine cavity and/or tubes by endometrial tuberculosis were rarely so profound or specific as to be manifest in the hysterosalpingogram.

Of 62 patients with partial or complete tubal occlusion in primary sterility, 26 (40.6 per cent) had genital tuberculosis, 24 verified by biopsy and 2 by culture. Of the 71 women with latent genital tuberculosis, 46 were followed over eight years. Two died of generalized tuberculosis, three had pelvoperitonitis after biopsy and two after insufflation and one had spontaneous adnexitis. In one case of endometrial tuberculosis, pelvoperitonitis developed after salpingography. None of the women with latent tuberculosis became pregnant during observation, and many had been sterile almost 20 years.

**Penetration by Spermatozoa through Zona Pellucida of Rabbit Ovocytes Impregnated in Vitro.** R. Moricard, J. Bossu and F. Moricard<sup>9</sup> (Paris) describe a method by which sperm

(9) *An. brasil. ginec.* 30:81-92, August, 1950.

can be demonstrated in the zona pellucida or cytoplasm of the rabbit ovocyte. Passage of at least one sperm through the zona pellucida was observed in 15 of 21 ovocytes. In five instances sperm were seen to penetrate the cytoplasm and in one instance two sperm penetrated the cytoplasm. In several sections the heads of sperm were cut in two, making their penetration into the ovocyte unquestionable. The authors conclude that sperm pass through the zona pellucida in about 75 per cent of cases.

**Semen Quality in 1,000 Men of Known Fertility and in 800 Cases of Infertile Marriage** was studied by John MacLeod<sup>1</sup> (Cornell Univ.). The fertile men had pregnant wives at time of study, the "infertile" ones had presented themselves for study of infertile marriage and were chosen before completion of studies establishing the responsibility in either partner. Average ejaculate volume for the fertile men was 3.4 cc., as compared with 3.6 cc. for the "infertile" men, a statistically significant difference. The poorest specimens in the "infertile" group contributed largely to this difference. The average in 300 azoospermias, not included in this group, is 2.72 cc.

Grand mean counts and total counts were 107 and 350 million/cc. respectively, for fertile males and 87 and 293 million for "infertile" ones. There is no significant difference between these means, but they hide rather than show the essential difference. Thus, in the fertile group, only 25 per cent fell below 54 million/cc., with 5 per cent between 1 and 20 million, whereas the first quartile of the "infertile" group fell below 30 million/cc. and 17 per cent were between 1 and 20 million. Of the fertile group, more men fell in a 60-79 million total count group than in any other, whereas the mode in the "infertile" series was in the 1-19 million group. The fertile group reach a peak count somewhat faster after previous emission than the "infertile" group, and a waiting period of at least one week is necessary in the latter to provide maximal counts.

Not all "infertile" men were really so. Conception finally resulted in more than 50 per cent of the wives of 666 of these followed one to four years. Again, average sperm count in the "conception" class, 100 million/cc., did not differ significantly from the "nonconception" class, 92 million/cc., but the

(1) *Fertil. & Steril.* 2:115-139, Mar.-Apr., 1951.

modal group in the first lay between 40 and 60 million/cc. as compared with 1-20 million/cc. in the "nonconception" class, exactly the same as in the total "infertile" series. There remained a number of cases in the nonconception class in which sperm count was normal by all standards and responsibility of infertility lay in the wives. Elimination of this category would have changed the data of the "infertile" and nonconception groups.

Morphologic examinations were not completely analyzed. Standards of normal and abnormal are rather elastic. In general, specimens with good counts and motility correlated with the normal complement of normal morphology, but specimens with low counts in the fertile group had consistently better morphology than in the "infertile" group. There was no correlation, in the fertile group, of time taken to produce conception and quality of semen.

"Count" thus remained the most important factor. The really significant observations are in the 1-20 million/cc. group, and 30 million/cc. is a level that can be regarded as borderline of subfertility, rather than 60 million/cc., formerly accepted. Compensating factors of good motility and morphology, however, were present in the 1-20 million/cc. specimens of the fertile men, and these must always be considered.

[I should like to emphasize that 29 per cent of the men in the fertile group had sperm counts below 60 million/cc. as compared with 44 per cent of the "infertile" men. Only 5 per cent of the fertile men and 17 per cent of the "infertile" men had counts in the 1-20 million bracket. I concur with MacLeod that the figure of 60 million should be given up as an arbitrary level for fertility. Even though MacLeod considers 30 million/cc. to indicate subfertility, we must remember that some men with lower counts may procreate children.—Ed.]

**Clinical Interpretation of 1,000 Semen Analyses among Applicants for Sterility Studies.** Ernest W. Page and Florence Houlding<sup>2</sup> analyzed semen specimens for sperm density, percentage of motile sperm two hours after collection and percentage of normal sperm heads. Subjects were arbitrarily divided into three groups: a group of 129 men whose wives conceived within six months of analysis, designated fertile; that of 800 men whose semen contained sperm but whose wives did not conceive within six months, designated fertility unknown; that of 71 men with azoospermia, termed sterile. Incidence of azoospermia of 7.1 per cent was lower than i

(2) *Fertil. & Steril.* 2:140-151, Mar.-Apr., 1951.

other reported groups (12.5 per cent) perhaps because this series consisted of private patients among whom incidence of gonorrhoea is lower. Twenty-five per cent of "fertile" men and 42.9 per cent of "unknowns" had sperm densities lower than 60 million/cc.

Valid statistical analysis of data obtained and determination of probability of fertility rests on three assumptions. (1) Of all men whose semen show values above the median for the fertile group (82 million/cc., 54 per cent motility, 88 per cent normal morphology), at least 90 per cent are fertile. (2) Based on this assumption, all densities above the cumulative percentage of 45 represent a probability of 90, and an arbitrary scale of 1 to 90 may be set up for density values below the median. Then, on this scale, a probability score can be obtained for each value by doubling the cumulative percentage found in the fertile group. Thus, if 3.1 per cent of fertile men have counts below 20 million/cc., a score of 6.2 can be given to such a count. A score scale might thus be made for all three factors. This simply means that of all men whose semen shows values below the median, the percentage who are fertile approximates the percentage of fertile men who are also below the median and show the same values. (3) Fertility of a man is more in proportion to the product of probability scores of the three factors than to the mean or average. A man who scores one-third in all three factors is only one-ninth as good a candidate for fatherhood as the man with median values throughout. This product was found to be the most valid index of the fertility of any single semen specimen.

**Male Factor in Fertility and Infertility: Analysis of Motile Activity in Spermatozoa of 1,000 Fertile Men and 1,000 Men in Infertile Marriage.** John MacLeod and Ruth Z. Gold<sup>3</sup> (Cornell Univ.) believe that spermatozoa which eventually reach tubal environment of the ovum pass quickly into the cervical mucus without an appreciable amount of seminal fluid. Thus seminal fluid is not a physiologic environmental medium for spermatozoa for long periods; in vitro studies of their survival in that medium, so far as motility is concerned, probably have no relation to their longevity in the female genital tract. Using the Hotchkiss method, the authors analyzed mo-

(3) *Fertil. & Steril.* 2:187-204, May-June, 1951.

tile activity of spermatozoa  $5\frac{1}{2}$  hours or less after ejaculation. In the infertile group, ejaculate volume tended to be higher; highest volumes were associated with semen specimens of poorest fertility as measured by sperm counts. With reference to activity, only 17 per cent of cases with less than 10 per cent active cells came from the fertile group, compared with 57 per cent in the 80 per cent (or over) active group. Critical level below which fertility was considered subnormal was 40 per cent active. Three per cent of the fertile and 10 per cent of the infertile group fell in the definitely poor motility quality classification (under 2). In contrast, 19 per cent of the fertile and only 12 per cent of the infertile group had high motility quality (over 3+).

In this study of large populations, percentage of active cells, even in high quality specimens, never approached 100; a good percentage active figure would be 75 and one between 50 and 60 would be average. There was inverse relation between time taken to produce conception in the fertile group and percentage active cells, time decreasing with increasing percentage active cells. Close correlation existed between percentage active cells and motility quality, irrespective of sperm count in both groups. But for any given quality the fertile group had a better percentage active than the infertile and, conversely, for any given percentage active the fertile group had better quality. Lower levels of normal male fertility for these aspects of semen quality may be estimated from these facts. Minimal level of normal fertility for spermatozoa count is 20 million/cc. (total sperm count of 50 million). Since minimal level for percentage active cells is 40 per cent, a total active sperm count in the ejaculate of 20 million is the lower level of normal fertility. Further, the 20 million active cells should have a motility quality (speed of movement) of at least 2.

**Sperm Survival at Estimated Ovulation Time: Comparative Morphology: Relative Male Infertility** was investigated by Melvin R. Cohen and Irving F. Stein<sup>4</sup> (Michael Reese Hosp.) in 45 married couples. Morphology of spermatozoa obtained at postcoital examination was studied and compared with analysis of semen previously obtained directly from the male. In specimens of mucus obtained  $1\frac{1}{2}$ -58 hours after

(4) Fertil. & Steril. 2:20-28, January, 1951.

coitus, surviving sperms were as active as those in freshly ejaculated specimens. Morphologically, however, they were superior in quality to those obtained from the same male by friction or withdrawal. In a directly obtained specimen of grade IV motility, there are always some sperms with grade 0, I, II and III motility. If these more sluggish spermatozoa are examined under high power magnification, some will appear normal, but most will show angulated heads, cytoplasmic extrusion and micro and macro forms. Therefore, it seems that the more normal actively motile sperms have greater endurance enabling them to survive longer. In one case, however, conception occurred despite greater survival of abnormal forms in the cervical mucus than in bottle samples. It is possible that some form of morphologically atypical sperm now classified as abnormal may be the unrecognized fertilizing agent.

Review of 194 couples with relative infertility revealed 33 conceptions (17.1 per cent) in couples given a guarded prognosis chiefly because of substandard sperm. These unexpectedly favorable results suggest the value of reconsideration of criteria for male fertility.

[Each year we find more and more articles in which the authors express astonishment that men with low sperm counts or with a higher than normal incidence of defective sperm are able to procreate. It is a serious matter to condemn a man as infertile simply because his sperm count is below 60 million or even below 30 million/cc., because many such men have been able to procreate. I fully agree with the authors that it is high time for a reconsideration of the criteria of male infertility.

Rubinstein *et al.* (*Fertil. & Steril.* 2:15, January, 1951) found that sperm migrate through the cervix, corpus and fallopian tubes 30 minutes after introduction into the vagina. They do this at any time in the menstrual cycle. The authors also found that the sperm may retain their motility in any and all parts of the female genital tract for at least 50 hours.

According to Cohen and Stein (*J. Urol.* 65:467, March, 1951), motile spermatozoa recovered from cervical mucus 1½-38 hours after coitus appeared normal when judged by the accepted standards for motility and morphology. Stained smears of cervical mucus post coitus showed a remarkable reduction in the percentage of abnormal spermatozoa from stained smears of semen direct from the male. Simmons also found that the percentage of normal sperm in cervical mucus was greater than that in the individual semen specimen.

Considerable publicity was recently given in the lay press to the steroid pregnenolone, said to have great value in male infertility. Tyler (*Fertil. & Steril.* 2:278, May-June, 1951) calls attention to his negative report on pregnenolone in 1948. He found that neither oral nor parenteral administration of this steroid had any clinical spermatogenic effect.—Ed.]



**Semen Studies and Fertility.** Edward T. Tyler<sup>5</sup> (Los Angeles) examined 2,500 semen specimens in analyzing 408 infertile couples; 211 men (51.6 per cent) showed impaired fertility. There was a general relation of sperm count with morphology and motility. In ranges of 1-19 million/cc., 94 per cent of specimens showed abnormalities of morphology and/or motility, whereas in ranges of over 200 million/cc. only 7.1 per cent showed any disturbance in these factors. However, necessity for complete semen study is indicated by the fact that many cases showed subnormal morphology and/or motility with counts above the normal limit of 60 million. In the entire group, there were 113 pregnancies. No pregnancies were observed when the sperm count remained consistently below 20 million; the greatest incidence occurred when it was above 100 million. Forty-three patients had complete azoospermia, caused in about 40 per cent by bilaterally hypotrophic testes, presumably on a developmental basis. Incidence of "constitutional" etiologic factors was compared in 188 subfertile and 163 normal patients. Pronounced malnutrition occurred about three times oftener in the subfertile group. Chronic fatigue was a complaint in 19.2 per cent of the subfertile and in 9.2 per cent of the fertile group. Obesity and excess use of tobacco appeared somewhat oftener in subfertile husbands. No real correlation was noted between occupation and subfertility.

Therapy consisted of endocrine and nonendocrine types. In the 43 patients with azoospermia there was no improvement with any treatment. Results of endocrine therapy were disappointing in 161 subfertile men with counts under 40 million/cc. and 201 with counts above 40 million. Most consistent improvement was obtained with thyroid in subthyroid patients with moderate seminal deficiencies. However, thyroid gave poor results when administered empirically to nonhypothyroid patients. Sperm motility was improved in only a few patients given testosterone and pregnenolone. Usually, endocrine treatment resulted in less than 10 per cent improvement. Constitutional, or nonendocrine, therapy included elimination of excessive use of alcohol or tobacco, weight reduction in obesity, correction of nutrition, improved habits of rest and exercise, high dosages of B complex with methionine and choline and prostatic massage. Patients with pretherap

(5) J. A. M. A. 146:307-314. May 26, 1951.

sperm counts under 40 million showed little change, but those with higher counts showed more improvement. Correction of severe malnutrition gave the best results, prostatic massage the poorest. Improvement of general health habits helped 36.7 per cent of patients, vitamin therapy about 23 per cent. The generally low percentage of improvement of sperm counts makes it mandatory to utilize the patient's sperm potential to the best advantage. This includes instructions in regard to timing of coitus, avoidance of intercourse at non-fertile times of the cycle and artificial insemination. The last probably does more than help in the journey itself; it may insure a large enough number of sperm reaching the cervical canal when diminished concentrations are present in the ejaculate. In addition, artificial insemination permits a large bulk of semen to remain in direct contact with the cervical os; if the fluid is placed on a speculum, there is little contact with acid vaginal secretions and considerable contact with favorable cervical secretions. Of 161 subfertile couples, artificial insemination was tried in 98 and resulted in 33 pregnancies; in the 63 couples not so treated, only 8 pregnancies resulted.

**What Constitutes Normal Semen?** Henry C. Falk and Sherwin A. Kaufman<sup>6</sup> (Beth Israel Hosp., New York City) performed complete semen analyses on 100 men of repeatedly proved fertility. Their wives were all pregnant at the time of the study, had two or more children and had never had a spontaneous miscarriage. Age of the men did not appear to affect the results.

Volume of the ejaculate averaged 2.9 cc. and was not related to sperm count/cc. No constant relationship was seen between viscosity and turbidity and any other phase of the analysis.

Motility estimation revealed an average of 61.4 per cent active cells after 3 hours, of 46.5 per cent after 6 hours and of 26.5 per cent after 12 hours. Nine specimens showed a relatively low percentage of motile forms and eight of these also exhibited poor quality of motion.

Spermatozoa count/cc. was less than 60 million in 15 of the 100 men. Seven had counts below 40 million. Average count for all men was 100.7 million. Average total count was 295 million. Eighteen had a total count below 150 million, **12 having counts/cc. below 60 million.**

(6) *Fertil. & Steril.* 1:489-503, November, 1950.

Morphologically, average percentage of normal forms was 88.4. Abnormal forms ranged from 3.0 to 30 per cent, average 11.6 per cent.

No specimen was poor in every phase of the analysis. A third were deficient in one or more respects according to present standards, but all these had at least one good compensating feature. No single aspect of semen must necessarily be of top quality to effect fertilization, but good morphology, although not absolutely necessary for fertility, is perhaps a more stabilizing influence than any other factor.

**Male Factor in Sterility.** C. O. McCormick, Jr.<sup>7</sup> (Indianapolis) examined 200 semen specimens from 178 married men over two years, using Farris' method. Examinations were made because of complaints of at least one year's involuntary sterility. The number of active sperm in the total ejaculate, collected after five days' abstinence from coitus or emission, was computed. Speed or drive of the active sperm was determined and morphology studied to obtain the percentage of normal oval forms. The standards of fertility used define a highly fertile male as having over 185 million active sperm in the ejaculate; a relatively fertile male, 80-184 million; a subfertile male, 1-80 million, and a sterile male, 0.

Eighty men (45 per cent) were highly fertile, 43 (24 per cent) relatively fertile, 45 (25 per cent) subfertile and 10 (5.6 per cent) azoospermatic. Volume of the ejaculate, speed of the sperm, percentage of active sperm and percentage of oval forms decreased as fertility decreased. Average amount of ejaculate of the sterile male is about 33 per cent less than that of the highly fertile male.

Pregnancy occurred in 20 cases while the couples were being treated for infertility. Semen examination showed that 11 husbands were highly fertile, 7 relatively fertile and 2 subfertile. All specimens were examined within at least four months of conception. Rechecking showed the only change in fertility rating to be in one man who had been relatively fertile when first examined. At the time of re-examination he was highly fertile.

McCormick recommends the Farris method as an easy, accurate procedure for determining the potential degree of fertility of the male.

(7) Am. J. Obst. & Gynec. 61:1020-1024, May, 1951.

**Appraisal of Therapy for Infertile Men** by usual criteria—the change in seminal constituent and the production of pregnancy—is unreliable because wide physiologic fluctuations in character of semen take place. Absence of spermatozoa, however, in three separate, properly collected ejaculates is a persistent defect, and spermatozoa rarely appear without removal of initial fault. Twenty men, with persistent azoospermia and without any related physical defect, were studied by Robert S. Hotchkiss<sup>8</sup> (New York Univ.). Bilateral testicular biopsies secured before treatment in each showed mitotic figures and spermatogenesis at least to the reduction division stage; a few spermatozoa were sometimes present. Bioassays for pituitary gonadotrophins in urine showed no pattern correlating biopsy and excretion of this hormone. A short course of sheep pituitary extracts was given to all patients and semen examined periodically thereafter. Spermatozoa were found in only one patient after treatment; this suggests that azoospermia is not always an irreversible condition, although it hardly proves the efficacy of treatment given.

Criteria to judge present methods of treatment of individual males with subnormal sperm counts are not available. Valuable data can be derived by analyzing effects of treatment on groups of subjects rather than individuals. Any treatment which materially elevates the average counts in a group of men deserves recognition, for such average is little affected by individual physiologic variations if the group is large enough. Another valid criterion is the presence of sperm in males heretofore azoospermic.

**Improvement in Spermatogenesis Following Depression of Human Testis with Testosterone.** Carl G. Heller, Warren O. Nelson, Irvin G. Hill, Edward Henderson, William O. Maddock, Edwin C. Jungck, C. Alvin Paulsen and Glenn E. Mortimore<sup>9</sup> studied pretreatment control testicular biopsy specimens from 20 healthy males, 15-46, who were residents of mental institutions. More than were anticipated showed defects in spermatogenesis. Changes were similar to those in infertile men with oligospermia. The men were given injections daily for 24-99 days or pellet implantations of testosterone. Testicular biopsy was done at intervals for a year.

(8) *Fertil. & Steril.* 2:152-161, Mar.-Apr., 1951.

(9) *Ibid.* 1:415-422, September, 1950.

In all, spermatogenesis was damaged, as judged by the appearance of the second specimen taken at cessation of treatment. There were decrease in size of seminiferous tubules, sclerosis and hyalinization of basement membrane and tunica propria of tubules, necrosis and sloughing of germinal elements, arrest of sperm formation and decrease in germinal elements, spermatids and spermatocytes disappearing more rapidly than spermatogonia. All showed absence or atrophy of Leydig cells.

Biopsy specimens taken 5-31 months after cessation of testosterone treatment all showed decided improvement over those studied at the end of the treatment period. Each was either remarkably better than the initial specimen or, if the initial specimen had been rated excellent, was rated equally good. The most striking phenomenon was the disappearance of hyalinization of the seminiferous tubules.

In one patient with an elevated gonadotrophin level, moderate testicular damage and sperm output of 3-4/low power field, 100 mg. testosterone daily for one month caused initial suppression of sperm output. However, 23 months later, sperm output was 63 and 58 million/cc.

As a result of testosterone administration, despite temporary damage, testicular morphology and function may be ultimately improved over pretreatment status if the testis is originally less than excellent.

In the discussion, Heller pointed out that these results do not constitute suggestions for definitive treatment, for it is not known what type of a testis will respond, what type will recover or what type will be depressed and stay depressed.

**Experimental Recanalization of Fallopian Tubes in Macacus Rhesus Monkey** is reported by Mario A. Castallo<sup>1</sup> (Jefferson Med. College). Intubated salpingostomy was performed under dial anesthesia, using different materials in each of four animals, no. 32 silver wire, no. 26 stainless steel wire, fine whalebone filament plus no. 26 stainless steel wire and fine caliber polyethylene tubing. Result of the procedure is shown in Figure 67. After four weeks laparotomy was again done on each monkey; serial sections were made and studied.

Recanalization and regeneration of fallopian tubes took place after intubation in all four animals (Fig. 68). How-

(1) Fertil. & Steril. 1:435-442, September, 1950.

Anchor sutures

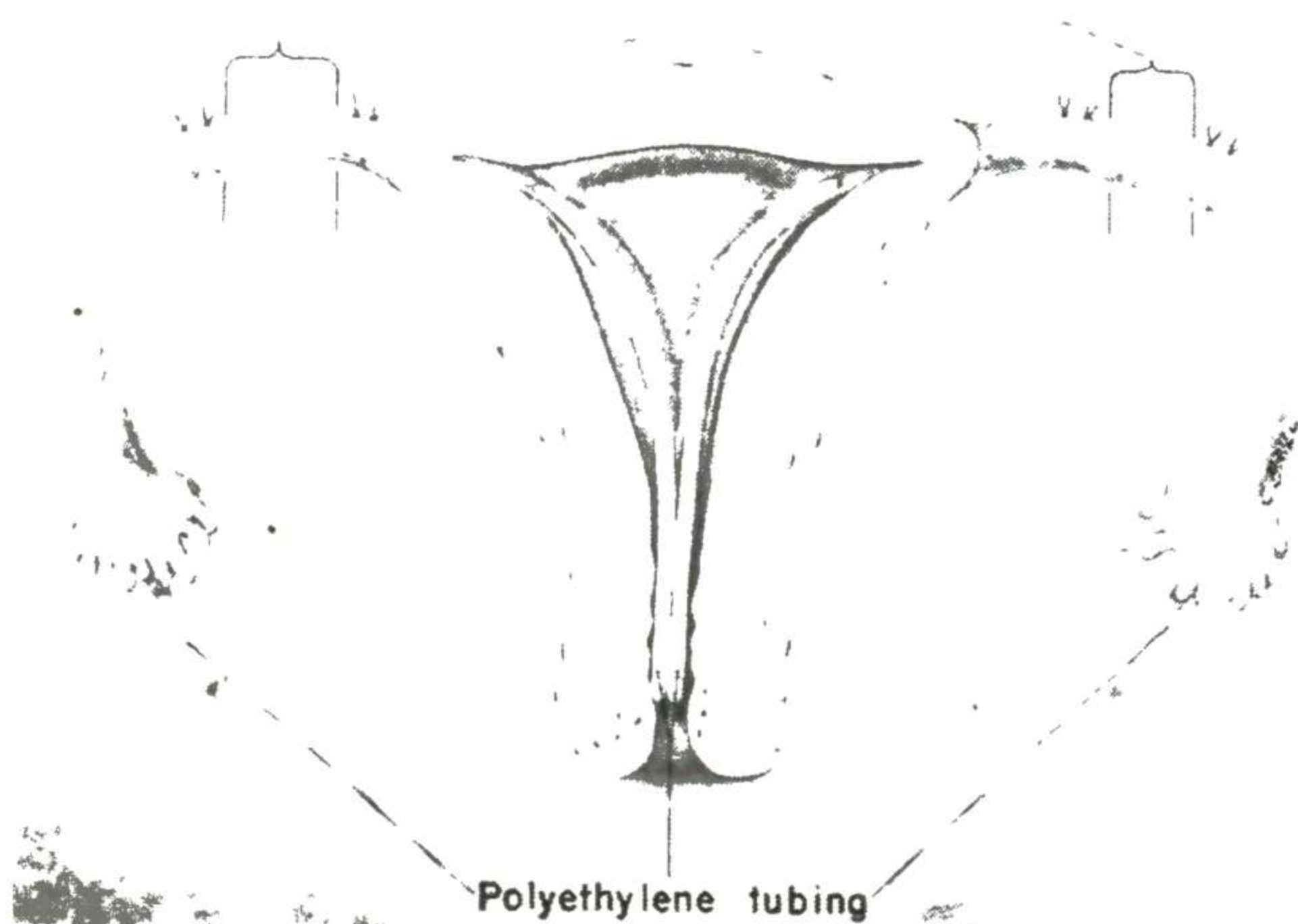
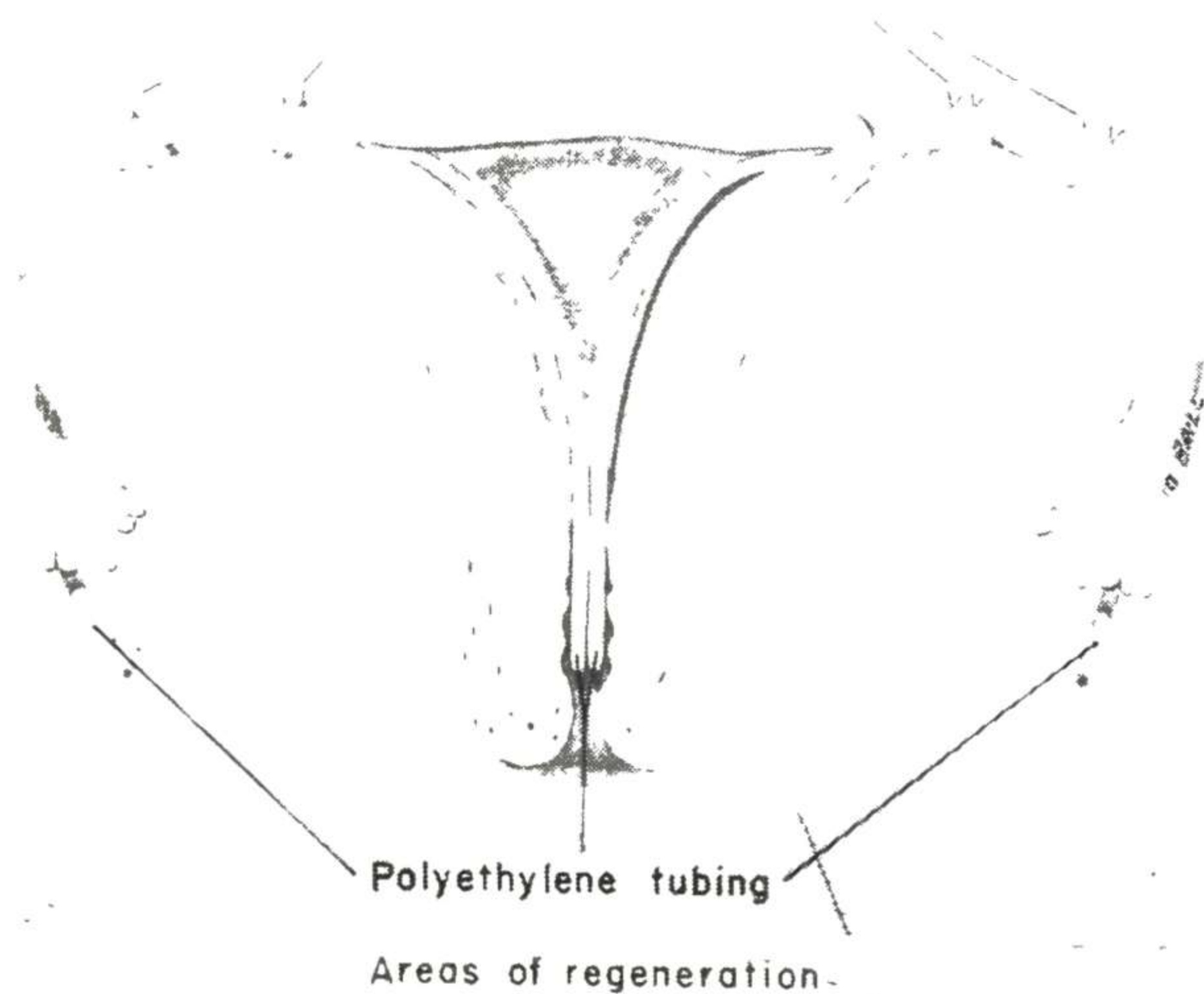


Fig. 67 (top).—Polyethylene tubing in situ after removal of middle section of fallopian tube.

Fig. 68 (bottom).—Diagram showing areas of regeneration of tubes.

(Courtesy of Castallo, M. A.: Fertil. & Steril. 1:435-442, September, 1950.)

ever, results with silver wire and steel wire filaments used in intubation were unsatisfactory, with inflammation, fibrosis and adhesions; whalebone produced fibrosis. The polyethylene tubing was the most innocuous bridging agent, producing no fibrosis. Possibility of overcoming human sterility by plastic surgery on occluded fallopian tubes by this method seems favorable.

**Artificial Insemination with Husband's Sperm** is discussed by Frederick M. Hanson and John Rock<sup>2</sup> (Harvard Univ.). Indications are (1) faulty spermatozoa reception, (2) hostility of endocervical secretions or (3) inability of husband to deposit sperm in vagina, according to some authors; others find it rarely of any value. Semen is commonly deposited in the uterus, cervix or vagina. Intrauterine deposition involves danger of endometritis, salpingitis and peritonitis from irritation by whole semen and infection from contaminated material. Uterine contractions, stimulated by a foreign body, may result in expulsion of the specimen. Intracervical insemination has the same drawbacks, especially if the injection is forceful enough to cause some material to reach the upper regions. Deposition in the posterior fornix is therefore preferable, combined with adjunctive measures such as previous alkaline douching, cleansing of the vagina by the physician before insemination and keeping the patient supine 30 minutes after the procedure.

Ejaculates were washed with Locke's solution and centrifuged at 3,500 rpm without injury to sperm. Common methods of intrauterine, intracervical or vaginal insemination were used in 92 patients, with an average of 4.2 inseminations/patient. Treatments were given during a period of  $14 \pm 2$  days before estimated onset of menstruation, but only 50 per cent actually fell within this period. Of 92 patients actually inseminated in the  $14 \pm 2$  day period, 7 were impregnated, with definite oligospermia in only 3, premature ejaculation in 1, hypospadias in 2 and unexplicable failure of conception in 1. Three of these seven had been treated with unwashed and four with washed semen.

After this series, two new methods were used to deposit the maximal quantity of sperm near the cervix. (1) A plastic

(2) *Fertil. & Steril.* 2:162-174, Mar.-Apr., 1951.

cervical cap with a short piece of tubing attached to a hole near its rim was placed over the cervix after the vagina was cleansed of mucus. Through the opening of the tube at the introitus the cap was filled with semen, the tube plugged and the patient allowed to go about her business for three hours; the cap was then removed. (2) A cervical plug was made by shortening a hard rubber Thomas pessary to  $\frac{1}{2}$  in. and boring a small hole through it lengthwise, and a needle stop was placed  $\frac{1}{2}$  in. from the distal end. In some patients this plug was placed in the cervix: 0.7-1 cc. concentrated semen was injected through the hole with a needle and expulsion of the plug was prevented by a gauze tampon.

Forty-two patients were inseminated by either of these methods, one to six inseminations (but only one in each cycle) being used for each patient. Treatments were timed by reference to temperature charts. Ovulation was assumed to occur at the time of slight temperature drop just preceding a significant rise, but since variation is so slight, ovulation time was estimated before treatment. One pregnancy resulted from 22 inseminations with cap technic and two pregnancies in 38 patients through pessary insemination. Only 14 women were inseminated at ovulation time, just before significant rise in temperature, and thus the three pregnancies represent 21 per cent success. One of these pregnancies ended with a normal delivery; the second, after one pessary insemination, in a tubal pregnancy and the third, after one cap insemination, in abortion during the third month.

Reports of husband insemination are not common in the literature. Only Whitelaw presents results from cap insemination with untreated semen, and he obtained 14 pregnancies in 32 women with only two abortions. Artificial insemination with husband's semen is thus a worthwhile procedure.

[My results with artificial insemination using the husband's sperm have been less than half as good as when using donor's semen. There are times when the husband's sperm should be used for artificial insemination, not only in the rare cases of hypospadias and inability to maintain an erection but also in some cases of deficient sperm.

Lamson, Pinard and Meaker present in the following article a discussion of sociologic and psychologic aspects of artificial insemination. They say that donor semen is undoubtedly destined to be used more and more as time goes on, but sociologic and psychologic contraindications are numerous and important. Incalculable harm will be done if practi-



tioners neglect these and start using donor insemination as a sort of assembly line technic aimed at mass production, as a routine manipulation of life or as an impersonal regimentation of the human reproductive power.—Ed.]

**Sociologic and Psychologic Aspects of Artificial Insemination with Donor Semen** are discussed by Herbert D. Lamson, Willem J. Pinard and Samuel R. Meaker<sup>3</sup> (Boston Univ.). In most sterile matings, responsibility is divided between the partners, each of whom shows some degree of infertility. In about 10 per cent of cases the fault lies wholly, and in another 20 per cent chiefly, with the male. Statistically, barren marriages prove less stable and are at least twice as likely to break up as are those with children; suicides are twice as common among married, childless persons as among parents. However, studies have shown that unhappiness and poor marital adjustment are much more prone among those who do not desire children than among those who cannot have them. Children do not necessarily assure success in marriage, and couples who state that divorce is inevitable unless they can have a baby are harboring an illusion which it is of dubious value to encourage.

Donor insemination is not illegal, nor is it considered immoral by most groups, but since it does overstep conventional mores, it requires particular evaluation of psychologic aspects. A wife denied motherhood frequently adjusts to the situation. However, she may become resentful, and devaluation of her husband's masculinity is bound to follow and add greatly to existing tension. Three sorts of reaction have been listed in wives of sterile men. The masculine-aggressive woman, insisting on a child of her own body, forces consent from her husband and is a ready but rarely an ideal candidate for insemination. Other women accept childlessness but require their husbands to achieve material success as proof of masculinity. The truly motherly woman channels her feelings toward other persons or objects, real or symbolic.

Men find it easy to allocate their productive impulses to other goals, but sterility may create feelings of inadequacy because of their inability to satisfy their wives' desires. To some, donor insemination may aggravate this feeling, creating jealousy of the unknown donor and resentment toward

(3) J. A. M. A. 145:1062-1064, Apr. 7, 1951.

the child. Artificial insemination in such families invites emotional disaster. Other men have basically opposite attitudes, are undisturbed by the idea of another man's intrusion, welcome the child and soon identify themselves in the role of father. Most men belong to an intermediate group, in which reluctance and hesitation at the outset are overcome in order to make the wife happy, obtain a child the man desires or discharge guilt feelings. This group requires careful psychologic evaluation; the husband may make a good, permanent adjustment, or the attitude of acceptance may be unstable and transitory and one of resentment, hate and disgust may develop later.

## OPERATIVE TECHNIC

**Perineotomy**, a perineal plastic operation designed to increase the size of the introitus, is rarely required but, when indicated, gives excellent results, according to John W. Huffman<sup>4</sup> (Northwestern Univ.). The clearcut indications include (1) dyspareunia due to congenital deformities of perineum or hymen, (2) dyspareunia due to scars of vulva or perineum, (3) congenital or acquired perineal abnormalities, discovered premaritally, which will interfere with coitus and (4) rarely chronic leukorrhea and vaginitis due to poor vaginal drainage. Simple incision of the hymen is usually not sufficient, for the size of the introitus depends more on the height of the perineum than on the width of hymen. Usually, when the hymen is thick and firm the perineum will be high and rigid. To ensure relaxation of the perineum with enlargement of the introitus, the perineum must be incised deeply in the midline.

**PROCEDURE.**—The operator's left forefinger, placed in the rectum, puts the rigid perineum under tension and serves as a guide for the perineal incision (Fig. 69). Incision is made dorsally through the hymen, through the perineal skin, the perineal body and the posterior vaginal mucosa (Fig. 70). With traction on the sides of the incision, scissors dissection separates the vaginal mucosa from underlying muscle sufficiently to allow mobilization without tension (Fig. 71). The hymenal ridge is freed laterally. Good hemostasis beneath the mucosal flap is essential to prevent postoperative hema-

(4) *Surg., Gynec. & Obst.* 92:355-359, March, 1951.

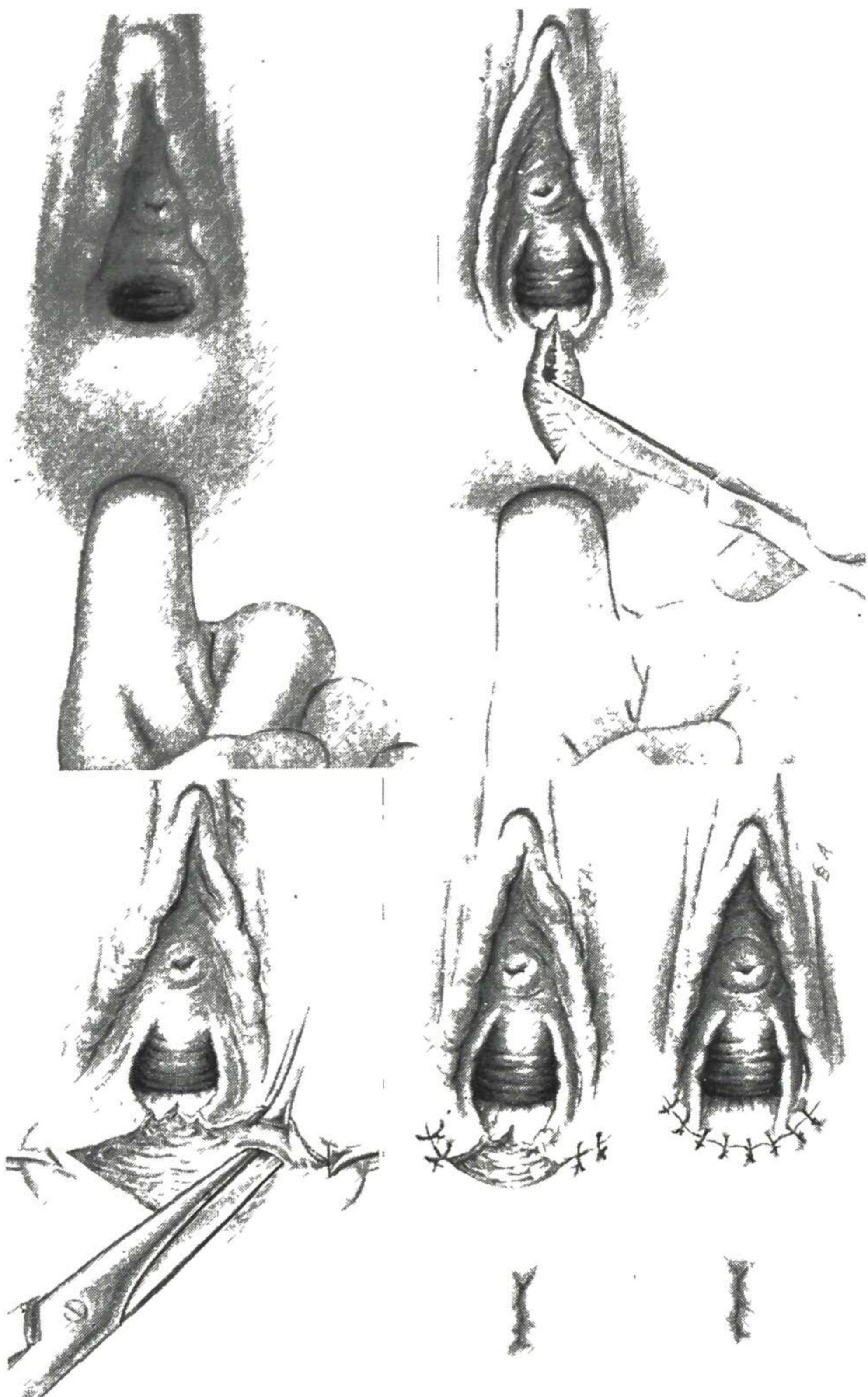


Fig. 69 (top left).—Surgeon's left forefinger in rectum serves as guide for incision and protects the rectum.

Fig. 70 (top right).—Incision through hymen, perineum and posterior vaginal mucosa.

Fig. 71 (bottom left).—Dissection of vaginal mucosa from underlying muscle.

Fig. 72 (bottom center).—Closure with interrupted sutures.

Fig. 73 (bottom right).—Completed operation. Hymen forms two curtain-like lateral folds and vaginal mucosa a troughlike floor for the introitus.

(Courtesy of Huffman, J. W.: *Surg., Gynec. & Obst.* 92:355-359, March, 1951; from Curtis and Huffman: *Textbook of Gynecology* [Philadelphia: W. B. Saunders Company, 1950].)

toma. Interrupted anteroposterior fine catgut sutures are used to unite the vaginal mucosa to the perineal skin; underlying muscle is not sutured (Figs. 72 and 73).

In 32 patients with dyspareunia, this operation gave good results in 28 and poor results in 1; 2 could not be traced. In eight patients with premarital lesions, results were good in six, poor in one, and one patient was not followed. Poor vaginal drainage and vaginitis were relieved in two patients.

**Culdocentesis.** Dan W. Beacham and W. D. Beacham<sup>5</sup> analyzed over 500 cases at Charity Hospital from 1947 to 1950. Culdocenteses were usually done when either hemoperitoneum or abscesses partially or entirely situated in the culdesac were suspected. About 55 per cent were done in clinics or admitting rooms, 30 per cent in examining rooms for inpatients and 15 per cent in operating rooms. Anesthesia was rarely used. The short period of maximal pain was usually tolerated without untoward effects.

**TECHNIC.**—Patient is placed in lithotomy position of abdominopelvic examination. After palpation, the cervix and posterior vaginal fornix are exposed by speculum and the posterior cervical lip grasped and elevated with a tenaculum. The fornix is sponged dry and an antiseptic solution applied. An 18 gauge spinal needle is thrust into the center of the culdesac or into the palpated mass in a direction parallel to the uterine body (Fig. 74). Depth of insertion rarely exceeds 2 cm. Suction is applied by syringe and, if no fluid is obtained, is maintained as the needle is slowly withdrawn. The end of the needle should not wander. Usually the needle should be withdrawn completely in one minute. If venous or arterial blood or feces is aspirated, a repeat aspiration is made with another set. If nothing is obtained on the first attempt, the needle is reinserted with a change of direction and/or position. Usually not more than three aspirations are performed at one time. Aspirations, if unsuccessful, may be repeated again in several hours. Fluid obtained should be examined immediately.

Clear or faintly cloudy fluid from the peritoneal cavity or adnexal cysts should be studied by smear. Definitely cloudy fluid from similar structures and frank pus which indicates an abscess or peritonitis should be studied by smear and/or culture. All blood aspirated should be observed for six minutes for coagulation; that from a vein or artery will clot. Blood that does not clot indicates a hemoperitoneum or blood-filled cyst.

Most patients treated surgically for ectopic pregnancy have some degree of hemoperitoneum, but recognition may

(5) *New Orleans M. & S. J.* 103:283-288, January, 1951.

be difficult. Culdocentesis is the simplest and most practical means of positive identification. Before 1947 culdocenteses were done in less than 30 per cent of ectopic pregnancies and accurate preoperative diagnoses made in less than 65 per cent. During the last 13 months of this study, aspirations were performed in 90 per cent, with 95 per cent correct preoperative diagnosis. Further, over 80 per cent of these patients were operated on less than six hours after hospitalization.

Of 194 cases of hemoperitoneum aspiration failed in 4.8

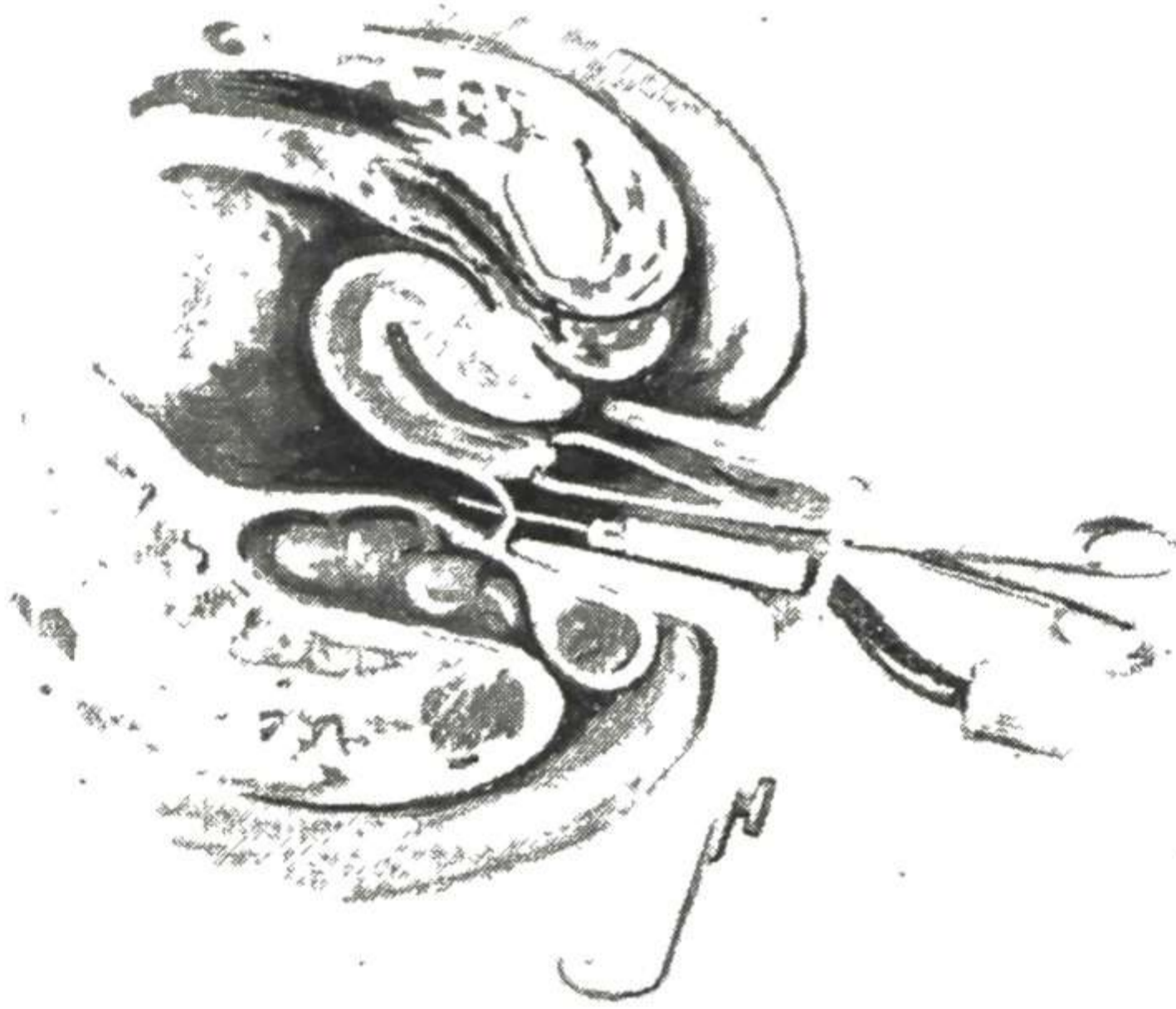


Fig. 74.—Aspiration of the culdesac. (Courtesy of Beacham, D. W., and Beacham, W. D.: *New Orleans M. & S. J.* 103:283-288, January, 1951.)

per cent, primarily because of technical difficulties which usually can be overcome in subsequent aspirations. In over 500 aspirations mistaken diagnoses led to unwarranted laparotomy in six cases. Routine observation of blood coagulation will correct such errors.

[Culdocentesis or aspiration of the contents of the posterior culdesac is a controversial procedure. Some gynecologists deny that it has any value and insist that it may even be dangerous, whereas others find it of the greatest value, particularly in cases of suspected ruptured ectopic pregnancy. I have used it in many cases to prove the presence of blood in the peritoneal cavity. I use it also almost routinely in cases of pelvic abscess (1) to remove some of the pus and (2) to use the needle point as the site of the incision into the posterior culdesac. The operation is simple and entails almost no risk. As emphasized by Beacham and Beacham, when blood is aspirated it is difficult to tell whether the blood is from an artery or vein or whether it has been aspirated from the posterior

culdesac. Blood aspirated from a vein or artery will clot, and all blood which is aspirated should be observed for six minutes to determine whether or not coagulation will take place. If the blood does not clot it is evident that it has been obtained from a hemoperitoneum or a cyst filled with blood.

In the ectopic pregnancies reported by Douglas, 52 patients had culdesac aspirations and blood was obtained in 47 of them. Schmelzer (*Zentralbl. Gynäk.* 72:968, 1950) also found pelvic puncture to be extremely useful in 49 cases of extrauterine pregnancy.—Ed.]

**Prolapse of Uterus: Review of 722 Cases Treated by Parametrial Fixation Operation.** Morris A. Goldberger and David Zakin<sup>6</sup> consider the vaginal approach alone preferable, in general, to the combined vaginal and abdominal approach. Of 334 postmenopausal patients, 159 had experienced menopause 5-35 years before. There was first degree prolapse in 63.7 per cent, second degree in 23.5 per cent and third degree (complete protrusion) in 12.8 per cent. Of 580 cases in which the cervix was clinically described, it was clean and/or atrophic in 91 and grossly diseased in 489; microscopic examination of 584 cervixes revealed disease in 582.

Parametrial fixation of the uterus was done in 665 cases, of the cervical stump in 40 and of the vaginal vault in 1; parametrial advancement of the uterus was done in 19 cases and of the stump in 1. Routine dilatation and curettage did not reveal malignancy. Only 11 patients, 10 of whom had previous plastic vaginal surgery, did not require colporrhaphy. Anterior and posterior colporrhaphy and perineorrhaphy were done in 651, anterior colporrhaphy in 35 and posterior colporrhaphy and perineorrhaphy in 25.

Postoperatively there were 35 cases of proved urinary tract infection (cystitis and pyelitis). Thrombophlebitis appeared in 15 patients, with radiologic evidence of pulmonary infarction in 4. Femoral veins were ligated in 2 patients, 1 of whom died of embolism; the other 13 recovered with conservative therapy. There was one other death due to a nursing accident. Follow-up in 665 patients (92 per cent) from 2 months to 10 years showed cure of uterine prolapse in all but 7. Associated vaginal relaxations recurred in 146 cases: 86 cystocele, 31 rectocele, 23 cystorectocele, 5 urethrocele and 1 enterocele. Most of these were asymptomatic and would have been overlooked by questionnaire follow-up. Tubal ligations were done in 35 of 192 women of childbearing age. Six

(6) *J. Mt. Sinai Hosp.* 17:571-595, Mar.-Apr., 1951.

patients became pregnant; four delivered without recurrence and in two pregnancy was therapeutically interrupted. In 2,989 collected cases there were 238 deliveries with recurrence of prolapse in 40; parturition thus greatly predisposes to recurrence.

Parametrial fixation presents many advantages. It is conservative, technically simple, anatomically sound and preserves blood supply to pelvic structures. The operation is entirely extraperitoneal, which makes drainage simple, avoids peritoneal inflammation and makes shock less likely. The procedure is well tolerated by elderly patients and can be done under local anesthesia if necessary. Morbidity and mortality are low, and recurrence of uterine prolapse is uncommon. In younger women, menstrual function and reproductive potential are conserved. Vaginal delivery after the operation is often feasible, although cesarean section is advised in most cases, particularly if cervical amputation has been high. Parametrial fixation can be used in all degrees of prolapse, including complete procidentia.

[This is an excellent review of the literature and a thorough study of a large series of patients treated by parametrial fixation. I agree with the authors that pregnancy after a parametrial fixation operation is best treated by cesarean section because in most cases the cervix has been amputated.—Ed.]

**Enterocoele: Analysis of 52 Cases.** Enterocoele or, more correctly, posterior vaginal hernia, is a hernia of the layers of the body cavity wall, i.e., vaginal mucosa, its supporting fascia and peritoneum, in addition to intra-abdominal contents (Fig. 75). The sac of peritoneum dissects beyond its lower normal limits, between the vaginal mucous membrane anteriorly and the rectum posteriorly to emerge through the vaginal introitus. On the other hand, cystoceles and rectoceles are sliding hernias.

According to John C. Weed and Curtis Tyrone<sup>7</sup> (Tulane Univ.), enterocoele is primarily a disease of senescence. In 52 patients, average age was 56. Enterocoele often followed surgical procedures, especially vaginal hysterectomy when the uterosacral ligaments were not properly approximated and the culdesac inadequately obliterated. It also occurred after the Le Fort operation. The trauma of childbearing, effects of the erect position, development of fascial weakness

(7) *Am. J. Obst. & Gynec.* 60:324-332, August, 1950.

associated with the aging process and congenital defects are also causative factors. In 23 patients, prolapse of the uterus, cervical stump or vaginal vault was also present, giving rise

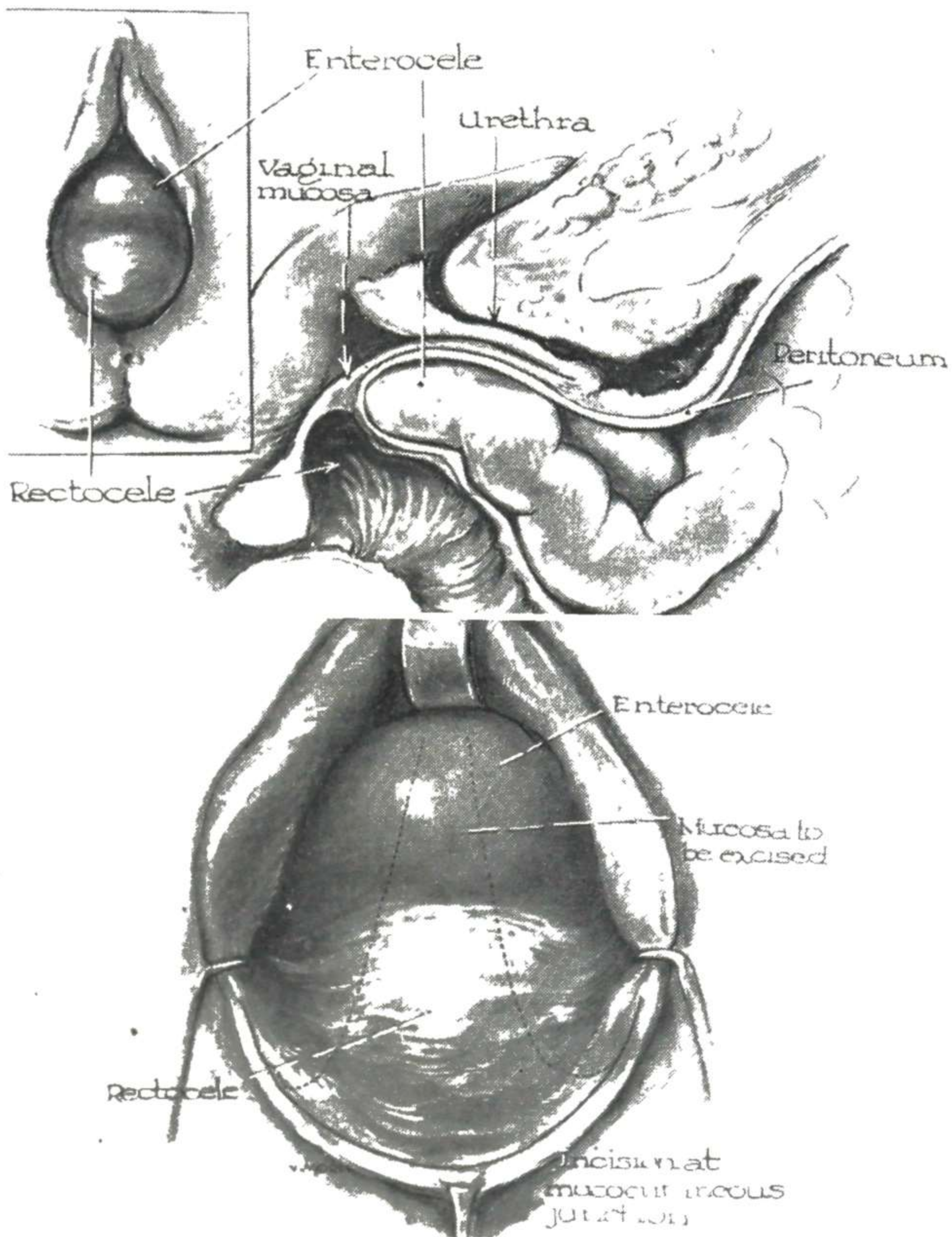


Fig. 75 (top).—Enterocele without prolapse of vaginal vault. Sagittal section showing extent of hernial sac.

Fig. 76 (bottom).—Incision of posterior vaginal mucosa.

(Courtesy of Weed, J. C., and Tyrone, C.: *Am. J. Obst. & Gynec.* 60:324-332, August, 1950.)

to “dragging sensations” and a sense of the “organs falling out.” Symptoms of enterocele alone were rectal fulness, inability to defecate, fecal impaction, feeling of incomplete emptying of the bowel and occasionally backache. Often the



hernia did not protrude except on straining or coughing or when a patient assumed erect posture.

For repair of enterocele, the vaginal approach offers the

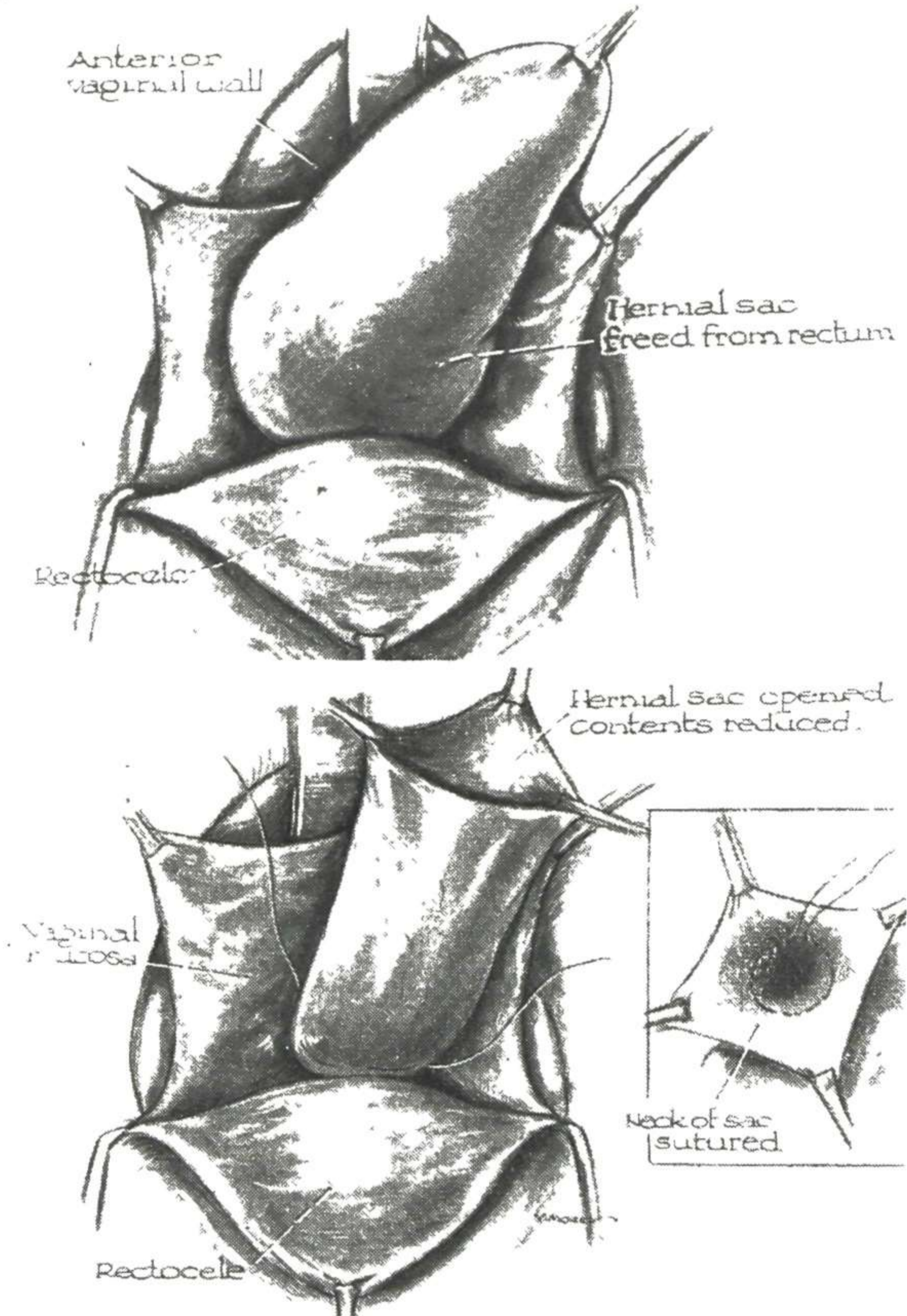


Fig. 77 (top).—With posterior vaginal mucosa elevated, hernial sac is dissected free from rectum and vaginal mucosa.

Fig. 78 (bottom).—Hernial sac is opened, its contents reduced and high ligation done.

(Courtesy of Weed, J. C., and Tyrone, C.: *Am. J. Obst. & Gynec.* 60:324-332, August, 1950.)

greatest advantages. The technic is shown in Figures 76-81. The posterior fascial layers should be repaired to obtain permanent cure and high ligation of the sac performed. There

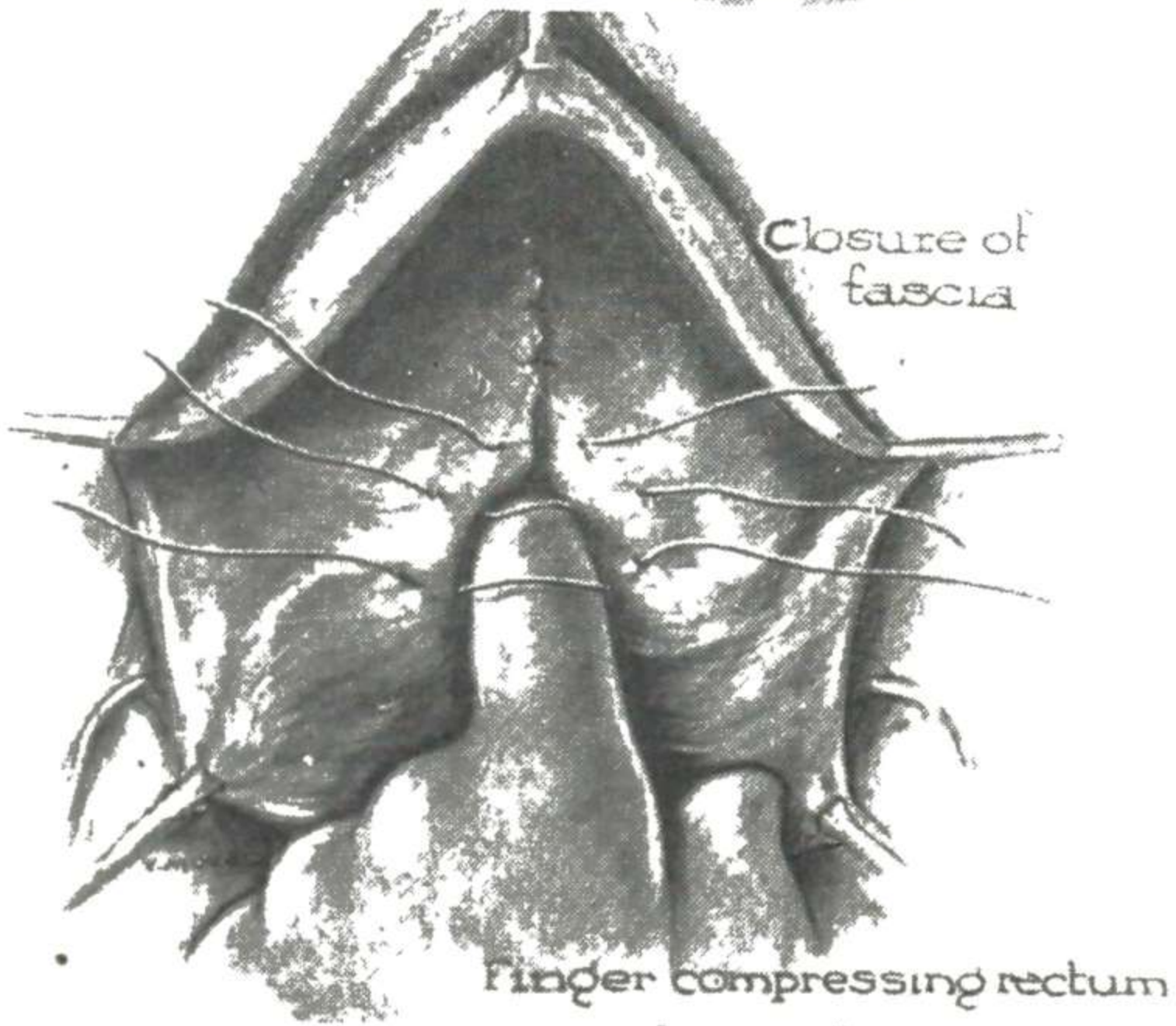
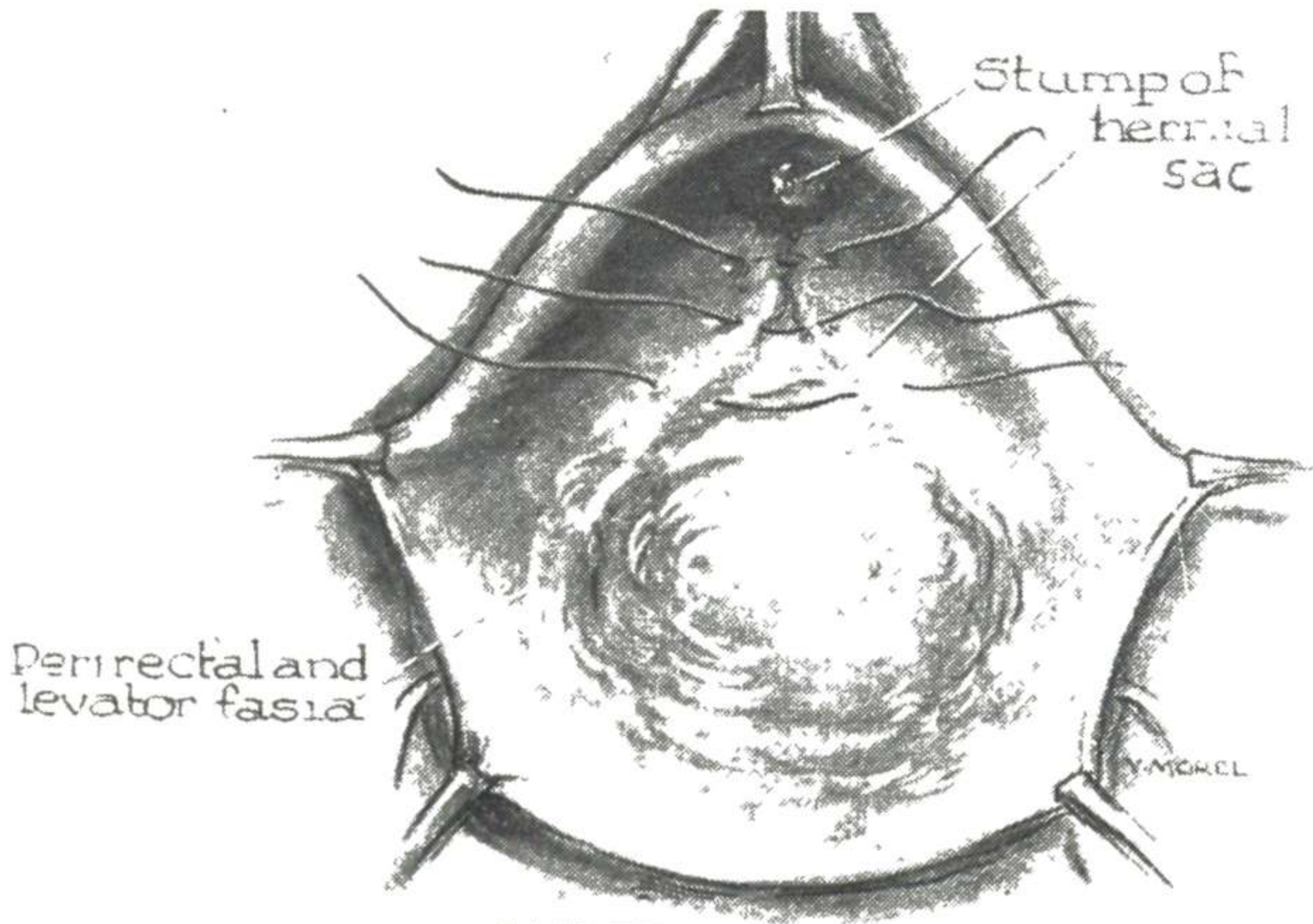


Fig. 79 (top).—Ligated stump of sac is buried by placing endopelvic fascia over it, continuing down to levator and fascia, which is approximated.

Fig. 80 (bottom).—Second row of sutures further supports posterior wall; this completes perineorrhaphy.

(Courtesy of Weed, J. C., and Tyrone, C.: *Am. J. Obst. & Gynec.* 60:324-332, August, 1950.)

were no deaths in this series and morbidity rate was 20.7 per cent.

[In the discussion of this paper Folger mentioned that in the University Hospitals, Cleveland, enterocele was recorded 95 times in 52,996 admissions. If a surgeon does not bear in mind the possibility of an enterocele, he will usually overlook the condition. Occasionally after repair of a cystocele or rectocele there is a so-called recurrence which is in reality an enterocele overlooked and not repaired at the time of the

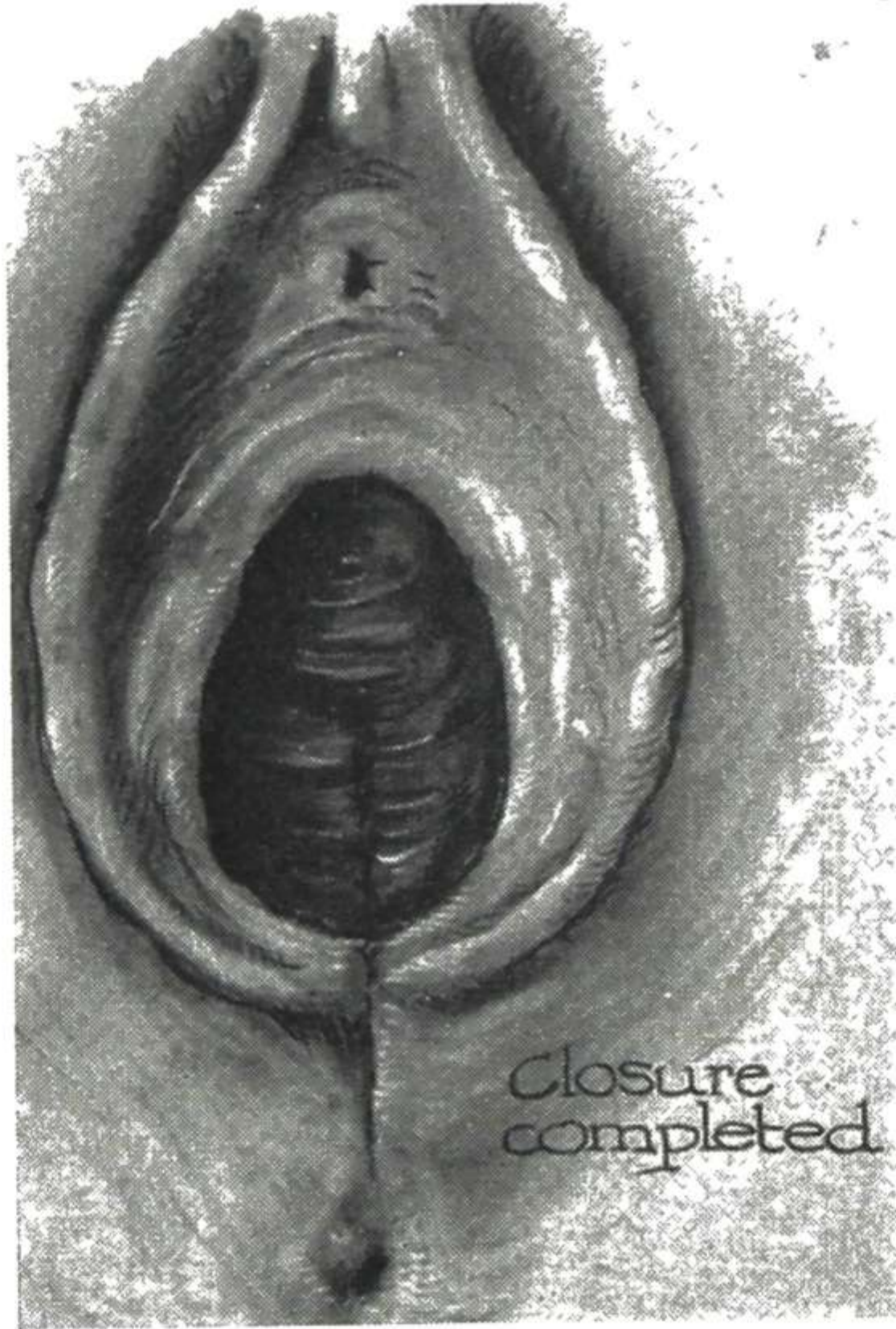


Fig. 81.—Complete posterior repair. (Courtesy of Weed, J. C., and Tyrone, C.: *Am. J. Obst. & Gynec.* 60:324-332, August, 1950.)

plastic operation. To establish the diagnosis of an enterocele, both a vaginal and a rectal examination is necessary. Furthermore, one should use a speculum in all cases to try to obtain the bulge produced by the enterocele. In some instances, the diagnosis can be made only with the patient standing up. Repair of an enterocele is essentially that of any abdominal hernia: the peritoneal sac must be isolated, ligated and removed and the remains pushed back and covered by fascia and muscle.—Ed.]

**Manchester Operation of Colporrhaphy in Treatment of Uterine Prolapse**, including amputation of the cervix during the childbearing age, does not preclude subsequent delivery through the birth canal. However, because of danger of uterine rupture attendant on pelvic delivery after extensive amputation of the cervix, Louis E. Phaneuf<sup>8</sup> (Tufts College)

(8) *Am. J. Surg.* 82:156-162, July, 1951.

uses the Manchester operation largely for patients past child-bearing age. Before surgery, cystoscopy and pyelography are done and disorders corrected; antibiotics and sulfonamides are useful. Decubitus ulcers on the cervix or vaginal walls are healed by bed rest with daily mild antiseptic and astringent douche.

**TECHNIC.**—The cervix is dilated and uterine cavity curetted. Transverse incision is made in the anterior vaginal wall where it joins the cervix, and the superior edge is made taut with Allis forceps. Separated from the bladder with sharply pointed curved scissors pointed against it, the anterior vaginal wall is incised in the median line to 1.5 cm. below the urinary meatus. The bladder is separated from the vagina and raised by Allis forceps. The uterovesical ligament is cut, freeing the bladder and exposing bases of broad ligaments (parametria). Three no. 1 chromic catgut sutures are introduced in bases of broad ligaments and left untied. The posterior vaginal wall is dissected from the cervix, which is amputated below the lower suture in the broad ligaments. Three or four no. 1 chromic catgut sutures attach the posterior vaginal wall to the cervical canal; these sutures are tied and cut. The lateral vaginal wall is attached to the anterior lip of the cervix by three no. 1 chromic catgut sutures which are left untied. The three sutures in the broad ligament are tied and cut. Interrupted sutures of no. 0 chromic catgut are placed in musculofascial tissues on the sides of bladder, tied and cut. Cystocele has been corrected. Excess vaginal wall is resected on each side; enough is retained to bring the vaginal wall edges together under tension. Sutures approximating the vaginal wall to the anterior lip of the cervix are tied and cut. Interrupted no. 0 chromic catgut sutures starting at the cervix and ending at the upper angle of the vaginal incision below the urinary meatus close the anterior vaginal wall. The pelvic floor is repaired. Some sutures in the anterior vaginal wall show above the repaired perineum.

Results were satisfactory in the 126 patients operated on (oldest, 80). The first patient suffered a recurrence, a medium-sized cystocele, indicating that the deep tissues should be approximated independently of the vaginal walls. Incision higher on the posterior vaginal wall close to the cervix usually prevents a lax posterior fornix (which occurred in a few early cases).

Postoperative urine retention is avoided by using a Malecot self-retaining catheter for seven days and gantrisin® as an antiseptic. Suture of the vaginal mucosa to the cervical canal with no. 1 (40 day) chromic catgut almost eliminates secondary hemorrhage from the cervix. Occlusion of the

cervix is prevented by dilatation with graduated dilators before reconstructing this organ. If indicated, a stem pessary may be worn for 10-12 postoperative days. Resection of the vaginal flaps so that they come together without tension prevents vaginal adhesions; any adhesions disclosed by examination on the 12th postoperative day are broken up, while thin and superficial, with a finger lubricated with Irish moss jelly. The vagina is packed lightly with petrolatum gauze for 48 hours to prevent recurrence. Leaving the wall slightly lax avoids narrowing of the vagina; the deep structures by approximation furnish support; the resected vaginal walls merely act as covering.

**Vaginal Plastic Surgery in Treatment of Lacerations and Displacements of Female Genital Tract: Study Based on 1,143 Patients Operated on from Jan. 1, 1938, to Jan. 1, 1948.** Using 27 technics, Louis E. Phaneuf<sup>9</sup> (Tufts College) carried out 2,176 procedures on 1,143 women, 16.2 per cent of whom were over age 60. Coronary thrombosis, cerebral hemorrhage, bronchopneumonia and biliary disease caused four deaths. All types of anesthesia were used, with local and spinal anesthesia offering many advantages. Three important factors govern results: age and general condition of the patient, condition of the tissues that must be approximated for support, and type of work the patient expects to do postoperatively. The normal recurrence rate of about 5 per cent increases as postoperative years increase.

A simple effective vaginal hysterectomy for prolapse, seldom complicated by postoperative posterior enterocele, is done with lateral fixation of the pedicles (Figs. 82 and 83).

**TECHNIC.**—The uterus is extruded, and a circular incision made in the vaginal wall (Fig. 82, *A*), which is then separated from the uterus in all directions (*B*). A small opening is made in the culdesac of Douglas with scissors, the opening enlarged with the fingers, and peritoneal edge of the culdesac of Douglas picked up with a fine catgut suture, with ends held long (*C*). The bladder and ureters are pushed upward away from the uterus, the anterior peritoneal culdesac is opened and the peritoneal edge picked up with a fine catgut suture, the ends held long (*D*). The uterine fundus is delivered through the anterior or posterior culdesac, whichever is more convenient—in this instance through the posterior culdesac (*E*). Because of excessive length of the cervix, as downward traction was made on it the uterine fundus appeared

(9) *Am. J. Obst. & Gynec.* 60:1068-1087, November, 1950.

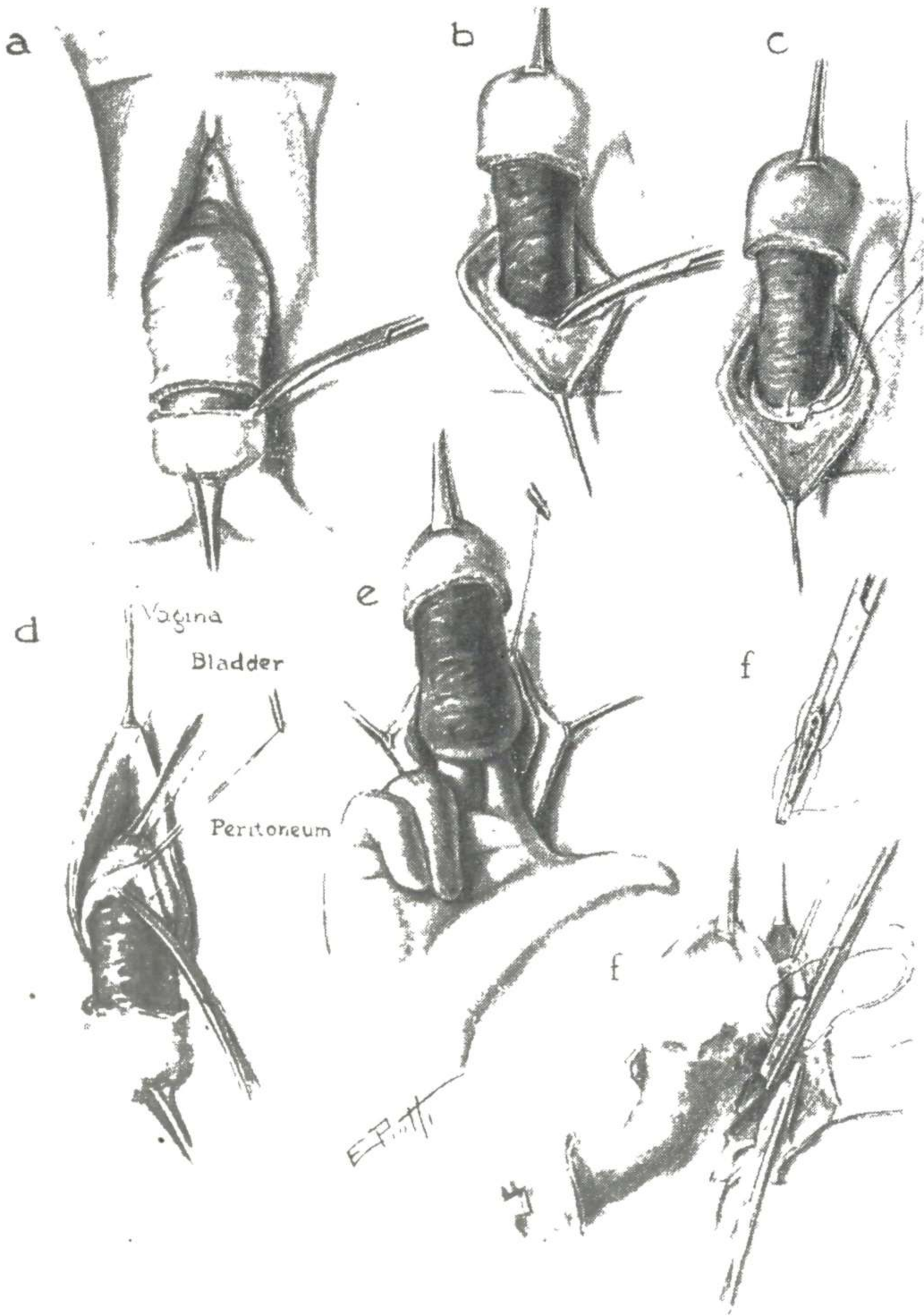


Fig. 82.—Vaginal hysterectomy with lateral fixation of pedicles. (Courtesy of Phaneuf, L. E.: *Am. J. Obst. & Gynec.* 60:1068-1087, November, 1950.)

anteriorly, under the symphysis, and was so held (*F*). The left broad ligament is clamped in two sections. The lower section includes the uterosacral and cardinal ligaments and vaginal and uterine vessels; the upper section includes the tube, ovarian ligament, round ligament and upper part of the broad ligament. Three clamps must sometimes be used when the broad ligament is very wide. Clamps are replaced by pulley sutures of chromic catgut (*F'*).

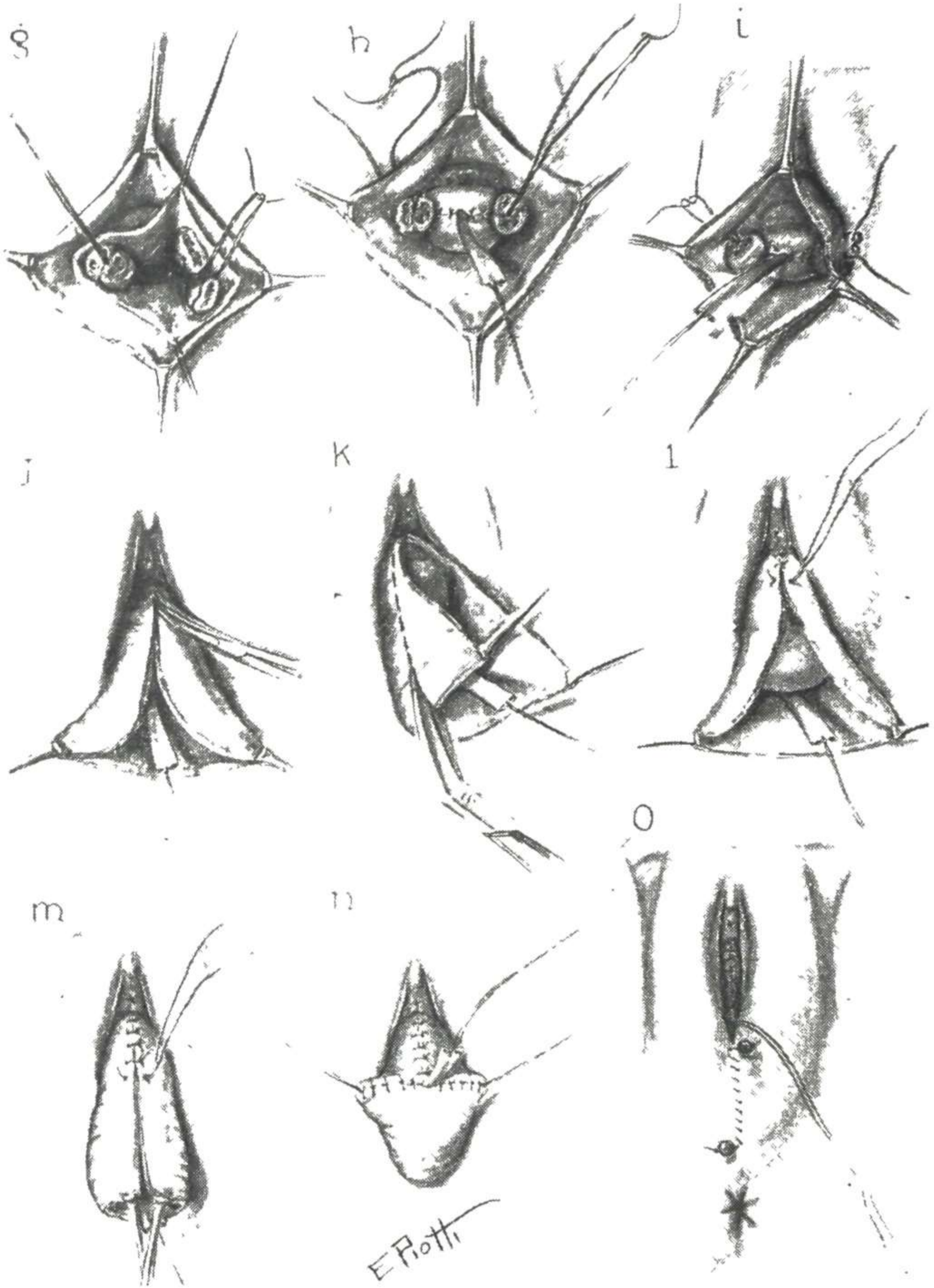


Fig. 83.—Completion of operation after removal of uterus. (Courtesy of Phaneuf, L. E.: *Am. J. Obst. & Gynec.* 60:1068-1087, November, 1950.)

The right broad ligament is treated in the same manner. The uterus is removed and the broad ligament pedicles of each side are tied together with chromic catgut, the ends held long.

Peritoneal edges, above and below, are held by fine catgut sutures (Fig. 83, *G*). The peritoneum is closed with interrupted sutures of fine chromic catgut (*H*). A small Penrose tube, held by a fine silk suture at its vaginal end, drains the peritoneal cavity.

The broad ligament pedicles are not extraperitoneal. On the right the two ends of the suture holding the pedicles are passed through the vagina laterally. The sutures holding the pedicles are passed on each side of the vagina laterally and tied (*I*). Traction is made on the anterior vaginal wall by means of Ochsner or Allis forceps (*J*). The anterior vaginal wall is separated, by means of scissors, from the bladder and urethra, to a point 1.5 cm. below the urinary meatus, incised in the median line and dissected from the bladder and urethra on each side. The excess of vaginal flap on each side is resected, leaving a wide triangular denuded area (*K*). The flap consists of the muscular layer of the anterior vaginal wall with its overlying mucosa. The anterior vaginal wall is closed from the urethra downward with interrupted chromic catgut sutures (*L* and *M*) to the transverse incision, which is closed in a transverse direction (*N*). The drain, which is removed at the end of 48-72 hours, is seen in the center. The lateral fixation sutures are cut, the vagina is returned to the pelvis, and the vault pulled upward by the pedicles as soon as traction is released. The perineum is repaired in four layers (*O*). Any enterocele is appropriately treated. The ends of the silk suture on the drain are held with a small strip of adhesive plaster. No knots are tied in the skin; the ends of the fine catgut suture are held with lead shot.

[Phaneuf has had a most unusual and extensive experience in gynecologic surgery. He has employed practically every type of vaginal plastic operation which could be used to repair vaginal lacerations and displacements. There are several points of interest in this article. Apparently Phaneuf performed what is now known as the Spaulding-Richardson operation before it was popularized by Spaulding or Richardson. Likewise, Phaneuf has long used a modification of the Manchester operation which he called the Alexandroff principle. I was amazed to find that Phaneuf performed bilateral trachelorrhaphy 144 times and unilateral trachelorrhaphy 17 times even if the operations on the cervix were done for the most part as one step in general pelvic repair. I rarely repair a cervix surgically. Mild pathologic processes in the cervix can be remedied by electric cautery. I am not worried about scars because they do not lead to cancer or cause any other trouble in most instances. In women past 45 whose cervix is really bad, the uterus is generally enlarged and troublesome. In such cases, a vaginal hysterectomy is better than cervical repair. The following statement by Phaneuf concerning his excellent results in perineorrhaphy deserves emphasis: "I attribute whatever success I may have had with these operations to careful sharp dissection, complete hemostasis, free mobilization of the structures involved, approximation of the tissues without tension, layer by layer with fine suture material, and meticulous nursing by nurses highly trained in this work." This analysis of operations performed by a master gynecologic surgeon is worthy of careful study.—Ed.]

**Intracavitary Radium at Time of Vaginal Plastic Operation** for benign uterine disease is not used by many gynecologists, despite clear indications, apparently because they fear that irradiation will hamper healing. Lennard L. Weber<sup>1</sup>

(1) Am. J. Obst. & Gynec. 60:371-378, August, 1950.



(Mount Sinai Hosp., Philadelphia) therefore analyzed results in 131 consecutive patients who underwent simultaneous repair of the vagina and intrauterine radium implantation for benign disease in 1928-47. In none was there delayed healing or wound breakdown. All complications were those of the immediate postoperative period, chiefly minor difficulties which are common after vaginal plastic procedures when radium is not used. Asymptomatic pyuria was noted in 18.4 per cent of patients and difficulty in voiding in 13 per cent. Only one patient had perineal wound infection, although 78.5 per cent showed some form of chronic cervicitis. Anatomic results of vaginal repair were considered successful in all patients but one in whom faulty technic was apparently to blame.

Most patients received radium for some form of abnormal bleeding (menorrhagia in 35.1 per cent, metrorrhagia in 27.5 per cent and menometrorrhagia in 19.8 per cent). Despite the change in optimal dosage for radium-induced menopause from 1,200 to 2,400 mg.-hr. over a period of years, analysis revealed that 1,200 mg.-hr. was adequate in all cases. Only one patient had any form of vaginal bleeding after the third postradiation period and she had been given repeated doses of estrogenic substance.

All patients had dilation and curettage. In one, the endometrium showed early adenocarcinoma. She received 2,400 mg.-hr. radium and underwent total hysterectomy and bilateral salpingo-oophorectomy six weeks later. Examination of the uterus after removal showed no evidence of carcinoma. In no patient had endometrial carcinoma developed 1-20 years after intrauterine use of radium. In one, papillary adenocarcinoma of the ovaries developed 15 years later.

No reason was found for avoiding use of intracavitary irradiation at the time of performing any type of vaginal colpoplasty.

[I am one of those who have hesitated to use radium at the time of a vaginal plastic operation, but I should add that during the last few years I have rarely employed radium for benign conditions since I encountered several cases of carcinoma of the endometrium a few years after radium was used to stop hemorrhage associated with hyperplasia of the endometrium. It is gratifying to read that in Weber's series no patient developed carcinoma of the endometrium during 1-20 years after intrauterine radium therapy for benign disease. In large groups reported from Phila-

delphia and New York there were many cases of carcinoma which followed radium therapy.—Ed.]

**Review of 500 Elective Operations for Pelvic Prolapse on Women over Age 60.** A. C. G. Frost<sup>2</sup> (Vancouver, B. C.) found 28 cases (5.6 per cent) of operative shock and 6 (1.2 per cent) of pulmonary embolus, of which 4 (0.8 per cent) were fatal. In three of the fatal cases there were varicose veins of the legs. Hypertension was noted in 62.8 per cent of the patients but does not appear in itself to be a contraindication to surgery if there is no cardiac or severe renal damage present.

In most cases the operation consisted of repair of cystocele and rectocele with or without amputation of the cervix. On over 10 per cent suspension of the uterus was performed, but Frost does not believe this operation is justified for this condition. No anticoagulation therapy was administered to any patient. In retrospect Frost believes anticoagulation therapy may have reduced deaths from embolism. In severe varicosities in elderly women it may be advisable to refrain from surgery or to carry out ligation of the veins before operation. Early ambulation on the first and second postoperative days is also suggested.

Frost believes that the operative risk is more than offset by the comfort and relief afforded these more or less incapacitated women who otherwise may be confined to sedentary life. This is especially important since life expectancy of the white American woman is 68.6 years and some authorities say it soon may reach 75.

[Today chronologic old age seldom deters us from operating. We perform all types of operations on very old women, most of them under direct infiltration anesthesia. However, all old women who are to be operated on should have a complete examination by an internist, with particular attention to the cardiovascular-renal systems. Most old women who have hypertension, cardiovascular disease, renal disease or other disturbance can be prepared for necessary surgery so that there will be only slight risk in operating.—Ed.]

**To What Does the Halban Operation Owe Its Efficacy?** G. Cotte and J. Mathieu<sup>3</sup> believe this simple operation lends itself to all types of anatomic conditions associated with a displaced uterus, even to eversion. It leaves the uterus in normal position, thereby facilitating evacuation of physiologic

(2) *Am. J. Obst. & Gynec.* 60:489-495, September, 1950.

(3) *Lyon chir.* 45:769-772, October, 1950.

secretions as well as treatment of pathologic processes. Its superiority to other methods lies in the Halban technic for creating a solid floor beneath the bladder.

A deep plane is found and the incision carried down to the bladder. The fibrous planes of the two edges of the incision are grasped with forceps. In the midline the fascia is thin but when dissected back from the cut edges becomes satisfactorily dense. If carried too far laterally, the dissection may endanger the venous plexus near the bladder and cause bleeding. In brief, the wall of the vagina should be incised through its entire thickness and the edges turned back on themselves as the dissection on the fibrous plane proceeds. In this way a very resistant fascia is isolated.

The authors are convinced that there is such a fibrous plane at the level of the anterior wall of the vagina between the mucosa and the bladder and that the efficacy of the Halban operation is due to suturing of the fascia to the anterior surface of the isthmus under tension. Amputation of the cervix and closure of the peritoneal vesicovaginal culdesac, less important steps in the procedure, are often superfluous.

**Total Colpocleisis for Pelvic Eventration** was used by Herbert D. Adams<sup>4</sup> (Boston) in 30 patients with prolapse of vagina following supravaginal or total hysterectomy or with extreme procidentia associated with huge enterocele. This operation completely obliterates the vagina, but the disadvantage of loss of marital functions was disregarded by the patients, who were old or extremely incapacitated by their symptoms.

**PROCEDURE.**—The operation is done under spinal anesthesia with patient in lithotomy position. The bladder is emptied, perineum prepared and cervix or vaginal apex grasped with a tenaculum. The mucosa of the anterior aspect of the vagina is incised from urethra to cervix or vaginal apex, flaps elevated from bladder as far as labial margins (Fig. 84) and mucosa of posterior aspect incised and elevated as in standard perineorrhaphy (Fig. 85). The cervix, if present, is then amputated, and with vaginal apex as focus a purse-string suture is placed (Fig. 86) and a series of inverting sutures placed around it (Fig. 87), thereby reducing the prolapse. This brings bladder and rectum back into normal position. The pelvic fascia is plicated (Fig. 88) and the levator and transverse perineal muscles brought together to obliterate t

(4) Surg., Gynec. & Obst. 92:321-324, March, 1951.

vagina (Fig. 89). The excess of lateral vaginal mucosa is removed, mucosa and perineum closed (Fig. 90), leaving a small 2 cm. dimple just below the urethra to provide unobstructed urinary flow from the urethra.

A modified procedure has been used for patients with procidentia with huge enteroceles. With lesser prolapse, a

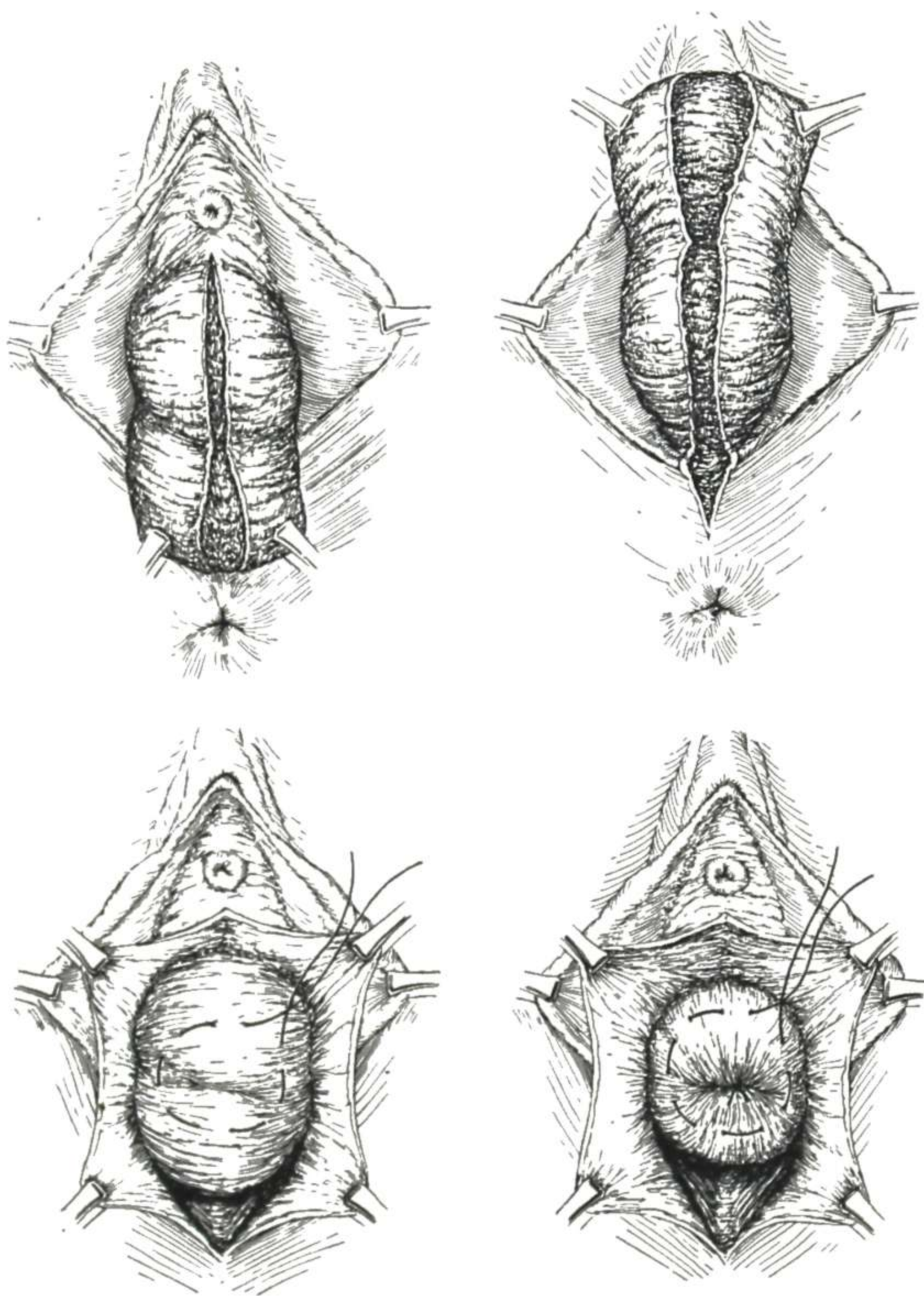


Fig. 84 (top left).—Mucosal incision of anterior aspect.

Fig. 85 (top right).—Mucosal incision of posterior aspect.

Fig. 86 (bottom left).—Purse-string suture around apical vaginal scar.

Fig. 87 (bottom right).—Series of purse-string sutures to invert bladder and rectum and reduce prolapse.

(Courtesy of Adams, H. D.: *Surg., Gynec. & Obst.* 92:321-324, March, 1951.)

modified Manchester-Fothergill procedure with amputation of cervix and plication of cardinal ligament behind the stump rather than anterior to it (Fig. 91) is effective in preventing

recurrence of the hernia. Marked procidentia associated with huge enterocele, however, is best managed by vaginal hysterectomy, plication of cardinal and broad ligaments and total colpocleisis.

[Colpocleisis should be reserved for very old women, particularly

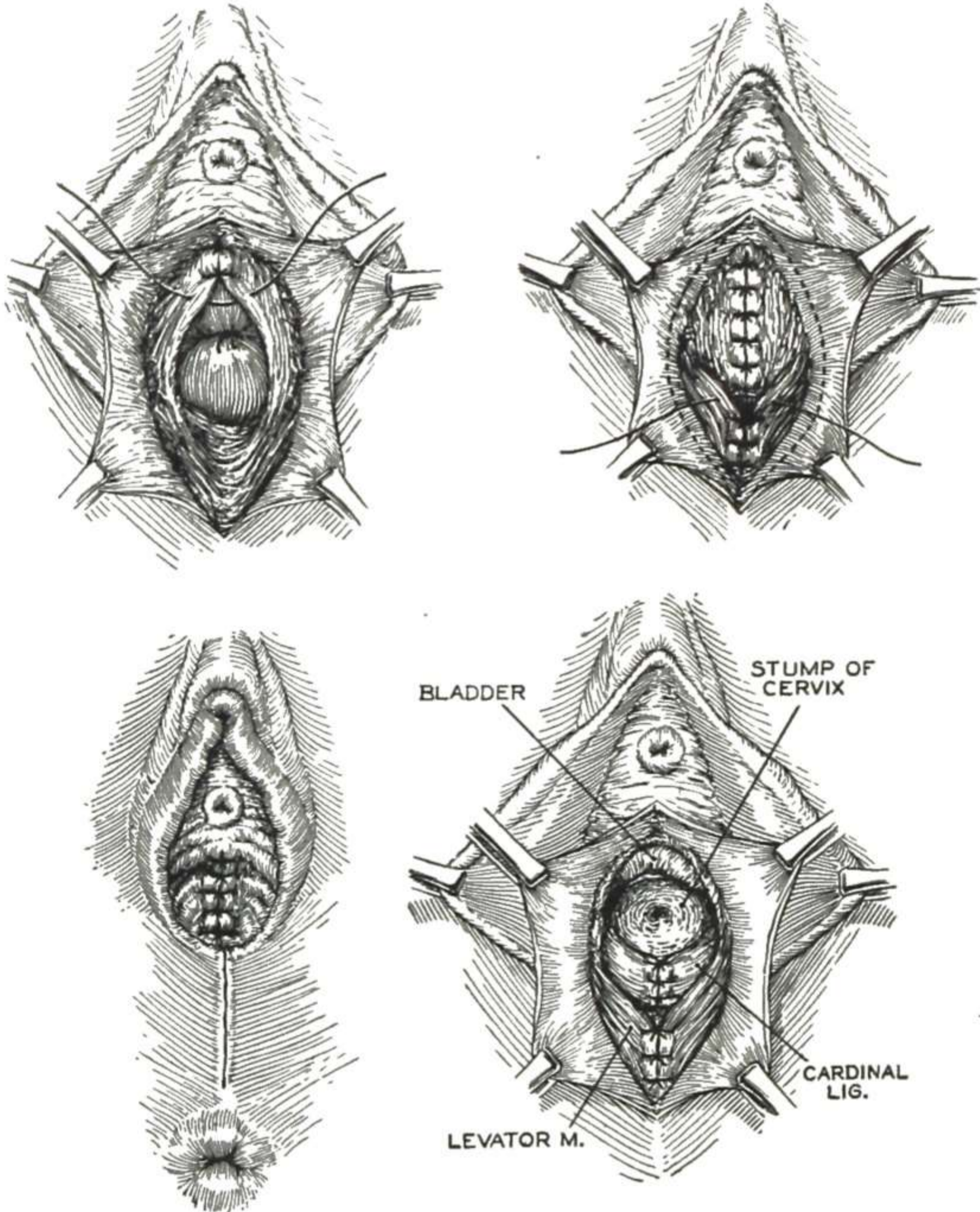


Fig. 88 (top left).—Plication of pelvic fascia.

Fig. 89 (top right).—Plication of levator and transverse perineal muscles to obliterate vagina.

Fig. 90 (bottom left).—Completed operation after closure of mucosa.

Fig. 91 (bottom right).—Modified procedure showing plication of cardinal ligaments behind rather than anterior to cervix.

(Courtesy of Adams, H. D.: Surg., Gynec. & Obst. 92:321-324, March, 1951.)

those who are poor surgical risks. The operation can often be done under direct infiltration anesthesia.—Ed.]

**Plastic Repair of Pelvic Floor: Report of 31 Cases of Stress Incontinence and Demonstration of Film in Color Showing Operative Technic.** The purpose of the operation described by Axel Ingelman-Sundberg<sup>5</sup> (Karolinska Hosp.,

(5) Acta obst. et gynec. scandinav. (supp. 7) 30:318-327, 1950.

Stockholm) is correction of insufficiency of the pelvic floor, the chief cause of stress incontinence. The bladder neck is replaced to normal position behind the symphysis, using bladder ligaments (fascia pelvis) and pubococcygeal muscles as support. These muscles can be divided slightly back of the midpoint without losing their ability to contract. Usually no

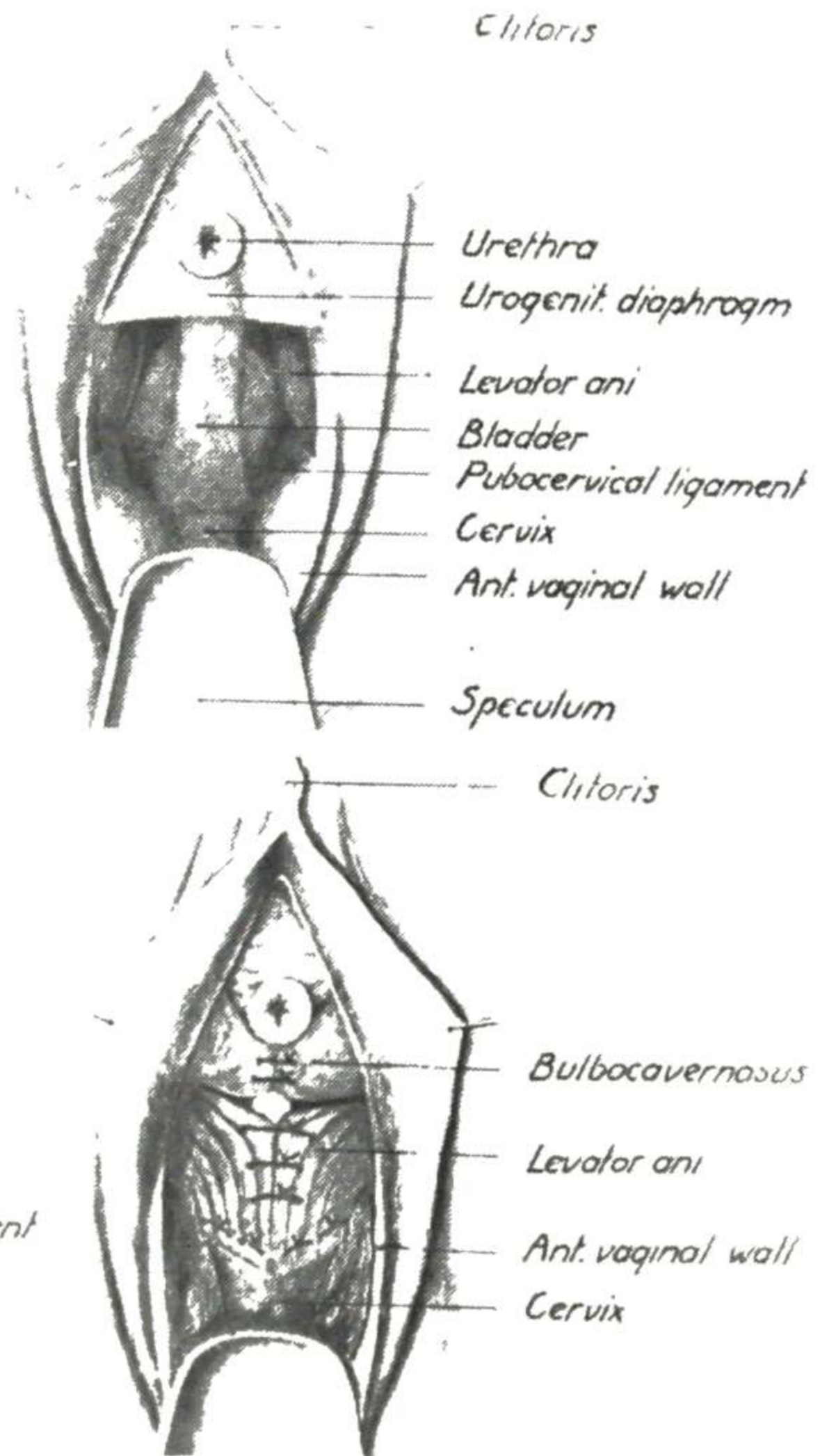
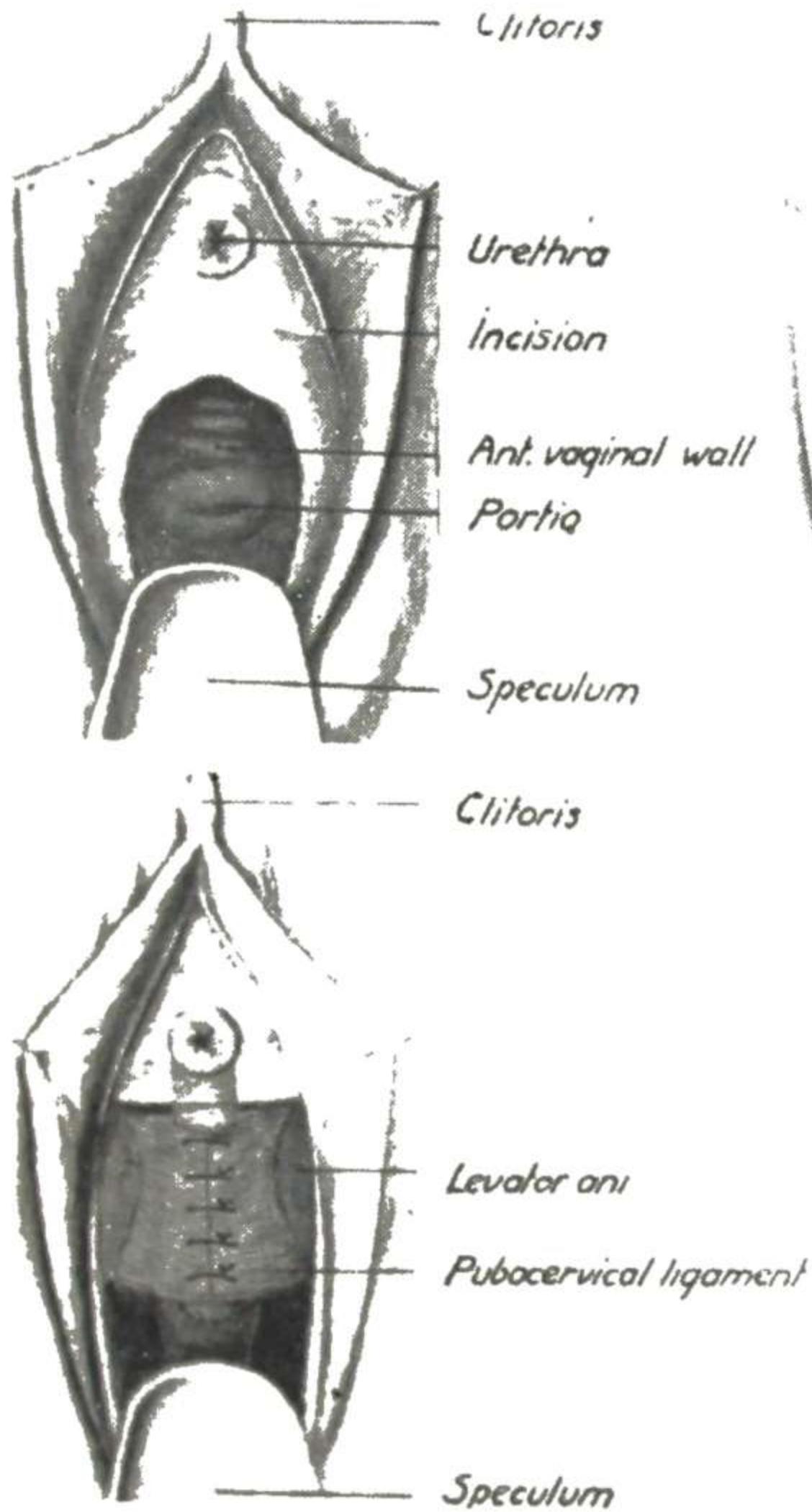


Fig. 92 (top left).

Fig. 94 (bottom left).

Fig. 93 (top right).

Fig. 95 (bottom right).

(Courtesy of Ingelman-Sundberg, A.: Acta obst. et gynec. scandinav. (supp. 7) 30:318-327, 1950.)

atrophy develops and plastic repair should be unlimitedly durable if nonresorbable sutures are used.

**TECHNIC.**—A triangular flap of mucosa is freed by dissection, with the apex near the clitoris and the base just above the vaginal inlet. A sleeve of mucous membrane is left around the urethral opening. Incision is then extended (Fig. 92). Anterior vaginal wall is dissected loose and urethra and bladder floor freed up to the

cervix (Fig. 93). During this procedure a soft rubber catheter is placed in the urethra. The bladder should be mobilized on both sides out to the pelvic wall to free bladder ligaments, which are then sutured in the midline with interrupted chromic catgut sutures to a fascial plate under the trigonum and bladder neck (Fig. 94). The posterior part of the plate is fixed to the cervix with a stainless steel wire suture. By blunt dissection the pubococcygeus muscles are freed to the symphysis and divided just back of the mid-

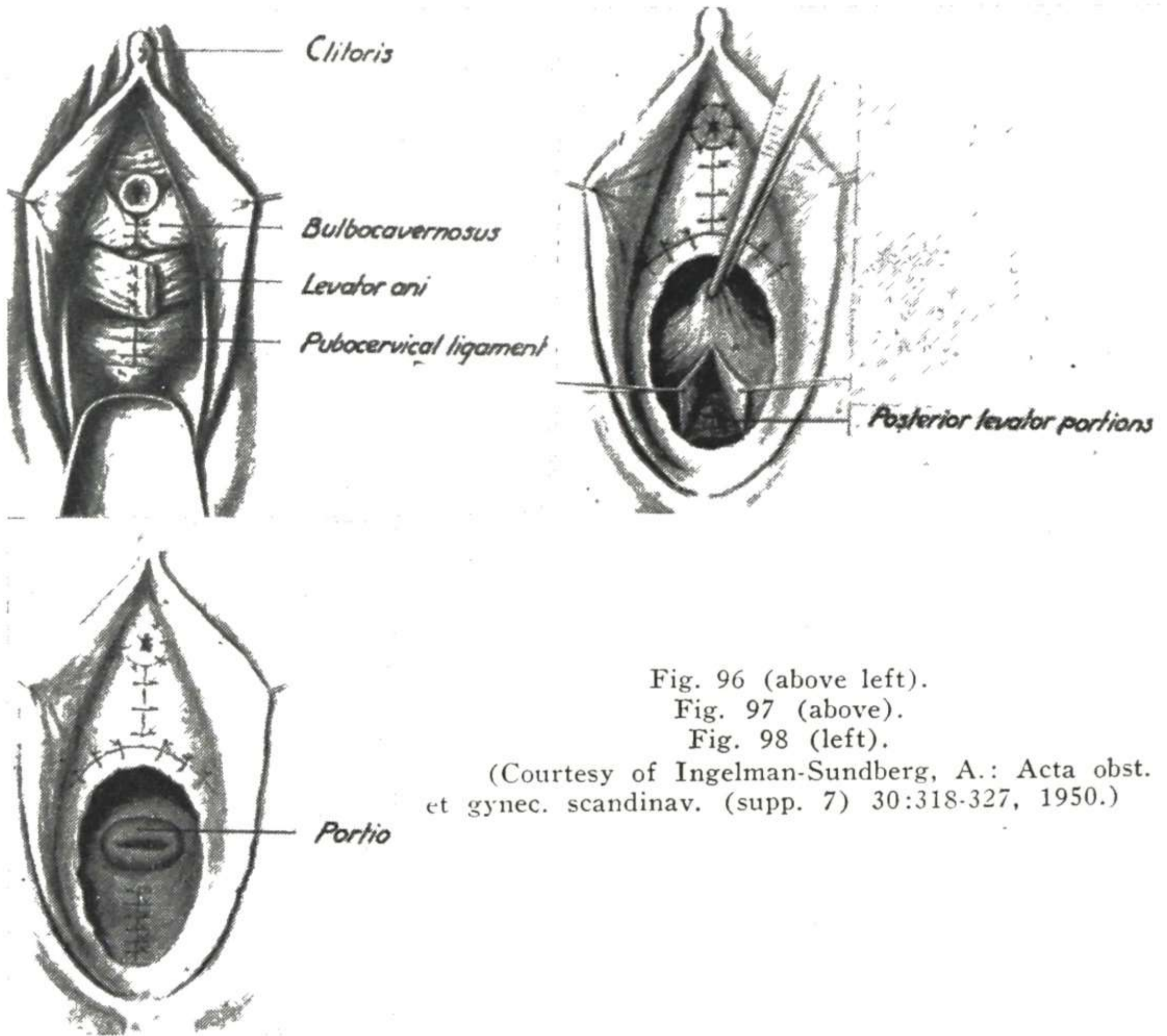


Fig. 96 (above left).

Fig. 97 (above).

Fig. 98 (left).

(Courtesy of Ingelman-Sundberg, A.: Acta obst. et gynec. scandinav. (suppl. 7) 30:318-327, 1950.)

point. In each of two posterior portions thus produced a suture with long ends is placed. The two anterior muscle portions are sutured with interrupted stainless steel wire sutures to a muscular support under the bladder neck outside the fascial layer. When muscles are well developed a muscular plate is made covering the whole bladder floor, and its posterior part is fixed to the cervix with stainless steel wire (Fig. 95). If this cannot be made without tension, muscles are sutured as a bridge under the bladder neck (Fig. 96). Vesico-vaginal interposition of the uterus is preferable if both bladder ligaments and pubococcygeal muscles are poorly developed. The corpus is then brought outside sutured bladder ligaments and fas-

tened to the periosteum of the pubic arch and to pubococcygeal muscles, which are sutured to lateral portions of the uterus with stainless steel wire. The bulbocavernosus muscle is freed and sutured in the midline to support the distal part of the urethra (Figs. 95 and 96). The muscle is sutured with two interrupted sutures of 00 chromic catgut and connective tissue on either side is sutured in separate layers with 000 catgut. The urethral orifice is sutured in the anterior part of the wound near the clitoris with fine catgut (000 or 0000); after any redundant portions of the vaginal wall have been trimmed, it is fastened with fine catgut against the underlying tissue and sutured as in Figure 97. Posterior portions of pubococcygeal muscles are now found through a longitudinal incision in the posterior vaginal wall so that after sufficient mobilization of the lateral vaginal walls the sutures applied previously are grasped with clamps and the muscles brought into the wound. They are then sutured together with several interrupted heavy chromic catgut sutures (Fig. 97). Proctoceles or enteroceles, if present, is repaired; any necessary perineal repair is made. After redundant tissue has been cut away, mucosa is sutured with fine catgut (Fig. 98) and the vagina sponged with gauze powdered with microcrystalline sulfathiazole and penicillin. An indwelling catheter is so placed that it can be fastened toward the symphysis without pressure on urethral sutures.

Tampon is removed 24 hours after operation and the catheter removed when the patient can empty bladder without residual urine. Fluids are forced and the patient encouraged to move freely in bed and sit in a chair one hour daily. She can walk in 10-14 days and is usually discharged in 16 days with instructions to take daily exercises to strengthen musculature.

Of 31 patients with stress incontinence operated on by this method and followed two to four years, 28 were completely cured; 3 sometimes had slight incontinence on coughing or sneezing. Two had normal deliveries following operation. There were no relapses. Chief advantages of this technic are: (1) provision of muscular support which, unlike one made by connective tissue, does not stretch; (2) location of muscular suspension to one side of birth canal proper which at time of future delivery will not be exposed to direct separation by fetal head.

**Sphincteric Function Established by Kinking Urethra.** Most methods for re-establishment of function of the urethral sphincter when it is paralyzed or destroyed, as often happens in vesicovaginal fistula, utilize transplants of surrounding muscles, such as the bulbocavernosus, levator ani or muscles of the thigh or abdominal wall, but results have not been



good. Axel Ingelman-Sundberg<sup>6</sup> (Karolinska Hosp., Stockholm) used a method based on lowering of the bladder floor during micturition. By transplanting the urethral meatus upward, a kink is produced in the urethra by the edge of the symphysis or by a strategically placed bone graft so that it remains occluded except at micturition.

**TECHNIC.**—An incision is made in the vulvar mucosa parallel to the sagittal plane and the mucous membrane mobilized so that a mucous tube with a circumference of 25 mm. can be made as a prolongation of the urethra. A soft rubber catheter is placed in the urethra and the mucosa sutured around it. The bulbocavernosus muscle is freed on both sides and the connective tissue on its posterior surface brought together over the new urethra by means of interrupted sutures. The muscle is then sutured in the midline. Fascia of the anterior surface and adipose tissue are sutured over the muscle in separate layers. The vaginal wall is dissected free and the bladder neck inspected. If it is sagging downward, the "bladder ligaments" are sewed together in the midline to assure sufficient kinking. The mucous membrane is sutured. The catheter is left in place for 14 days unless suprapubic drainage is provided. The patient is allowed to move freely in bed and fluids are forced. After two weeks the patient is allowed to stand up and after three weeks she can be discharged.

This procedure gave good results in 10 patients, with slight residual incontinence on coughing or sneezing in only 2. In one, this was completely remedied by wearing a pessary and the other was comfortable enough without one.

[Kegel and Powell (J. Urol. 63:808, 1950) used their physiologic method of treatment of urinary stress incontinence in about 300 cases. In 70 per cent muscular relaxation was the dominant factor accompanied by only moderate loss of co-ordination. In 30 per cent the neurogenic factor was dominant. Approximately one third of this group were completely relieved and another third were greatly relieved but had fatigue. The remaining third was comprised of patients unable to learn to contract the perineal muscles. See the 1949 YEAR BOOK (p. 402) for Kegel's perineometer and its use in overcoming urinary incontinence.—Ed.]

**Methods and Technics for Surgical Correction of Stress Incontinence.** Virgil S. Counseller<sup>7</sup> (Mayo Clinic) reports results in 578 patients surgically treated in the past five years. In many patients incontinence was associated with other pelvic conditions requiring surgical treatment, such as cystocele, urethrocele, prolapse of the uterus or of a retained cervical stump, menometrorrhagia, small fibroids and recurring uterine polyps. In some cases incontinence was the patients'

(6) Acta chir. scandinav. 101:1-10, 1951.

(7) J. A. M. A. 146:27-30, May 5, 1951.

primary concern, but in most it was incidental to other pelvic disorders.

Advanced age, crippling arthritis and severe cardiac disease almost always contraindicate surgical correction of incontinence. Patients with little, if any, cystocele, those with a congenitally short anterior vaginal wall and those who have begun to have atrophic contractions of the vaginal walls are poor candidates for any plastic procedure on the urethra or vesical neck for incontinence. In patients with extensive scarring from previous vaginal operations, incontinence is usually due to fixation of the urethra and vesical neck in scar tissue and the sphincteric mechanism is unable to contract or relax. The best treatment for this type of incontinence is to open the anterior vaginal wall, separate the urethra and vesical neck from the vagina and posterior surface of the pubis and elevate these structures by an iodoform gauze pack placed around the urethra and under the vesical neck. The pack is left in position 8-10 days and then replaced with a second pack. This pack is left in five to seven days until the bladder remains elevated by itself and does not become re-attached to the vagina or pubic bone. If incontinence develops in later years in patients who have not had children, then the loss of the supporting structures must be considered due to atrophy unless it is a result of some degenerative disease of the central nervous system. Some form of muscle training or re-education as suggested by Kegel is useful.

The Kelly operation, consisting of the placing of one or two mattress sutures so that they will tighten the muscle layer in the vesical neck and posterior third of the urethra, was performed on 227 patients. Results were poor in 10 per cent; 5 per cent had some improvement and 85 per cent complete relief. The Kelly operation was done as a secondary operation on 21 patients with poor results in 14 per cent, some improvement in 10 per cent and good results in 76 per cent. The modified Kelly operation, which involves a little more suturing, gave poor results in 6 per cent, some improvement in 7 per cent and good results in 87 per cent. With the more extensive Kennedy operation results were poor in 7 per cent, improved in 8 per cent and good in 85 per cent. Good results were obtained in only 48 per cent when this operation was done as a secondary procedure. High incidence of poor

results in secondary operations seems to indicate that patients with scarring and fixation of the vesical neck should be treated by one of the more extensive suprapubic operations.

[Everyone who performs gynecologic operations should study the original article for its valuable information. Re-study of the papers by Kelly and Kennedy on the cure of stress incontinence will also be of great benefit to some surgeons. I fully agree with Counseller that the vast majority of cases of stress incontinence can be cured by means of the Kelly or Kennedy operation. However, in view of the good results obtained with the Kegel perineometer, most patients for whom an operation is planned should first try this instrument. Some women can avoid an operation by use of the perineometer.—Ed.]

**Management of Urinary Incontinence in Women** following childbearing, subsequent to either supracervical or total hysterectomy or resulting from vesicovaginal fistula is discussed by Walter J. Reich, J. Lester Wilkey, Mitchell J. Nechtow and Harold E. Silverman<sup>8</sup> (Chicago). Management of incontinence following childbearing should include a careful systemic inventory, urine culture and antibiotic therapy. Surgically, the urethrovesical platform is restored, with utilization of intrinsic bladder musculature, intrinsic musculature of the urethra and sphincter urethrae muscle, uteropubic fascia, bulbocavernosus muscle and pelvic floor. The patient is told to return about three weeks after operation for urethral dilation to alleviate vesical spasms and to minimize cicatrization about the urethra.

The probable cause of incontinence subsequent to supracervical or total hysterectomy is improper technic of reflection of the vesical peritoneum and its fixation with abnormal trigonal contraction. Utilization of the maximal amount of reflection of the vesical peritoneum and transverse suturing of the uterosacral ligaments during hysterectomy has minimized the vesical symptoms that follow this procedure.

Incontinence due to vesicovaginal fistula was studied in a large number of cases. The improved results obtained were attributed to more careful preoperative study, antibiotics, wider mobilization of the bladder and use of spinal anesthesia. The patients were first hospitalized for a complete physical check-up to rule out factors which might produce immediate or delayed postoperative nonclosure. The cystoscopist performed combined intravesical and intravaginal study, noting

(8) J. Internat. Coll. Surgeons 14:188-193, August, 1950.

particularly the relation of the fistula to such definite landmarks as the two ureteral openings, interureteric ridge and urethra. Spinal anesthesia is preferred for these operations because of the great relaxation. Important in postoperative therapy is administration of antibiotics, depending on results of cultures.

**Vaginal Hysterectomy as Safety Measure in Genital Prolapse.** According to Julian Ocejó,<sup>9</sup> prolapse should be treated by the vaginal approach unless some other surgical condition is present which requires the abdominal route. In any case, posterior colpoperineorrhaphy is necessary. The Manchester operation is indicated in young women, and vesicovaginal interposition and the Spalding-Richardson procedure in women near the menopause. After the menopause vaginal hysterectomy is done and in very old women, a Le Fort colpocleisis. Because of the probability of recurrence of prolapse after vaginal hysterectomy, many authors recommend use of interposition after the climacteric. Ocejó proposes a combination of vaginal hysterectomy and interposition, having the advantages of both without their disadvantages. It consists of extirpating the whole cervix and endometrium and, from the remaining uterine musculature, constructing a firm, permanent and well vascularized support interposed between bladder and vagina.

**PROCEDURE.**—The cervix is closed with three stitches, and the suture ends grasped with clamps to permit manipulation of the uterus. An inverted T incision is made and the anterior wall of the vagina dissected. The bladder and prevesical fascia are freed and the cervicovesical ligaments severed near the cervix. Dissection of the cervix is continued up to the Douglas pouch, which is opened. The cardinal ligaments are clamped and sectioned. The forefinger is introduced behind the uterus to facilitate the opening of the vesicouterine fundus. Staunching of blood on both uterine borders is done with intestinal coprostasis clamps. Both uterine horns are sectioned between ligatures and transverse incision is made in the posterior wall of the fundus, reaching the anterior wall after passing below the uterine horns. The two parts of the incision are continued along the anterior wall 1 cm. apart and meet again behind the isthmus, thus removing the whole endometrium and cervix. Most of the myometrium, its vascular and ligament connections are spared. The myometrium is sutured longitudinally, forming a support interposed between the bladder and vagina. Provisional hemo-

(9) *Rev. cubana obst. y ginec.* 13:58-71, Mar.-Apr., 1951.

stasis is removed, and the anterior peritoneum is closed as low and as tightly as possible. The muscular support is fixed on the lower border of the pubis at each side of the urethra. The cardinal ligaments are joined with each other and the isthmus; the uterosacral ligaments are shortened, joined together and folded over the isthmus. The posterior peritoneal pouch is closed and suture of the vagina begins by joining it with the uterosacral ligaments. The sides of the vagina are trimmed, the prevesical fascia and vagina sutured and, after cutting the sutures, the vaginal wall rises.

### **Role of Vaginal Hysterectomy in Operation for Prolapse.**

E. Held<sup>1</sup> (St. Gallen, Switzerland) reviews 70 vaginal hysterectomies plus anterior colporrhaphy and colpoperineoplasty among 1,000 operations for prolapse and incontinence. In 60 patients hysterectomy was included because of a diseased uterus or recurrent prolapse—the principal reason for adding hysterectomy to the reparative procedure. In the other 10 the uterus was small, no longer undergoing menstrual changes and showed primary prolapse.

All but one patient was past 40: the oldest was 72. There was one surgical death, due to massive pulmonary embolism. Among the other 17 complications were bronchitis, nonfatal pulmonary embolism, cardiac complications, abscess of the stump (2 cases), mechanical ileus and fever for several days. Of the 56 patients followed one to nine years, 2 were not cured, 3 improved satisfactorily and 51 were entirely well. Of 36 with relative urinary incontinence, only 1 was not entirely cured by the operation.

[A vaginal hysterectomy is by no means part of an operation for cure of prolapse of the uterus. The uterus should be removed if it or the cervix is diseased or if the patient has menometrorrhagia. In Held's series of 925 prolapse operations, a vaginal hysterectomy was performed in only 7.5 per cent. This is a low frequency. Ricci (Am. J. Surg. 79:377, 1950) has abandoned all but two procedures in treatment of prolapse of the uterus; vaginal hysterectomy, and high amputation of the cervix. Occasionally he performs a colpectomy. I use several different operations, depending on the conditions present, but most frequently use (1) the Manchester operation with amputation of the cervix, (2) vaginal hysterectomy with a repair operation, (3) an extensive plastic operation, and (4) occasionally the Le Fort operation.—Ed.]

**Vesical and Enterovesical Fistulas.** Virgil S. Counseller<sup>2</sup> (Mayo Clinic) states that vesical fistulas may be multiple and may involve the ureter, intestine and vagina. Patients become dejected and extremely worried and, because of uriniferous

(1) *Gynaecologia* 130:22-30, July, 1950.

(2) *S. Clin. North America* 30:1223-1234, August, 1950.

odors, most of them prefer to stay home. Paramount in their minds is the question of cancer. Another important factor is the altered family relation, especially during the sexually active period.

Uncomplicated vesicovaginal fistula is the commonest type in the group mentioned. The behavior of vesical tissue in general always favors surgery because this tissue has the ability to heal or reconstruct itself if given a chance.

The type of vesical fistula most commonly seen today occurs after some surgical abdominal or vaginal procedure, usually total abdominal hysterectomy. To avoid this accident, surgery should be done under direct vision and without trauma or production of hemorrhage. A fistula after vaginal hysterectomy undoubtedly is produced in about the same manner as that after abdominal hysterectomy; i.e., by a suture through the entire bladder wall or by incision in the bladder wall. In either instance the occurrence is unobserved at operation. Prevention of a fistula after irradiation for cervical carcinoma is usually the radiologist's problem.

Clinical investigation before repair should be most complete. A ureterovaginal or ureterovesicovaginal fistula can be caused by catching the ureter within about 1 in. of the ureterovesical orifice. Management of such a fistula is somewhat complicated. The kidney on the involved side must be considered. An excretory urogram should be made in every instance of vesical fistula.

When there is a ureterovesical or ureterovesicovaginal fistula with a sound kidney on the opposite side, nephrectomy on the side of the fistula is usually indicated. If the fistula is only ureterovaginal, no additional procedure need be done on the bladder because the patient will be dry. If there is a bladder opening or a ureterovesicovaginal fistula, the vaginal opening can be closed subsequently.

Immediate repair of a vesicovaginal fistula is inadvisable. The patient should be allowed to recover completely from surgery and wear a catheter, if necessary, before repair is attempted. The patient is advised to wear pads and let the urine flow constantly rather than to wear a catheter which may inflame the urethra and bladder. Repair should be postponed until all inflammation has disappeared and adequate

blood supply is restored to the injured tissues; four months is the minimal and perhaps six months the maximal time needed.

Causes of failure of repair of vesical fistula are, in order of decreasing importance: (1) inadequate exposure from various positions, (2) failure to excise all scar tissue, (3) too early operation, (4) bladder closure under too much tension, (5) accumulation of blood between vaginal wall and bladder or hemorrhage directly into the bladder and (6) failure to use the method of closure which protects the upper and lower angles of the suture line.

[This is an excellent article based on extensive experience with a most distressing illness. It should be carefully studied by surgeons before they attempt to repair any vesical, ureteral or enterovesical fistula. Particular attention should be paid to the advice concerning prevention of bladder and ureteral fistulas.

Charlewood (South African M. J. 24:232, 1950) reports 72 cases of vesicovaginal fistula in which the Sims paring technic with excision of the fistulous tract and without use of the silver wire gave an over-all cure rate of 94 per cent. This is an extraordinary result. Ordinary 20 day chromic surgical gut was used. Galló and Chacon (Ginec. y obstet. México 6:14, Mar.-Apr., 1951) describe a simple, anatomic transcolic ureterocolostomy.—Ed.]

**Ureterovaginal Fistula.** Gershom J. Thompson and Virgil S. Counseller<sup>3</sup> (Mayo Clinic) report 35 cases, in most of which fistula developed during convalescence from gynecologic procedures: 3 deliveries of large infants, 1 colpotomy, 1 abdominal suspension of uterus and tubal ligation, 7 vaginal and 23 abdominal hysterectomies. In two of six hysterectomies for malignancy, Wertheim's operation was performed. The injury was not recognized for several days and sometimes months after operation. The authors feel that passing ureteral catheters before difficult pelvic operations is helpful.

Suspicion of injury is aroused by pain in the flank and sometimes high fever and elevation of pulse rate after surgery. Diagnosis is sometimes difficult. If indigo carmine placed in the bladder appears in the vagina without delay, vesicovaginal fistula is almost certain; if it fails to appear in the vagina but a vaginal pack becomes soaked with urine, ureterovaginal fistula can be diagnosed. In one case, reflux of dye through the dilated ureter was misleading. Ureteral leakage spurts while that of the bladder does not, and this

(3) J. Internat. Coll. Surgeons 25:479-487, April, 1951.

can be well demonstrated with intravenous indigo carmine. Usually obstruction prevents passage of a catheter, but in several of the present cases the catheter could easily be passed up to the renal pelvis, probably because a stitch included only part of the ureteral wall. The excretory urogram often shows dilatation of the renal pelvis and ureter above the obstruction; sometimes, however, the kidney or ureters are not outlined at all. Of 34 cases, 8 had no pyeloureterectasis, 27 had varying degrees of dilatation and 5 had nonfunctioning kidneys, although sufficient urine was drained from the vagina to require the constant wearing of a pad. Use of an inlying ureteral catheter is justified if it is passed easily, indicating absence of obstruction. However, unless conservative measures succeed early, surgery should be done.

Reimplantation of the ureter into the bladder is the ideal operation, especially if dilatation or infection do not complicate the picture and if the injury is close to the bladder. Ureters were reimplanted in 11 patients by bringing the ureter diagonally through the bladder wall and allowing it to protrude 1-2 cm. into the vesical cavity, as is done in uretero-intestinal anastomosis. In 20 patients with one normal kidney, discouraged by unsuccessful attempts at repair or deprived of function in the other, nephrectomy proved the easiest solution.

**Changes in Squamous Epithelium Following Surgical Treatment of Absence of Vagina: Preliminary Report.** Frank E. Whitacre and Roland H. Alden<sup>5</sup> (Univ. of Tennessee) cover a Pyrex glass mold with a skin graft from the abdomen or thigh and suture it to the introitus epithelium for six months, with removals for cleansing. There have been differing opinions as to whether the transplanted epithelium grows in this position or is gradually replaced by invading introitus epithelium. The fact that in Negroes the vaginal and introitus epithelium are pigment free furnished a means of determining this, provided the graft retained all or some of its pigment. The biologic point of interest was what happens to thin, pigmented, hirsute, keratinized skin with underlying tissues, sweat glands and ducts when placed in a position normally occupied by the vagina which is relatively thick, unpigmented, weakly cornified and devoid of sweat glands and hair.

(5) *Ann. Surg.* 133:814-818, June, 1951.



With a full thickness skin graft an artificial vagina was constructed for a young Negro woman. No remarkable change was noted in biopsy specimens taken over more than six months. Ten months after surgery, biopsy was done, 1 mg. estradiol benzoate in oil was given intramuscularly on the first and third day and another biopsy done on the fifth day. This was an attempt to determine if estrogens in this amount would mobilize glycogen within the transplanted epithelial cells as might be expected from previous reports. None was found in the biopsy specimen taken after estradiol injections, and further estrogen administration was not possible as the patient insisted on leaving the hospital. Estradiol benzoate, 2 mg., was sufficient to influence normal vaginal epithelium. No change was detected in thickness of epithelium, number of mitoses in the stratum germinativum or in glycogen content. Loss of hair, sweat glands, reduction in large elastic fibers and reduction of pigment were negative changes making the explant more like normal vagina, although the hyperplasia of epithelial cells and increase in number and height of dermal papillae give positive modifications leading in the same direction. The degree of keratinization of the stratum corneum, the number of keratohyalin granules in the stratum granulosum and the amount of epithelial glycogen are skin characteristics not materially altered during the study.

The skin graft substitute vagina apparently survives as such and is not replaced by invasion of epithelium from the introitus; histologically the explant is modified, gaining some but not all the characteristics of normal vaginal mucosa but never losing certain characteristics of skin.

**Improvement in Technic of Constructing Vagina.** Lawrence R. Wharton<sup>4</sup> (Johns Hopkins Hosp.) makes vaginal forms of balsa wood and sutures the exposed edge of the graft to the cut edge of the vestibule (Fig. 99), thus fixing both the graft and the form, preventing rotation and descent and allowing adequate drainage without occlusion of the dissected space. After three weeks, the sutures are either absorbed or loosened so that the form can be slipped out. The graft stays in place. Another form can be introduced without inconvenience.

(4) Am. J. Obst. & Gynec. 60:871-874, October, 1950.

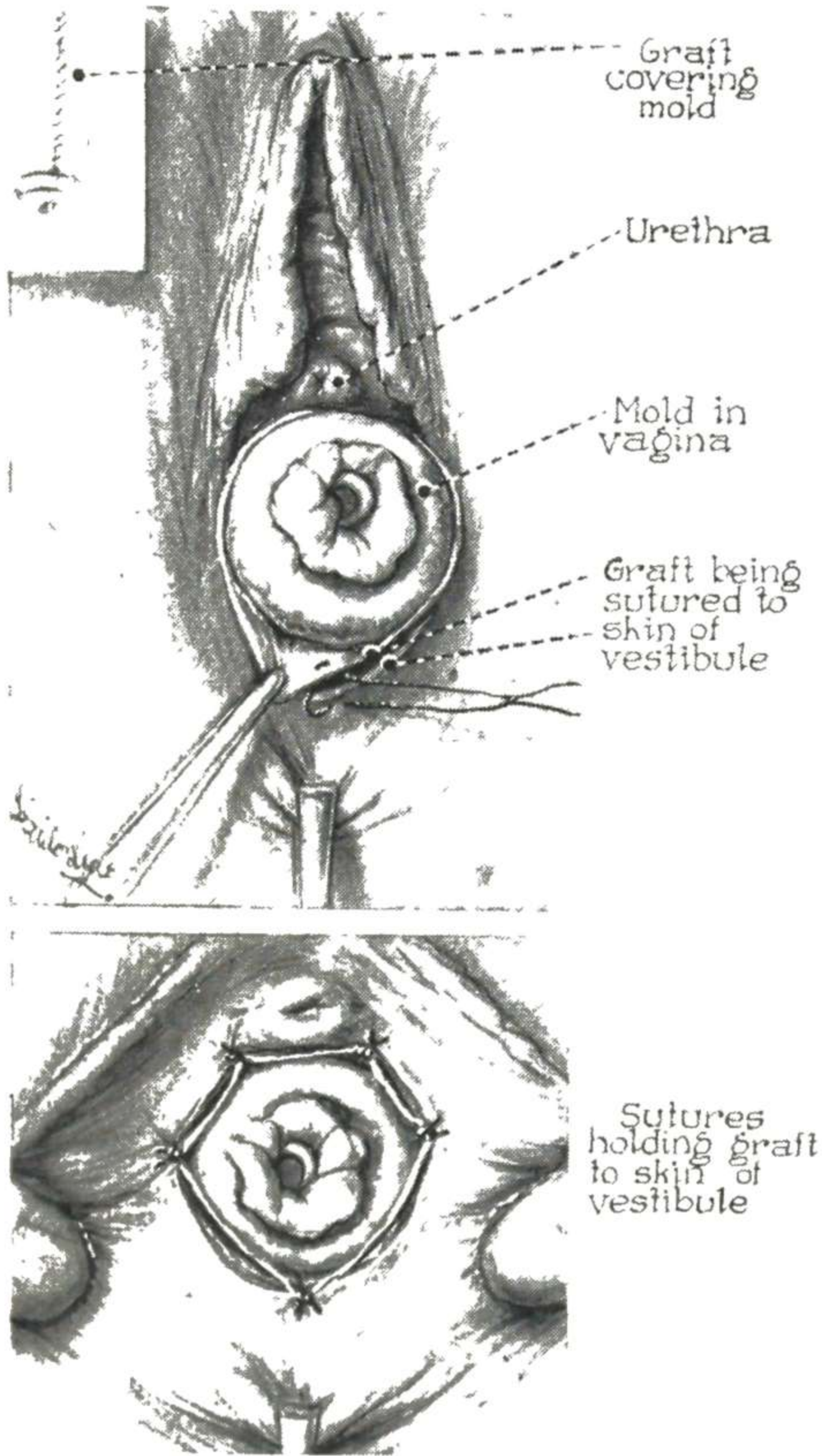


Fig. 99.—New method of fixing form and skin graft in space dissected for vagina. (Courtesy of Wharton, L. R.: *Am. J. Obst. & Gynec.* 60:871-874, October, 1950.)

In one case, a vaginogram taken after five months showed a deep and commodious vagina; the orifice was normal and the external genitals showed no deformity or scar. In another case, biopsy specimen from the apex of the constructed vagina showed normal, healthy, squamous epithelium.

**Technical Principles in Myomectomy with Special Reference to Hemostasis.** I. C. Rubin<sup>6</sup> (St. Louis, Mo.) points out that, unlike hysterectomy, myomectomy conserves men-

(6) *J. Mt. Sinai Hosp.* 17:565-570, Mar.-Apr., 1951.

struation and the power of reproduction. Since uterine fibroids interfere with conception and pregnancy by blocking the access of spermatozoa to the uterine cavity or tubes or by associated peritubal and periovarian adhesions, myomectomy is indicated when motherhood is desired. Before myomectomy, uterotubal insufflation should always be done to determine patency and degree of function of fallopian tubes and hystero-graphy to determine configuration of the uterine cavity and presence of submucous fibroids or polyps. Submucous fibroids may be removed vaginally preliminary to or abdominally during myomectomy. Polyps are removed by preliminary curettage.

Technical steps making the operation safer than before are (1) removal of as many fibroids as possible through each incision; (2) incising anterior wall whenever possible and covering the wound with the sigmoid serosa or sigmoid epiploica if posterior incision is necessary; (3) making incision as far as possible from uterine ends of tubes; (4) making sure that lumen of tube is not closed by suture.

TECHNIC.—Tumors are cut into deeply; each half is grasped with a tenaculum and enucleated. One or more tumors extending into the uterine cavity may be enucleated without entering the cavity, the mucous membrane being gently peeled from the myoma capsule. The uterine cavity must be entered to remove any submucous fibroids which have broken through mucous covering. As many fibroids as possible are removed through the same incision, extending it as required. Small subserous fibroids are twisted out with a single tenaculum hook with negligible bleeding. Fine catgut suture unites the serosa. When deeper tumors are removed, continuous or interrupted suture will obliterate the enucleated cavity. A seromuscular suture overlies the basic suture and a seroserosal suture completes the closure. Seromuscular segments are not removed to give a symmetrical appearance as the uterine surface resumes normal contour in about three months, and removal of too much uterine wall may weaken it in case of pregnancy or may cause necrosis. The whole wound area is covered by a flap of vesico-uterine peritoneum (particularly after removal of intraligamentous fibroids) and/or a suture is taken from the anterior parietal peritoneum across and behind the top of the uterine wound to the parietal peritoneum on the other side, fixing it in ventrosuspension: A heavy uterus may be supported by several fine sutures. When much bleeding occurs, the broad ligaments are compressed between the assistant's fingers until removal is completed, or an intestinal or thyroid clamp covered with rubber tubing is applied to broad ligaments. When fibroids of all kinds are present, particularly when multiple

and deep, an elastic ligature around the cervix, compressing the uterine vessels, affords preventive hemostasis. Galley needles are used to pass the ends of the tourniquet through an avascular area of the broad ligaments from one side to the other. Kelly clamps grasp the tourniquet on each side of the cervix. The ligature is pulled taut, crossed over and against the posterior cervix wall or lowest part of the lower uterine segment and clamped at the point of crossing by a toothless clamp. To avoid shock, ligature should be relaxed for a minute every 10 minutes, bleeding being controlled by compression with hot pads.

**Myomectomy** is discussed by F. Victor Rodrigues<sup>7</sup> (Univ. of Brazil). The two principal types of hysterectomy are total and subtotal. When the whole uterus is not removed, at least the entire corpus uteri is taken out. Hence the patient does not menstruate. For treatment of fibromas, extreme measures are taken; the organ bearing the tumor is sacrificed, whether wholly or in its menstruating part. Some surgeons remove only a portion of the upper part of the corpus uteri. This partial hysterectomy tends to preserve menstruation. In uterine myoma it is ideal to extirpate only the tumor and to leave the organ. This can be accomplished more often than most surgeons believe. Its psychosomatic importance is crucial and should not need to be emphasized.

From 1939 to 1950, 336 patients with uterine myoma were treated surgically, 230 by various types of hysterectomy and 106 (31.55 per cent) by myomectomy. Since there were 22 conservative hysterectomies, the number of conservative operations for myoma is increased to 128 (38.09 per cent), of which myomectomies constitute 82 per cent.

When the study was divided into four periods—1939-42, 1942-45, 1945-48 and 1949-50—the practice of myomectomy was found to have increased from 14.5 to 45.5 per cent. The increase was due to a decrease in hysterectomies in general and principally to a decrease in subtotal hysterectomies, which were reduced to an insignificant number. Of patients aged 41-45, 16.4 per cent had myectomy; of those over 45, 5.4 per cent (in these, conditions probably made myomectomy a simple operation). Even after age 40 myomectomy is advisable when it is not exceedingly difficult. If only those over 45 are excluded, myectomy represents 44.4 per cent of the total.

The ideal technic is to make one longitudinal incision

(7) *An. brasil. ginec.* 15:265-276, October, 1950.

in the middle of the anterior wall or transverse to the bottom (Bonney's "cowl" technic). Secondary incisions are made on the edges of the primary incision. The cavity can be easily opened. The nodules of the posterior wall can even be pulled out across it, as Bonney advises.

[For many years Rubin has been a staunch advocate of myomectomy. The points in technic which he describes are decidedly practical and will prove helpful to most surgeons.

Rodrigues' statistics indicate what can be done when one thinks in terms of myomectomy rather than hysterectomy. An increase in incidence of myomectomies from 14.5 to 45.5 per cent in 10 years is astonishing. Apparently the author and his associates are well satisfied with their results or they would not increase the incidence of myomectomy three-fold. I do not agree with Rodrigues that myomectomy should be performed in many women past age 40 because: (1) not many women past 40 want to have children; (2) there is a definite risk of recurrence of fibromyomas, and (3) since as far as we know the uterus serves no function except for procreation, there is no point in leaving the uterus in women near the end of the procreative life after they have already had all the family they desire. Also, there is some danger of the development of carcinoma, not because the patient had myomas but because of the natural incidence of malignancy of the uterus. One thing is certain, more myomectomies should be performed than have been done in the past, especially in women between 35 and 40.

Guerrero (*Ginec. y obst. México* 6:43, Jan.-Feb., 1951) reports on 640 cases of uterine myoma. No treatment was carried out in 26.7 per cent, hormonal or symptomatic therapy was used in 27.2 per cent, hysterectomy was done in only 7.3 per cent, partial hysterectomy with conservation of menstruation was done in 1.9 per cent, radiation was employed in 0.3 per cent and myomectomy in 36.5 per cent, the largest group of cases.—Ed.]

**Does Uterine Myoma Always Mean Operation?** Incidence, growth and development, types and symptoms of myomas are discussed by William F. Mengert<sup>8</sup> (Univ. of Texas). Treatment is not indicated until the tumor becomes larger than a three months' pregnancy. Then treatment would be indicated in a woman aged 20 but not necessarily in a woman of 45, providing both were symptom free.

Operations for myoma are myomectomy, subtotal hysterectomy, total hysterectomy and vaginal hysterectomy. Myomectomy is not as satisfactory as hysterectomy; if the reproductive function is not to be preserved, myomectomy is unsatisfactory. Total hysterectomy is preferred to subtotal hysterectomy. Size of the myomatous uterus may be reduced by myomectomy as a prelude to hysterectomy.

Irradiation has minimal, if any, effect on the tumor; it produces castration resulting in decreased pelvic blood supply

(8) J. Michigan M. Soc. 49:1302-1307, November, 1950.

and shrinking of tumors. Dilatation and curettage must precede external irradiation to ascertain absence of endometrial adenocarcinoma *before* treatment. A myomatous uterus larger than a three month pregnancy should not be irradiated; but if complete disappearance of the myoma is unimportant and the woman is willing to chance sarcoma, external x-ray therapy can be used. Intercavitary radium is contraindicated because of technical difficulties in delivering a castration dose to the ovaries. Irradiation, when some therapy is necessary, should be reserved for women at or near the menopause, with operation reserved for younger women.

Myomas are associated with infertility. In absence of other known causes of infertility, myomectomy is justifiable. Myomas disturb pregnancy when they distort and encroach on the endometrium and uterine cavity.

Pregnancy should be ruled out before contemplating surgery when there is a midline symmetric tumor of soft consistency. Differential diagnosis at the time of operation may be made from inspection of the round ligaments, insertion of a needle into the center of the mass, or, if necessary, by direct inspection. Most women with myomas will become pregnant, carry through to term and bear healthy children without serious sequelae.

[The question asked in the title, "Does uterine myoma always mean operation?" can be answered with an emphatic "No." In fact, most fibromyomas of the uterus require no treatment. This must be repeated over and over because many uteri are removed because they contain small fibromyomas. Most fibromyomas are entirely harmless and even when large sized remain harmless, with few exceptions. Women with myomas should be checked twice a year and eventually, with the change of life, the tumors diminish spontaneously. However, when fibromyomas are associated with profuse uterine bleeding at each menstrual period, surgery or irradiation must be instituted.—Ed.]

**Conservative Treatment of Salpingitis Complicating Myomata Uteri** refers to preservation of the involved tube and its accompanying ovary as opposed to their usual removal. H. C. Falk, Carl Mandelbaum and George Blinick<sup>9</sup> (Harlem Hosp.) report results in 135 consecutive cases of uterine myomas complicated by inflammatory adnexal disease in which hysterectomy was done and one or both tubes and ovaries left in situ unless ovarian or tubo-ovarian abscess or severe cystic ovarian disease were present.

Surgical treatment of salpingitis is rare in private prac-

(9) Ann. Surg. 132:247-252, August, 1950.

tice, for antibiotic therapy is usually begun early; however, in city hospitals patients are seen later when palpable masses are often present and antibiotic therapy is of doubtful value.

Analyses of the results of salpingectomy reveal unsatisfactory mortality, morbidity and reoperation rates; reoperation for symptomatic cystic ovaries and/or bleeding from the retained uterus is necessary in 5-10 per cent of cases. As a result, most gynecologists prefer hysterectomy and bilateral salpingectomy; the reported mortality rate is 4.1-18.4 per cent despite antibiotics.

The authors have used bilateral cornual resection in treatment of recurrent salpingitis. Concepts underlying this operation are based on bacteriologic and histopathologic evidence that gonorrheal infection from the endocervix reaches the tube by direct extension along the epithelium of the endometrium and endosalpinx. Interruption of this epithelial continuity prevents reinfection from the cervix ascending to the tube. The tube does not reinfect itself. Thus, on resolution of the existing inflammation in the retained tube, cornual resection results in cure. Hysterectomy for uterine disease is, in effect, a cornual resection.

The clinical cure rate in this series was 85 per cent, with improvement in 14 per cent. Postoperative complications were noted in 16 per cent. There was one death four days postoperatively. In addition to these encouraging treatment results, ovarian function is preserved in the younger women. Incidence of reoperation for cystic ovaries is reduced because the vascular supply to ovaries is least jeopardized and, consequently, cystic degeneration less likely.

**Clinical Evaluation of Falk's Procedure.** For chronically recurring gonorrheal salpingitis, when three or more severe acute attacks have interfered with employment, Charles R. Freed and Robert A. Kimbrough<sup>1</sup> (Univ. of Pennsylvania) use the Falk procedure. This is based on the fact that gonorrhea of the tube is self-limited. Interruption of the pathway of spread of gonococci from an infected cervix and endometrium comprises the rationale for the procedure. Thus, salpingectomy is avoided with its interference with ovarian blood supply and consequent ovarian cyst formation, which often necessitates oophorectomy later.

(1) *Am. J. Obst. & Gynec.* 60:416-421, August, 1950.

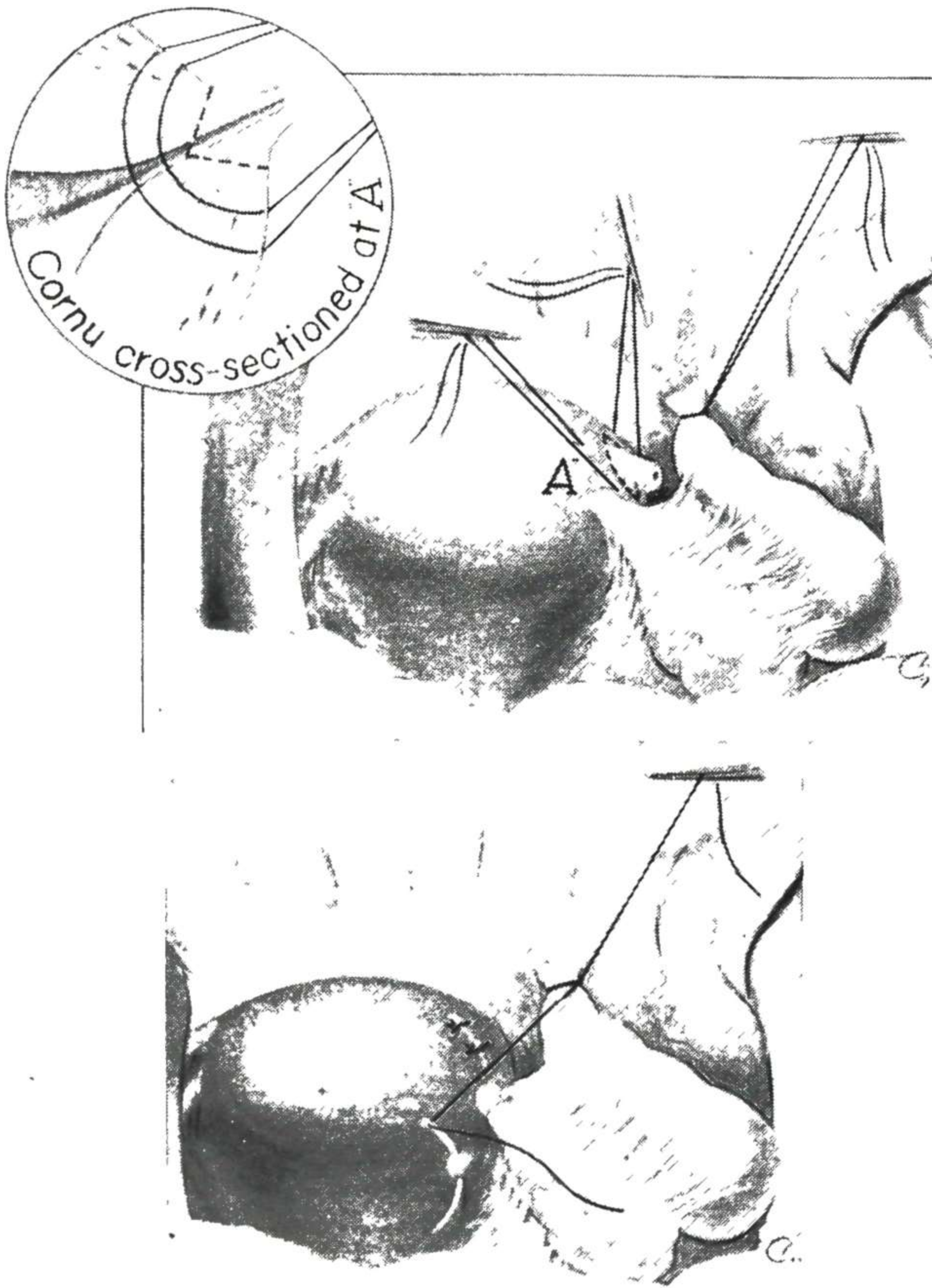


Fig. 100 (top).—Right tube has been ligated and resected. Sutures have been placed through cornu. Dotted line indicates direction and depth of incision.

Fig. 101 (bottom).—Cornual sutures have been tied. Needle in posterior wall of uterus denotes placement of free end of tube.

(Courtesy of Freed, C. R., and Kimbrough, R. A.: *Am. J. Obst. & Gynec.* 60:416-421, August, 1950.)

On hospitalization the patient is given 100,000 units of penicillin intramuscularly every three hours with 0.5 Gm. sulfamerazine and 0.5 Gm. sulfadiazine orally every six hours. When acute symptoms subside, temperature is normal for at least seven days, white count is below 8,000, sedimentation rate is decreasing and a pronounced or persistent temperature



rise does not follow gentle bimanual examination, the patient is ready for operation. Penicillin and sulfonamide therapy is continued until the temperature has remained normal for 24 hours postoperatively.

The Falk procedure was performed on 62 patients with an average age of 25. Ninety-five per cent were Negroes. In most, duration of salpingitis was 8-12 months and 45 per cent had had incapacitating pain for 10-14 days. Although half had pelvic masses, this was not found to be an index of the number or severity of symptoms.

TECHNIC.—When the abdomen is opened, tubes and ovaries are examined with minimal disturbance of adhesions. If a cystic or abscessed ovary is found, tubal resection is contraindicated. The tube to be resected is ligated about  $\frac{1}{2}$  in. from the uterus and the suture ends left long. The tube is severed and a generous stump left. Parallel sutures are placed deeply through the cornual portion of the uterus with the ends held apart by an assistant (Fig. 100). An Allis clamp is placed on the cornual stump, and while gentle traction is exerted on the clamp, the cornu is excised with a wedge type elliptic incision, with care not to cut the previously placed cornual sutures. These sutures are tied after excision of the cornu, effecting immediate hemostasis (Fig. 101). The long end of the suture used to ligate the tube is rethreaded on a round needle and a deep bite is taken in the posterior surface of the uterus just below the attachment of the ovarian ligament. Tying of this suture pulls the cut end of the tube against the uterine wall under the suspensory ligament of the ovary. The round ligament is utilized to cover the cornual portion in a modified Coffey suspension. The remaining tube is similarly resected.

In a high percentage of cases the resected tubes were 3-5 cm. in diameter. Average number of postoperative hospital days was 9.7. The only case of morbidity was one complicated with acute tonsillitis. Ninety-two per cent of the patients were followed for at least six months. Pelvic diathermy was used when palpable adnexal masses were present at the time of discharge. Usually adnexal tenderness had completely subsided within three weeks after operation and masses usually disappeared in four to six weeks, 61 per cent having no mass remaining, 33 per cent having only mild residual adnexal thickening and 6 per cent having definite masses. Only three patients complained of pain, and examination revealed no adnexal lesion to account for this symptom. Dyspareunia was almost always relieved. In three patients, severe gonorrhoea developed later but none had evidence of salpin

gitis. Clinical relief was obtained by 95 per cent; none required subsequent operation.

**Conservative Surgery in Gynecology.** The type of operation for diseases of the pelvic organs in women of childbearing age must be chosen carefully. Operative procedures depend on the patient's age, size and location of growths, parity and to some extent on the patient's wishes. Robert James Crossen<sup>2</sup> (St. Louis) advises young women with myomas to have children early so that hysterectomy can be done later if necessary. If other factors have been excluded in infertile patients with myomas, myomectomy should be considered. When location of the tumor will interfere with pregnancy or delivery, myomectomy should be done before the patient becomes pregnant. Myomectomy is sometimes necessary during pregnancy; miscarriage can usually be prevented by administration of large doses of diethylstilbestrol postoperatively. In multiparous women in their middle or early thirties, high hysterectomy with preservation of menstrual function is usually preferable to complete or supravaginal hysterectomy. In general, hysterectomy should be limited to women over 40.

A second field for conservative surgery is disease of the fallopian tubes. In women of childbearing age the operation should not constrict the tube or interfere with its peristaltic movements, especially when the ovary on one side is removed but the tube preserved. Great care should be taken not to injure the overlying tube or its blood supply in removal of parovarian cysts. In the infertile patient whose tubes are found closed after repeated Rubin tests, hysterosalpingography is indicated. The type of plastic operation to open the tubes depends on location of the block. When tubes are occluded at the fimbriated end, salpingostomy is indicated. When the block is in the proximal or middle portion, the closed distal portion is excised and the remaining portion conserved. When the block is at the interstitial portion with the distal part of the tube open, implantation may be done by one of several methods. In all cases, the farther the block is from the uterus, the better the chance of success.

In many young women ovarian cysts or tumors can be resected and normal ovarian cortex preserved. Persistent ovarian cysts, 2-3 in. in diameter, or enlarging cysts or tu-

(2). *Texas J. Med.* 46:746-750, October, 1950.

mors demand investigation. However, when a polycystic ovary is only slightly enlarged, with perhaps a thickened capsule, the advantages of surgery should be carefully considered. Decortication of the ovary should be done in only carefully selected patients. Only when other treatment methods have received thorough trial should operation be considered. When both tubes have been removed or no tubal lumen exists, Estes' operation is the preferred procedure.

In endometriosis in women of childbearing age, surgery should be delayed as long as possible unless an ovarian cyst is present. If operation is necessary, ovarian activity should be preserved if possible. Even if small areas of endometriosis must be left, it is worth the risk in women under 35. If the remaining areas of endometriosis become active, troublesome symptoms can be stopped by radiation therapy. Reports on use of hormones to control symptoms and progress of endometriosis have been encouraging but are not conclusive.

[This article is important because it cannot be emphasized too often that gynecologic surgery is often too radical. In many women the uterus and at least one ovary or a good part of it can be preserved. Of course, it is much easier to remove an organ than to perform conservative surgery on it. Sometimes myomectomies are difficult and bloody, whereas hysterectomy is nearly always an easy operation and it is much easier to remove an entire ovary than to resect dermoid, chocolate and even serous cysts. In young women with endometriosis it is important to preserve ovarian function even though it may be easier to remove both ovaries. Also, in selected cases reconstruction operations should be done on the fallopian tubes to try to restore their function.—Ed.]

**Hysterectomy: Personal Experience with 2,000 Consecutive Cases.** Curtis Tyrone with John C. Weed<sup>3</sup> (Tulane Univ.) believe that hysterectomy should be part of any pelvic procedure on a woman near the menopause or in a younger woman if the family is complete or pregnancy impossible. In this series, 691 patients had not been relieved by previous conservative pelvic surgery, and Tyrone's experience shows that hysterectomy is almost without risk and restores the patient to complete health. There were 1,457 total abdominal operations, 170 supravaginal and 373 vaginal. The last is contraindicated when pelvic structures are fixed or the cervix cannot be drawn to the vaginal outlet. Of the abdominal techniques, the total is preferred since it eliminates the possibility of cervical and endometrial malignancy.

(3) Ann. Surg. 133:819-827, June, 1951.

Indications were: fibroids, 873 (only when causing symptoms or rapidly growing); endometriosis, 495; uterine prolapse, 373; uterine fibrosis, 161; cervical stricture, 143 (most after previous plastic surgery or conization); functional bleeding, 128 (most after fair trial of conservative measures, including radium, which was followed by endometrial malignancy in 12 of 48 patients); uterine malignancy, 107; ovarian cysts, 85, and pelvic infection, 61.

Spinal analgesia was used in 1,187 cases, in recent years being given 90 per cent of the time. On the operating table an infusion of 5 per cent glucose in physiologic saline, to 2,000 cc., was given, with further infusions only if fluids could not be taken by mouth. Special methods were used only when indicated. Chemotherapy and antibiotics were prescribed only for pelvic cellulitis, peritonitis or wound and urinary infections. Vigilance was maintained against thrombosis and embolism and special measures were used only on suspicion of trouble. Ambulation as early as the day after operation is important in reducing complications. Present hospital stay seldom exceeds eight days.

Of 576 patients listed as having postoperative complications, 291 had only temperature elevations to 100.2 F. or over for two consecutive days. Of the 285 with identifiable complications, three-fourths had urinary difficulties, usually related to catheterization and principally after vaginal operations. The only urinary tract injuries occurred with vaginal operations: one accidentally severed ureter, one opened bladder and one vesicovaginal fistula. A fatal embolism was the sole instance of thrombosis or embolism. Venous ligation prevented intravascular clots in a few cases, and superficial vein ligation was successful in nine cases of thrombophlebitis. Other complications included 20 wound infections, 5 infections and 3 abscesses of the cuff in vaginal procedures, postoperative bleeding, readily controlled, in 9 patients and occasional intestinal obstruction, ileus, pelvic, cellulitis and peritonitis. There were four deaths (0.20 per cent), three in poor risk patients and one of embolism following suggestion of thrombophlebitis early in convalescence.

**Changing Indications for Hysterectomy in Climacteric Woman.** The records of 271 women, aged 40-55, who had had

hysterectomies were analyzed by J. Robert Wilson and M. Joseph Daly<sup>4</sup> (Temple Univ.).

When bleeding near the menopause requires control, total hysterectomy is preferred to subtotal in cases in which the risk is minimal and in physiologically young women, because (1) bleeding can be controlled permanently without suddenly precipitating the menopause, (2) any symptoms associated with subsequent cessation of ovarian function may be treated without fear of producing reactivation of the endometrium with bleeding and (3) development of uterine cancer, which may be increased in these patients, is prevented.

Requirements before hysterectomy include careful pre-operative evaluation, replacement of blood to a level of at least 11 Gm. hemoglobin and careful diagnostic study to rule out malignancy. In physiologically young women removal of ovaries is unwarranted; in postmenopausal women or those with symptoms of ovarian failure, ovaries may be removed. Contraindications to hysterectomy are: (1) absence of well founded indication; (2) advanced cardiovascular renal disease, uncontrolled diabetes, blood dyscrasias and extreme obesity; (3) poor hospital facilities and an inexperienced surgeon. Indications for surgery are: (1) bleeding from a benign lesion sufficient to require control; (2) bleeding requiring control and associated with any condition contraindicating irradiation; (3) bleeding which because of the physician's ability or physical facilities can be controlled more safely by surgery than by radiation; (4) bleeding from a uterus which may be removed in conjunction with an indicated vaginal plastic procedure.

Contraindications to irradiation are: (1) absence of subjective menopausal symptoms, (2) presence of small fibroid tumors which can produce symptoms other than bleeding because of their location or because of degeneration or infection, (3) presence of ovarian tumors over 5 cm. in diameter, (4) old pelvic inflammatory disease associated with pelvic adhesions (adherent loops of bowel may be overirradiated and become necrotic), (5) cervical and uterine infections, which may spread laterally after irradiation, (6) vaginal relaxation or prolapse, (7) firm association of irradiation and cancer in the patient's mind. Irradiation should be given only

(4) Am. J. Obst. & Gynec. 60:1088-1100, November, 1950.

experienced persons. Size of the uterus is important because it may prevent adequate dosage from reaching the gonads and tumor degeneration may follow decrease in blood supply. Pedunculated tumors are generally better managed surgically. In general, if irradiation is contraindicated, hysterectomy is the method of choice for control of bleeding.

[In the discussion of this paper, Kottmeier stated that, unlike most American gynecologists, he uses small amounts of radiations for benign uterine bleeding in the preclimacterum. At Radiumhemmet the dose is 40 mg. radium element screened by 0.5 mm. Pt left in the uterus for 16 hours, or a total of only 640 mg.-hr. radium. Results have been satisfactory. In the United States the dose of radium used to stop benign uterine bleeding in the preclimacterum varies between 1,200 and 2,400 mg.-hr. Novak said his experience has not shown an increased frequency of cancer of the endometrium after the use of radium and that the statistics of Corscaden and Gusberg require confirmation.

James Young of London referred to the study by Foulkes (*J. Obst. & Gynaec. Brit. Emp.* 56:648, August, 1949) of 169 cases of functional bleeding in which he proved two points. (1) In younger women, the results of curettage were relatively unsatisfactory, only 30 per cent of whom obtained adequate relief. (2) In older women, curettage was, in a high proportion of the cases, successful, with at least 60 per cent of women nearing the menopause obtaining clinically adequate relief.

Novak mentioned that many gynecologists have become increasingly radical, having in mind the possible development of adenocarcinoma in later life, and that this trend will encourage abuse of hysterectomy. With this I fully agree. I do not believe that a uterus should be removed without an absolutely valid reason, chiefly profuse menstrual bleeding. In women past 45 who have profuse bleeding one may use irradiation or hysterectomy. I do not favor irradiation, but find no fault with those who use it. In women under 40, profuse uterine bleeding should preferably be treated by hysterectomy, because ovarian function is essential and after radiation therapy ovarian activity ceases.—Ed.]

**Trend toward Complete Hysterectomy.** Complete hysterectomy has gained in popularity because of general recognition that it is dangerous to leave the cervical stump, according to Irving F. Stein<sup>5</sup> (Michael Reese Hosp.). Pelvic lesions should not be diagnosed solely on the basis of history and manual examination. Inspection of the region with a speculum is imperative and study of smears may be necessary for exact diagnosis. Of 561 hysterectomies, 94 per cent were total, with 60 per cent done by the abdominal route and 40 per cent by the vaginal. There was no operative mortality.

The type of hysterectomy to be performed depends on extent of the lesion and skill of the surgeon. Complete abdominal hysterectomy should be done prophylactically if cervical cancer is likely to be present or to develop. It eliminates the

(5) *West. J. Surg.* 59:6-12; January, 1951.

chronically inflamed cervix and makes prolapse of the vaginal vault unlikely. Vaginal hysterectomy is done for prolapse. Complete vaginal hysterectomy may be used to remove small fibroids, adenomyosis and fibrosis, if size and mobility of the uterus permit. When total hysterectomy entails danger to the patient because of increased vascularization or fixation to nearby structures or pelvic organs, subtotal hysterectomy is justifiable. Many symptoms, however, persist after this operation.

The fear of a shortened vagina after total hysterectomy is groundless. The procedure is not more difficult to perform than subtotal hysterectomy; results depend largely on the skill and judgment of the surgeon.

Stein recommends a time lapse of three years after subtotal hysterectomy has been performed before carcinoma of the cervical stump is diagnosed. If carcinoma of the stump is found in that period it probably was present at the time of hysterectomy. Such lesions could be eradicated by election of the total operation.

**Total Abdominal and Vaginal Hysterectomy: Comparison.** Michael L. Leventhal and Maurice L. Lazarus<sup>6</sup> analyzed 300 consecutive operations of each type. All were private practice patients and were operated on by 15 members of the gynecologic staff of Michael Reese Hospital. The senior men, those who did the greatest volume of work and are considered the more experienced technicians, removed the uterus vaginally 282 times and abdominally 245 times. The eight men with less experience did abdominal hysterectomy 55 times and vaginal hysterectomy 18 times, giving the impression that as the experience of the operator increases, his indications for vaginal surgery broaden.

The method of removal chosen appeared to be influenced by parity, size of the uterus and the abnormalities it contained. In the abdominal group, 103 patients were nulliparous and 197 parous, whereas in the vaginal group 5 were non parous and 295 parous. For comparison of size, a small uterus was considered one in which all growths did not exceed the size of an eight weeks' gestation. On this basis, in the abdominal group 219 uteri were large and 81 small, where

(6) *Am. J. Obst. & Gynec.* 61:289-299, February, 1951.

in the vaginal group 94 were large and 206 small. These figures reflect the opinion that it is preferable to remove larger tumors abdominally.

To compare morbidity, the standard used was an oral temperature of 100.4 F. on any 2 postoperative days, excluding the first 24 hours. After abdominal hysterectomy, morbidity was 27.3 per cent; after vaginal hysterectomy without additional plastic repair, 38.8 per cent, and with additional surgery, 39.3 per cent. Thus, with regard to over-all morbidity, the abdominal approach is somewhat safer than the vaginal. There was no difference in morbidity after vaginal hysterectomy when colpoperineorrhaphy was also done (38.1 per cent versus 35.8 per cent); but when it was combined with plastic procedures plus adnexal removal, morbidity was 52.5 per cent. Statistically, morbidity was not affected in either group by previous surgery. When previous surgery has been performed, choice of the vaginal route depends on the nature of postoperative residuals, not on the type of previous operation.

The percentages of urinary retention and urinary tract infection were higher when the vaginal route was chosen, whereas paralytic ileus, venous thrombosis, pulmonary embolus and ureteral injury were commoner in the abdominal group. There was one death; a nullipara, 66, who died suddenly of pulmonary embolus eight days after abdominal pan-hysterectomy. The ureter may be injured during vaginal hysterectomy when the adnexa are removed, but in removal of the uterus alone it is less likely to be compromised in vaginal than in total abdominal hysterectomy.

Average hospital stay for the abdominal group was 11.1 days and for the vaginal group 11.5 days, but 40 patients in the vaginal group had to remain over 2 weeks as compared with 23 of the abdominal group.

The authors concluded that vaginal hysterectomy should not compete with abdominal total hysterectomy but that each has its own indications and contraindications. Each patient should be evaluated individually, the type and extent of disease, previous surgery, presence of prolapsus, obesity and training and skill of the surgeon being considered.

[I fully agree with the authors that vaginal and abdominal hysterectomy should not be competitive operations. Each has its place, and all



surgeons who perform pelvic operations should be able to perform either operation with equal dexterity.—Ed.]

**Morbidity after Total Abdominal Hysterectomy**, as affected by preoperative vaginal preparation on the operating table, intraperitoneal use of sulfathiazole and simultaneous appendectomy, was studied by Joseph Hyde Pratt, Madison J. Lee, Jr., Walter F. Hasskarl, Jr., and Robert W. Brandes<sup>7</sup> (Mayo Clinic and Found.). Three series of over 100 patients each, in 1947, 1948 and 1949, formed the basis of the study. The surgical technic was the same during the three years, but in the later years pentothal<sup>®</sup> sodium and curare were administered intravenously more often in place of nitrous oxide-oxygen-ether. The only other change was earlier ambulation. Preoperative vaginal and perineal care of all patients was similar: vulva and perineum were shaved; soapsuds enema followed by a douche-containing soda bicarbonate was given the night before operation, and a second douche was given the morning of surgery. In 1947 patients were catheterized and the vagina wiped out with two merthiolate<sup>®</sup> sponges. In 1948 and 1949 the vagina was scrubbed with sterile soap and water, wiped out with merthiolate<sup>®</sup> and the patient catheterized. Five Gm. sulfathiazole crystals were given intraperitoneally to all patients in 1947 and 1948. Appendectomy was performed simultaneously in 54.8 per cent of cases in 1947, 49.0 per cent in 1948 and 55.5 per cent in 1949.

Morbidity was defined as an oral temperature of 100.4 F. or higher on any two postoperative days, excluding the day of operation. Morbidity was 42.3 per cent when sulfathiazole was used intraperitoneally and there was no vaginal preparation in the operating room, 16.7 per cent when sulfathiazole was used and the vagina was prepared in the operating room, and 23.1 per cent when the vagina was prepared in the operating room but sulfathiazole was not used intraperitoneally. In 1948 and 1949, morbidity was essentially the same regardless of whether or not appendectomy was done simultaneously. Over-all morbidity for the 323 patients in the three series was 27.2 per cent.

Pelvic malignant disease was present in 9.6 per cent in 1947, 18.6 per cent in 1948 and 11.9 per cent in 1949. Morbidity was 60.0, 21.0 and 35.7 per cent respectively.

(7) Am. J. Obst. & Gynec. 61:407-413, February, 1951.

The only death was in 1947. An obese, hypertensive patient with auricular fibrillation died on the sixth postoperative day, presumably of multiple emboli from mural thrombi. Thus, over-all mortality was 0.31 per cent.

The authors concluded that vaginal preparation with soap, water and antiseptic in the operating room is an important factor in lowering morbidity after total abdominal hysterectomy; that intraperitoneal use of sulfathiazole somewhat lowers morbidity but is less important than vaginal preparation, and that appendectomy performed simultaneously has no effect on morbidity and should be performed whenever there is no contraindication.

**Indications for Total Hysterectomy in Nonmalignant Conditions of the Uterus.** During or after the menopause Arnaldo de Moraes<sup>8</sup> advocates total hysterectomy as cancer prophylaxis for uterine myoma, severe functional hemorrhages, chronic pelvic inflammation, pain and adhesions, ovarian tumors, genital prolapse with uterine lesions, etc. At the University of Brasil uterine myoma is treated surgically, preceded by curettage, since surgery is more conservative than x-ray therapy. In young women, myomectomy is done or, when this is impossible, fundectomy, partial hysterectomy or myometrectomy. In women past 40 a total hysterectomy is preferred, to exclude the danger of cancer in the cervical stump. Tumors are often found in patients who have had subtotal hysterectomy.

The abdominal hysterectomy is chosen for patients with ovarian or large uterine tumors, patients previously operated on (e.g., cesarean section), after severe inflammatory endometritis and for multiparas with a long straight vagina. The vaginal route is selected for aged women, multiparas, when there is genital prolapse or when vaginal plastics are required. Local anesthesia is given, which produces little shock. For prolapse, the Fothergill technic is used for menstruating women, with or without amputation of the cervix; during or after menopause, a vaginal hysterectomy according to the Mayo technic is done, with colpoperineorrhaphy. Colpocleisis is done in elderly women.

[De Moraes and Stein agree with most gynecologists in the United States that whenever a hysterectomy is done regardless of whether the

(8) *An. brasil. ginec.* 30:119-128, August, 1950.

condition is benign or malignant, the cervix should be removed with the corpus. It has been definitely shown that in the hands of trained surgeons the risk is no greater for total hysterectomy than for supravaginal hysterectomy. With supravaginal hysterectomy there is risk of leaving an undetected carcinoma of the cervix and enough carcinomas of the cervix develop years after supravaginal hysterectomy to warrant almost routine removal of the cervix with the body of the uterus. However, total hysterectomy should not be done if it would jeopardize the patient's life or health. In such cases it is safer to leave the cervix than to persist in extensive manipulation which may traumatize the rectum or bladder or produce excessive bleeding.

Castallo and Wainer (*Am. J. Obst. & Gynec.* 60:406, August, 1950) reviewed the literature on the vagina following abdominal hysterectomy and found 167 cases of increased vaginal length—2.4 cm. after total and 1.6 cm. after supravaginal hysterectomies. This increase is seemingly due to several facts, including the inherent elasticity of the vagina, imbrication of the supporting ligaments in such manner as to give a definite lift to the vagina and shortening of the uterosacral ligaments. The technic of total hysterectomy described by Dallas (*California Med.* 74:92, February, 1951) prevents shortening of the vagina. At Stanford, 1944-50, mortality for total hysterectomy was 1.1 per cent and for the subtotal operation 1.4 per cent. Of course, many of the latter were done on seriously ill women.

In vaginal hysterectomy Burke (*J. Obst. & Gynaec. Brit. Emp.* 57:912, December, 1950) recommended that a thin layer of cervix be left attached to the ligaments in the bases of the broad ligaments because it increases the safety and ease of operation. In his 585 cases of vaginal hysterectomy done chiefly for prolapse, abnormal bleeding and fibromyomas, there were three deaths (0.5 per cent).

Falk (*Harlem Hosp. Bull.* 3:89, December, 1950) illustrated his technic of total abdominal hysterectomy with 62 excellent drawings. Approximately 140 of these operations are done each year, and there have been no cases of vesico-, recto- or uterovaginal fistulas following nor was the bladder injured in any patient.

In a symposium on hysterectomy (*Proc. Roy. Soc. Med.* 43:969, December, 1950), Kimbell suggested that the term panhysterectomy be abolished in favor of the term total hysterectomy with or without salpingo-oophorectomy. I long ago made this recommendation (*1941 YEAR BOOK OF OBSTETRICS AND GYNECOLOGY*, p. 398). At Samaritan Hospital for Women, among 2,569 total hysterectomies, the death rate was 1.4 per cent and among 910 subtotal hysterectomies, 1.6 per cent. In the total group the appendix was removed 502 times and in the subtotal group 58 times. In only one case was death attributable to the appendicular scar. White said that since the ovaries are not always removable during vaginal hysterectomy, it is not a suitable operation for carcinoma of the body of the uterus and should be given up in such cases. Plastic surgery to the ovaries is very difficult or impossible and appendectomy impossible at the time of vaginal hysterectomy. Green-Armytage reported 981 vaginal hysterectomies done chiefly for hemorrhagic states with a death rate of 0.8 per cent. For such cases he is opposed to use of radium with its subsequent disorders. Bourne saw no disadvantage to the patient in leaving a healthy nulliparous cervix and he is not convinced that incidence of carcinoma in the nulliparous, uninfected cervical stump is higher after subtotal hysterectomy than it is in the nullipara who has not had subtotal hysterectomy. Further, there are advantages to the patient in leaving

the cervix since the subtotal operation is quicker, does not disturb the supports of the vaginal vault and the cervix plays some part in a woman's sexual life. These statements are reminiscent of the article written by Robert Frank shortly before he died (1949 YEAR BOOK OF OBSTETRICS AND GYNECOLOGY, p. 434).—Ed.]

**Cervical Tumors after Subtotal Hysterectomy.** M. Dargent<sup>9</sup> reports 114 cases of cancer of the uterine cervix after subtotal hysterectomy. He accepts an interval of three years schematically to differentiate two kinds of tumor: an early type which he designates as epithelioma arising in the cervix where it existed before subtotal hysterectomy (55 cases) and a late type developing in the remaining cervical stump (59 cases). In 74.5 per cent of the first group the fault lay in erroneous diagnosis of metrorrhagia or fibroma. For them subtotal hysterectomy was an incorrect procedure and the surgical trauma it caused may have contributed to development of the neoplasm. Results after five years in these cases were obviously unsatisfactory.

The second type of tumor is different though in it also metrorrhagia or fibroma, diagnosed in 57.5 per cent, led to subtotal resection of the uterus. One of every four was operated on for inflammation of the adnexa with chronic cervicitis for 14-28 years. These conditions should always be regarded as precancerous and contributing to development of cervical cancer. Treatment in this late type of cervical stump cancer is usually satisfactory, with good results after five years.

In all series of cases there are some in which metastases or cancer of the uterus or ovaries develop early. Metastatic involvement in the early type of cases affected the rectum in seven, the bladder in five and the intestine in one. In the late group there were 11 metastatic tumors: 2 ileal, 7 rectal and 2 vesical, and all very serious.

Radiotherapy is dangerous because of the proximity of the bladder and rectum and is unnecessary if a cervicectomy and pelvic lymphadenectomy are done after simple irradiation of the vagina.

Dargent emphasizes the importance of (1) total hysterectomy in the presence of doubtful ovarian tumors, (2) thorough examination of the cervix and (3) Papanicolaou's test in metrorrhagia.

(9) Lyon chir. 45:827-836, October, 1950.

[Some authors maintain that when a cancer is found in the cervix within two years of a supravaginal hysterectomy the cancer was present in the cervix at the time of operation. Dargent considers three years the period of time for such a diagnosis. Actually it does not matter which period is used. Carcinoma of the cervix after hysterectomy is a good reason for performing a total hysterectomy whenever possible. This is done by most gynecologists. However, inexperienced or occasional operators are wise not to try to remove the cervix routinely. In their hands, more women would die or have distressing morbidity from trauma to the bladder, ureters and other structures as a result of the attempt to perform a total hysterectomy than would die of carcinoma of the cervix which would be found later. Even experts in gynecology frequently leave the cervix, particularly when the operation would be so traumatic and difficult as to endanger the patient. I refer particularly to cases of endometriosis in which rectum, vagina and cervix are all one mass and, if one persists in trying to separate the vagina and cervix from the rectum, harm may be done.

Lachmann (*Acta obst. et gynec. scandinav.* 30:169, 1950) reported 73 cases of cancer of the cervical stump discovered at the Stockholm Radiumhemmet among 521 cases of cancer of the cervix. Incidence of cancer in the cervical stump has been increasing in recent years in proportion to the increase in number of patients treated by subtotal hysterectomy. Stump cancer is likely to develop in about 1 per cent of patients after subtotal hysterectomy. This is the same as the incidence of cancer of the cervix in all women of the age group concerned. At Radiumhemmet the five year cure rate for cancer of the cervical stump was 59 per cent, which is more favorable than the five year cure rate for cancer of the cervix in general. Probably this is due to the fact that most patients with cancer of the cervix were treated at an early stage. It is important to remember that in cases of stump cancer in which cancer was probably present at the time of hysterectomy and was not diagnosed, prognosis is unfavorable. The five year cure rate in these cases was zero, whereas in the other cases it was 72 per cent.

Hendricks (*J. A. M. A.* 146:100, May 12, 1951) reported 28 cases of carcinoma of the cervical stump seen in 10 years, in 22 of which, onset of symptoms occurred more than five years after a subtotal hysterectomy. He pointed out that, in treatment of vaginal bleeding, accurate diagnosis of the primary pathology, not hysterectomy, should be the first thought. He believes that routine dilatation and curettage immediately before any pelvic surgery is too often neglected. It can be done with a minimum of time and effort at the time of preoperative catheterization. Had dilatation and curettage preceded laparotomy in some of the patients he reported, there would have been an excellent chance in each case of making a correct tentative diagnosis of carcinoma of the cervix before laparotomy. If at that time inspection of the cervix did not lead to a biopsy of the lesion, then the free bleeding resulting from the cervical dilatation would have aroused the operator's suspicion.—Ed.]

**Bilateral Polycystic Ovaries, the Stein Syndrome,** is characterized clinically by menstrual irregularity. Principal features are amenorrhea, history of sterility, masculine type of hirsutism and, less consistently, retarded breast development and obesity. This condition, resulting from an endocrine disturbance, in which the ovaries are similarly and simulta-

neously enlarged and show cystic changes which are irreversible and refractory to hormonal therapy, was first treated by ovarian wedge resection by Stein in 1929. Since then, he has operated on 76 patients. Menstrual function was restored in all 28 single patients and in 90 per cent of the 48 married

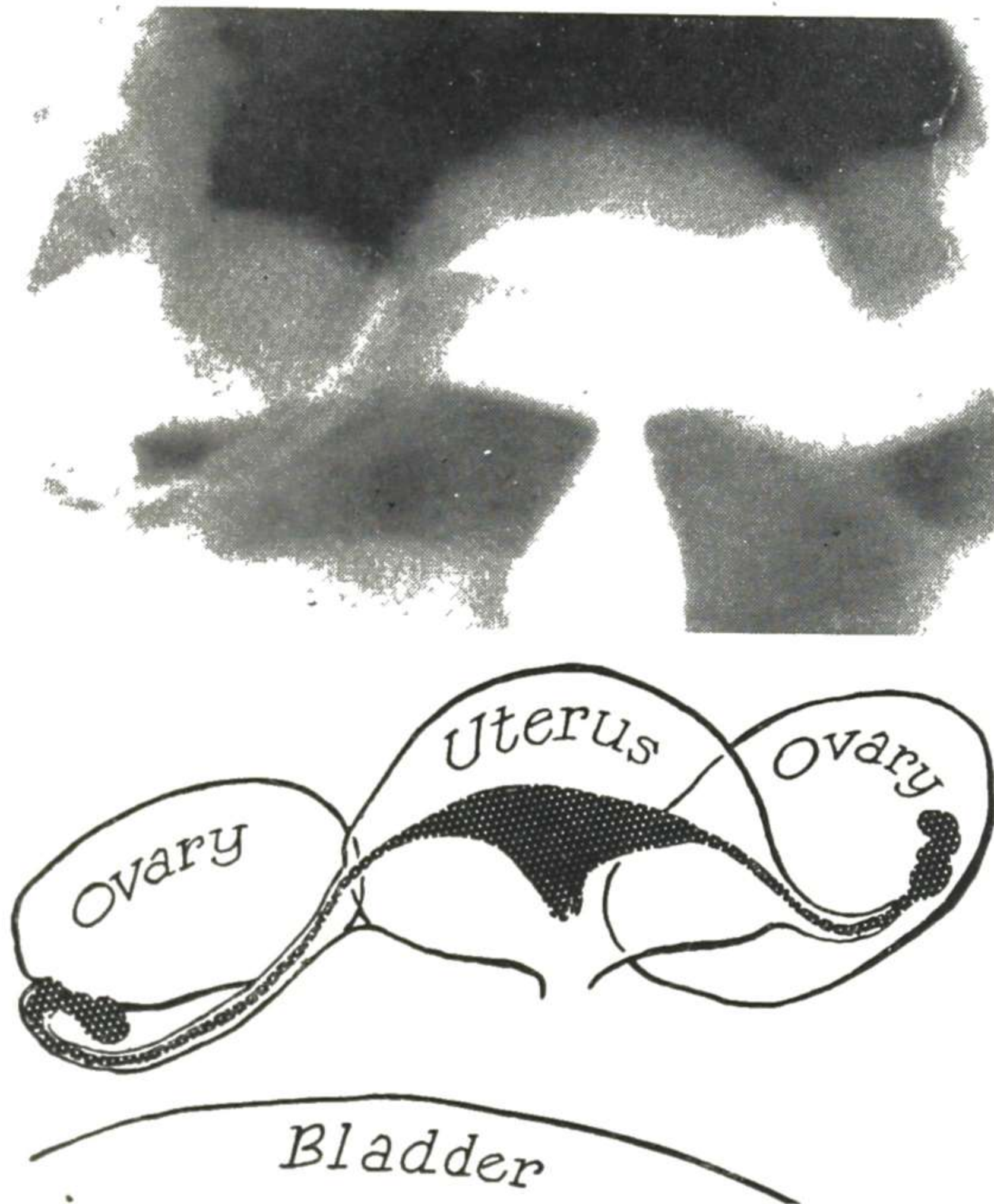


Fig. 102.—Bilateral polycystic ovaries. Combined gynecography. (Courtesy of Leventhal, M. L., and Cohen, M. R.: *Am. J. Obst. & Gynec.* 61:1034-1046, May, 1951.)

patients. Sixty-six per cent of the married patients conceived one or more times.

Michael L. Leventhal and Melvin R. Cohen<sup>1</sup> report 10 additional cases from Michael Reese Hospital. Diagnosis was based on a history of secondary amenorrhea; general physical examination usually revealed no stigmas of gross endocrine abnormalities. However, seven patients had hirsutism, although it usually occurs in only about 50 per cent. Secondary

(1) *Am. J. Obst. & Gynec.* 61:1034-1046, May, 1951.

sex characteristics were often normal. Pelvic examination revealed a normal or small uterus and bilateral, firm, smooth, nonsensitive ovarian enlargements. Pneumoroentgenograms of the pelvis were typical and diagnostic (Fig. 102).

After surgery, all patients had normal menstruation. Hairy growth was arrested in three and improvement occurred in the other four, although in none did it disappear. In these patients hyperplasia of the theca interna was a constant finding in removed ovarian tissue, with prominent luteinization of the theca in four. Experimental evidence supports the theory that thecal hyperplasia produces androgens, this being the factor apparently important in production of hirsutism, amenorrhea, sterility and enlargement of the clitoris. Quantitative variations in secretion of these steroids may account for the menstrual abnormalities, and it is also possible that progesterone or one of its derivatives may exert the androgenic effects seen in this syndrome.

Ovarian dysfunction, manifested by secondary amenorrhea and associated with polycystic changes in the ovarian cortex, was thought a reflection of dysfunction in the anterior pituitary-ovarian cycle. Whatever the pathogenesis, partial resection of the fibrous cortex with its contained cysts is usually followed by restoration of normal menstrual and reproductive function.

**Stein-Leventhal Syndrome.** The picture of genital insufficiency is closely connected with ovarian dysfunction. Stein and Leventhal described a syndrome in which ovarian disturbance apparently caused childlessness. Amenorrhea or oligomenorrhea, sterility and bilateral polycystic ovaries formed a characteristic triad, and hirsutism, obesity, underdevelopment of the breasts and pelvic pain were noted in some cases. Some patients never had normal menstruation, but in most the disturbance came with sexual maturity, first in the form of hypermenorrhea; later, with longer intervals, the flow became slighter. Variations of hirsutism appeared in half and obesity in only 1/10 of the patients, all of whom had normal basal metabolism.

Bimanual examination in some cases revealed palpable ovaries two to four times normal size, often tender and elastic. Stein used pneumoroentgenography to disclose disproportion between ovaries and uterus, but the method has

not been favored by other American investigators. Operation in all cases revealed enlargement of the ovaries mainly due to cysts (5-15 mm. in diameter) in the cortex. These, visible on the surface, did not actually protrude from the gland surface. Where the tunica albuginea was very thick, the ovaries were white with a glossy surface. Cysts dimly visible through the tunica albuginea formed gray patches. No ovarian wrinkling, recently ruptured follicles or corpus luteum were noted.

In almost 9,000 laparotomy records, Paavo Vara and Kalevi Niemineva<sup>2</sup> (Univ. of Helsinki) found 6 patients with symptoms of Stein-Leventhal syndrome, with no other apparent cause for irregular menses and sterility but with retroverted uterus—perhaps important.

Stein and Leventhal emphasize that the condition is not congenital, inflammatory or degenerative but is due to endocrine disturbance of unknown mechanism. Along with endocrine disturbance, Ingersoll and McDermott mention congenital fibrosis and thickening of the ovarian capsule as possibly hindering ovulatory function and causing polycystic changes. Thickness of the tunica albuginea causes menstrual disorders and sterility. The authors consider retroflexion a possible etiologic factor since it causes congestion and leads to thickening of the tunica albuginea until it becomes a mechanical obstacle to ovulation.

In ovarian surgery, which often involves inadequate operative indications, the Stein-Leventhal triad provides an unmistakable directive. Stein removes one half to three fourths of both ovaries, making sure that the position of the ovaries provides optimal blood circulation. With very painful menses and when technically feasible, the operation should be complemented by presacral neural resection as recommended by Cotte.

**Ovarian Resection—Ovariectomy—or Absolute Conservatism.** Herbert F. Traut<sup>3</sup> (San Francisco) states that ovarian surgery is done predominantly on the right side, probably owing to the wide use of the McBurney incision for appendectomy, which makes the left ovary inaccessible to the surgeon. It is obvious that ovarian pathology is not right sided,

(2) *Ann. chir. et gynaec. Fenniae* 40:23-33, 1951.

(3) *J. Michigan M. Soc.* 50:611-614, June, 1951.



and it is the lack of specific knowledge of ovarian pathology that leads to much of the needless, right ovarian surgery. An ovary or a portion of it cannot be removed without considerable risk of producing undesirable physiologic effects in later life.

Inadequate understanding of the life cycle of ovarian cysts has led to much radical surgery in their treatment. Benign cysts, such as graafian follicle cysts, corpus luteum cysts, simple serous cysts and endometrial cysts, are usually small. They grow slowly and seldom exceed 5-6 cm. in diameter. Because they often regress, small cysts can usually be watched if patients are co-operative and will return for examination from time to time. Dermoid cysts are more serious, since they do not regress and may cause an acute abdominal condition by torsion of the pedicle. If they tend to float up into the anterior abdomen when the patient is supine and if they show calcareous deposits on x-ray, removal by conservative surgery is best. Since about 20 per cent are bilateral, the other ovary should be examined. Inflammatory cysts are easily recognized because of their location between contiguous layers of peritoneum and because of adhesions which usually surround them. Radical surgery is rarely justified.

Serous cysts provide a more formidable consideration, first as to whether they are simple serous cysts or cystadenomas and, if the latter, whether they are unilateral or bilateral. Simple serous cysts are small, often unilocular and thin walled; they contain watery straw-colored fluid but have no papillary processes. Presence of papillary processes serves to differentiate between benign and possibly malignant cysts. Cancer of the papillary serous variety, which always arises in benign serous cystadenoma frequently is bilateral, cannot be cured. It is in this group of ovarian tumors that radical surgery is justified. Sometimes, however, even large cystadenomas give no gross indication of their character. Then the character of the cystic fluid becomes important. If it is mucoid or semislimy, there is usually no danger, because pseudomucinous cystadenomas are rarely malignant compared to the serous variety. On the other hand, if the fluid is straw-colored or bloody and does not feel slimy, radical surgery is indicated. Endometrial cysts should be treated on an individual basis, weighing the patient's age and her desire

to have children. It is often found that surgery can be obviated in part or completely by adequate dosage of androgens by mouth.

**Pathology and Present Treatment of Ovarian Cysts.** According to Ralph C. Benson<sup>4</sup> (Univ. of California), too much unjustified ovarian surgery is done today. The worst offenses are (1) removal of the entire ovary when only a small physiologic cyst is present; (2) removal of the ovary for a moderately large, benign cyst which could have been resected; (3) removal of both ovaries, either for surgical convenience or "to avoid cancer at some later date." Although the ovaries are apparently similar, ovulation and hormone production are not equally divided between them. Removal of a single ovary can therefore eliminate all truly active ovarian tissue. Except for extensive endometriosis, chronic tubo-ovarian abscess formation or malignant disease, conservation of both ovaries or a portion of both is almost always possible.

Parovarian cysts are not true ovarian cysts; they cause symptoms by pressure only and almost never become malignant. Germinal inclusion cysts are insignificant in size, are seen just beneath the surface of the senile ovary and have no proved clinical significance. Follicular cysts are also called retention or simple cysts. There is still debate as to whether they are actually functional, but they never become cancerous. When large, they compress the rest of the ovary and destroy much ovarian tissue except at the hilus. Pain due to torsion or dyspareunia may occur. Hemorrhage into the cyst, with rupture and bleeding, may constitute a surgical emergency. Lutein cysts, granulosa or theca, are not uncommon and are functional, non-neoplastic tumors. Persistent lutein cysts may result in discomfort, delayed menstruation and menorrhagia. Occasional rupture results in surgical emergency. Endometrial cysts are commonly associated with culdesac implants. Absence of papillary processes in these cysts aids in ruling out cystadenoma.

Neoplastic ovarian cysts, such as papillary cystadenoma and cystadenocarcinoma, are common. About one of five persistent ovarian cysts over 5 cm. in diameter is neoplastic. Usual age incidence is 45-65. Transition from benign to malignant is gradual, an important point in prevention of cancer.

(4) *Postgrad. Med.* 9:313-320, April, 1951.

There are two kinds of cystadenomas—serous and pseudomucinous. Incidence of the benign type is about 1:1. About 50 per cent of serous and 20 per cent of pseudomucinous cystadenomas are eventually bilateral, even before they become malignant. Some 50 per cent of serous and 5 per cent of pseudomucinous cystadenomas become malignant, the former constituting 70 per cent of all ovarian cancers, the latter only 2 per cent. After true malignancy is established, only about 20 per cent of cases can be arrested; the importance of early removal is therefore obvious. Cyst teratoma or dermoid cyst represents 10 per cent of cystic ovarian tumors. Since about 25 per cent are bilateral, when one is found at surgery the other ovary should be carefully examined.

True ovarian pain is uncommon. It is due to (1) torsion of the pedicle, (2) incarceration of the cyst in the pelvis, disturbing bowel and bladder function, (3) infection or cellulitis (endometriosis) of the adnexa and (4) malignancy and extension which produce ascites, pressure discomfort, etc. Clinical clues to pathologic trends in ovarian cysts are (1) persistent or enlarging cyst, (2) continued or severe abdominal pain, (3) bilaterality of cysts, (4) nodulation or firm irregularity, (5) evidence of hormone production and (6) ascites. Any of these may indicate laparotomy. If laparotomy is not done, further observation, often with hormone therapy, is the plan of management. In treatment of small polycystic ovaries less than 6 cm. in diameter, cyclic estrogen or androgen therapy is indicated. Curettage is indicated when uterine bleeding is excessive, and average function often follows this treatment alone. The ovary on the side of a tubal pregnancy should not be removed. Every effort should be made to keep as much normal ovary as possible, utilizing wedge resection or, as with dermoid cysts, removing the cyst with closure of the capsule. Ovarian cysts should never be aspirated at surgery for fear of spill. Puncture of cysts is worthless and decortification and splitting operations are unproved.

**Resection of Superior Hypogastric Plexus: Modification of Technic to Prevent Regeneration** between the cut ends is described by Frederick S. Wetherell<sup>5</sup> (Syracuse, N. Y.), with emphasis on total ablation of the plexus for relief from pelvic pain.

(5) Am. J. Obst. & Gynec. 61:738-742, April, 1951.

TECHNIC.—The patient is placed in the extreme Trendelenburg position. Spinal anesthesia is used since it decreases the bulk of the intestinal tract, lessening the need for packing. If necessary a rubber dam may be placed over the intestines before gauze packing to prevent adhesive bands. An incision is made 5 cm. above and to the left of the umbilicus (this eliminates forceful upward pulling). The peritoneum is incised from the level of the sacral promontory to 5 cm. above the aortic bifurcation after a small vertical incision is made in the posterior parietal peritoneum and a path 1 cm. wide made by inserting a curved scissors and carrying the blunt point first upward and then downward while pressing against the peritoneum. The posterior surface of the peritoneum is cleaned by blunt dissection to the lateral margins of the common iliac arteries. Tissues containing the nerve fibrils are mobilized, common iliac arteries and left common iliac vein are cleaned, main bundle of the plexus is cleaned from the vertebrae and the entire group is held by Allis clamps. Repeated drying of the field is essential for meticulous dissection. Fibers of the left intermesenteric nerve are cleaned from the left inferior mesenteric artery. When dissection is complete the bundle is grasped with a hemostat about 3 cm. superior to the aortic bifurcation and below at the point where it spreads out to form the inferior hypogastric plexus, the dissected portion is removed and the crushed ends are transfixed and tied. The proximal stump is firmly enclosed within the peritoneum as closure is begun and a transfixion suture passed through the peritoneum and stump. Peritoneal closure is continued with a running stitch and the distal stump left buried behind the peritoneum.

The last step prevents the possibility of regeneration of the plexus, although such regeneration has not been reported after the usual technic in which both ends are left behind the peritoneum.

[Wetherell was one of the pioneers in the use of resection of the superior hypogastric plexus for relief of dysmenorrhea. I began performing resections of the superior hypogastric plexus in 1931, and since then I have done many for the following four indications.

1. Primary dysmenorrhea, but only in patients in whom all the customary procedures, including analgesics, exercise, estrogen therapy and minor surgery, have failed. Results have been excellent.

In 1924 Cotte showed that pain arising in the midpelvic organs could be relieved by resecting the superior hypogastric plexus. In 1929 L'Hermitte and Dupont, and independently Leriche, suggested that a painful ovary could also be rendered insensitive by denervation. These workers soon realized that, owing to the cross link in the nerves between the ovaries, bilateral denervation was necessary for success. Their most recent technic is division of the two or three main ovarian nerve bundles in the mesovarium without interfering with the ovarian blood vessels. O'Donel Browne (1950 YEAR BOOK, p. 560) also advocates ovarian sympathectomy when the menstrual pain is of ovarian origin. He determines this by firm bimanual compression of the ovary while asking if the pain or discomfort thus produced resembles that experienced at the menses. Browne's technic for ovarian denervation consists of simple division of

both infundibulopelvic ligaments, their nerves and blood vessels and simple ligation of the stumps with catgut.

In 1939 Cooke (1940 YEAR BOOK, p. 359) operated on women under local infiltration anesthesia to determine the routes of pain conduction. From the standpoint of relief of dysmenorrhea he drew the following conclusions regarding the various types. In the cramping (uterine) type, presacral sympathectomy is wholly adequate; in the congestive (vascular) type, no effective nerve section had been devised; in the ovarian type, ovarian sympathectomy should be done, and in the peritoneal type, no operation is available for the areas outside the distribution of the presacral and ovarian plexuses.

2. Endometriosis in young women at the time of a conservative operation. Whether the sympathectomy benefits the endometriosis is questionable, but it does reduce pain in the culdesac, uterosacral ligaments and bladder following the operation. Also, it will prevent a good deal of pain if endometriosis recurs and will diminish pain during labor. This operation will not eliminate pain in the ovaries due to endometriosis unless the ovarian vessels are ligated and cut.

3. Pain due to carcinoma. Pelvic sympathectomy will almost completely relieve the intractable pain in about half the women with advanced carcinoma of the cervix. However, intraspinal injection of alcohol is simpler and effective in more cases. Nevertheless at the time of laparotomy for carcinoma of the cervix or the corpus it is advisable to resect the superior hypogastric plexus because, should the carcinoma recur, the pain will be less intense than if sympathectomy had not been done.

4. Rare cases of severe persistent pain in the lower abdomen not relieved by so-called exploratory operations which failed to reveal a cause for the pain. In these cases, pelvic sympathectomy may bring dramatic relief provided the patient has not developed a psychosis about the pain.

The technic most of us use is that described by Cotte, and we try to remove every single nerve fiber connected laterally with the superior hypogastric plexus. I remove the two hypogastric nerves which rest on the sacrum as well as the superior hypogastric plexus which lies on the lower lumbar vertebrae, and I do not tie the ends of the nerve tissue which is left behind. The piece of nerve tissue which I remove is at least 6 cm. long, and even though it is hard to believe that regeneration of the nerve tissue can take place across such a distance, such a possibility nevertheless exists. Therefore Wetherell's modification is a distinct improvement in the operation.

Every piece of tissue which is removed during a pelvic sympathectomy should be examined microscopically to be certain that nerve tissue and ganglions are present. Not infrequently an inexperienced surgeon has a failure because no nerve tissue was removed, only fat and connective tissue. Such failure cannot be charged to the operation.

Pelvic sympathectomy is generally a fairly simple operation, but there are some dangers, particularly to the ureters and large blood vessels. Because the operation is usually easy and results are excellent, it is being used too often for dysmenorrhea when laparotomy is not required. However, when the abdomen is opened for any reason in women who have severe dysmenorrhea, the superior hypogastric plexus should be removed as an accessory operation.—Ed.]

**Acute Appendicitis Incidental to Gynecologic Procedures** was diagnosed microscopically in 25 of 210 cases by E. M.

Rosset and A. S. Conston<sup>6</sup> (Mount Sinai Hosp., Philadelphia). This number represented an incidence of 12 per cent among 401 abdominal gynecologic operations performed in 1948-50. Failure to perform appendectomy in 191 cases was probably due to unwillingness to expose the patient to the increased risk of additional surgery, or to previous appendectomy. All patients with suspicious histories or signs of appendicitis were discarded from the series. Most patients were admitted on a nonemergency basis, waiting a week before entering the hospital.

Of the 25 patients, every patient with one or more of the clinical symptoms or signs considered criteria for diagnosis of appendicitis had a pathologic lesion other than appendicitis to account for it. Most were degenerating fibromyomas or salpingitis.

Histologic criteria for appendicitis were presence of an appreciable number of neutrophilic leukocytes in the mucosal stroma, with or without luminal exudate. This gave a higher incidence than those obtained with the criteria of standard pathology textbooks and of other pathologists, but on the basis of any of these criteria a significant number of cases of asymptomatic appendicitis do occur. To explain these cases the authors postulate occurrence of frequent episodes of inflammation without a predominant obstructive factor to produce symptoms.

The authors concluded that continuation of routine incidental appendectomy is advisable if risk to the patient is not increased. As a result of this practice a definite number of inflamed, although asymptomatic, appendixes have been excised.

**Is the Principle of Appendectomy during Gynecologic Laparotomy Correct?** Hans Heidler<sup>7</sup> (Vienna) performed appendectomy in 176 of 300 gynecologic laparotomies. In 50 other cases the appendix had already been removed. In 72 cases, the following contraindications were found: lengthy and difficult operations, 20; severe narcosis, 16; ovarian carcinoma, 16; radical surgery, 7; tubal pregnancies, 4; old age, 4; carcinoma of corpus, 2; severe anemia, 2; severe myo-

(6) *Am. J. Obst. & Gynec.* 61:1136-1141, May, 1951.

(7) *Wien. klin. Wchnschr.* 35:633-635, Sept. 1, 1950.

cardial damage, 1. In two additional cases, no ground was found for nonremoval, but appendectomy was not done. In only 9 appendectomies was the appendix macroscopically normal and in only 3 but slightly altered. Microscopically, 73 appendixes were chronically inflamed, 43 partially or totally obliterated, 16 inflamed and congested. There were four deaths, in only 1 of which could appendectomy have played a part. It is concluded that appendectomy in gynecologic laparotomies is of considerable value unless definite contraindications exist.

[The question of appendectomy at the time of a gynecologic laparotomy no longer causes vehement discussion. More and more appendectomies are being performed without harm because of use of the antibiotics and improvements in general surgical technic. Any appendix that is retrocecal or shows signs of causing trouble should surely be removed, and in most cases even a normal appendix should be removed at laparotomy. When an operation is difficult or time-consuming or there has been great loss of blood, the appendix should not be removed.

Taniguchi and Kilkenny (*Am. J. Ost. & Gynec.* 60:1359, December, 1950) reviewed 532 appendixes removed incidental to pelvic surgery and found that 10.5 per cent showed acute inflammation. They believe the appendix should be removed routinely in pelvic surgery whenever it is accessible. In this series there were no deaths attributable to prophylactic appendectomy.—Ed.]

**Prophylactic Use of Penicillin Vaginal Suppositories in Gynecologic Surgery.** Paul F. Fletcher<sup>8</sup> (St. Louis Univ.) compares results in 109 consecutive patients with those in 50 controls who underwent essentially the same type of surgery.

**TECHNIC.**—One suppository containing 100,000 units of calcium penicillin in cocoa butter was inserted in the vagina the night before and the morning of the operation. One or two suppositories were inserted on completion of the operation and before the patient left the operating room. After minor vaginal surgery a suppository was given once daily for six days. Patients having major vaginal surgery, abdominal or vaginal and abdominal surgery received two suppositories daily the first three postoperative days, then one suppository daily for three days. Occasionally a suppository was continued once daily for 10 or 12 days postoperatively. Early ambulation was used in all cases.

Of the 109 patients, 6 (classed as morbid) had temperature of 100.4 F. or higher on two postoperative days. In the controls, 15 of 50 had a similar morbid postoperative course. In both groups morbidity occurred only in patients undergoing major surgery. Corrected morbidity incidence for the 109 patients was 5.5 per cent; for the 50 controls, 30 per cent. Aver-

(8) *South. M. J.* 43:715-720, August, 1950.

age duration of morbidity in the controls was 3.3 days; in the suppository group, 2.16 days.

The number of days required for postoperative convalescence was reduced in the suppository group. Averages were: abdominal cases, 9.8 days; major vaginal cases, 10.2 days; "combined" cases, 10 days; minor vaginal cases, 4 days; incomplete abortion cases, 3 days. Averages for the controls were abdominal cases, 12 days; major vaginal cases, 11.6 days; "combined" cases, 10.7 days; minor vaginal cases, 5 days and incomplete abortion cases, 4 days.

Postoperative discomfort was noticeably reduced with use of suppositories. The odor and amount of vaginal discharge were greatly decreased, and rate of healing seemed to be increased.

**Effect of Penicillin Vaginal Suppositories on Morbidity in Vaginal Hysterectomy and on Vaginal Flora.** In 100 consecutive cases Samuel J. Turner<sup>9</sup> (Chicago Med. School) added to the usual preparation for vaginal surgery a cocoa butter suppository containing 100,000 units of crystalline potassium penicillin G, inserted vaginally 12-14 hours preoperatively. These patients had an average of 9.8 postoperative hospital days and a morbidity of 7 per cent. Of the seven febrile patients, three with cystitis responded well to urinary antiseptics or sulfonamides; of three without apparent cause for fever, two required no additional therapy and one responded to penicillin and sulfonamides. Bacteriologic study in 83 cases revealed almost complete inhibition of pyogenic cocci in vaginal cultures obtained a few hours after insertion of penicillin suppositories. All cultures contained some organisms before treatment, and 40 showed no growth after penicillin. There were no untoward reactions to the suppositories.

With the same preoperative treatment except for the penicillin suppository, morbidity in 56 vaginal hysterectomies was 37.5 per cent. In a control series of 210, morbidity was 34.8 per cent with an average of 11.2 postoperative hospital days; of the 73 febrile patients, 53 were treated with parenteral antibiotics and/or sulfonamides.

[From my limited experience with vaginal suppositories containing penicillin and from my observation of groups of cases in several hospitals in Chicago, I am convinced that penicillin vaginal suppositories do lower the morbidity following gynecologic operations. Despite this, operators

<sup>9</sup> (9) *Am. J. Obst. & Gynec.* 60:806-812, October, 1950.



should not be less meticulous in their operative technic nor should they break any rules of asepsis. Since there is no harm whatever in inserting a single vaginal suppository containing 100,000 units of penicillin the night before surgery, this should be done.—Ed.]

**Analysis of Deaths Occurring in 5,318 Gynecologic Operations** performed at Cook County Hospital during 1942-47 was made by J. P. Greenhill and Harold M. Loeff.<sup>1</sup> Results were compared with those of 6,022 operations performed at the same hospital in 1926-30. Of the 5,318 operations, 4,391 were major and 927 minor. There were 69 operative and postoperative deaths up to three months after surgery, a mortality rate of 1.3 per cent. The highest rate occurred in 1943, 2.16 per cent, and the lowest rates in 1946 and 1947, 0.7 and 0.67 per cent respectively (eight deaths each year). In the first series, 88 per cent of the operations were major; 213 deaths gave a mortality rate of 3.5 per cent. Although fewer major operations were performed during the second period, the number of hysterectomies increased by almost a third. There was a striking decrease in defundations and simple removal of the adnexa.

During the first period there were 551 total and 1,408 supravaginal hysterectomies, whereas during the more recent period there were 1,250 total and 1,415 supravaginal hysterectomies. The number of vaginal plastic operations decreased from 329 to 136, whereas the number of vaginal hysterectomies increased from 158 to 531. Of the 531, 336 were combined with a plastic operation. In the first period, 14 colostomies were performed, after which 11 women died; none were performed during the second period.

In general, mortality rates for the various operative procedures decreased, the one exception being an increase from 0.8 per cent in the first period to 1.2 per cent in the second when simple supravaginal hysterectomy was performed. This was probably due to the fact that in recent years the operation was usually limited to technically difficult cases and to patients who were poor operative risks. The lowest mortality rate during the second period was associated with vaginal hysterectomy.

In the first period infection was the cause of 48.8 per cent of deaths; in the second period, of 29 per cent. During the first three years of the second period when only the sulfona-

(1) *Am. J. Obst. & Gynec.* 61:340-347, February, 1951.

mides were available to treat peritonitis, 34 per cent of deaths were from this cause; in 1946 and 1947 when both penicillin and the sulfonamides were used, 12.3 per cent (one a year). Another favorable factor influencing the mortality from infection was the more conservative surgical attitude adopted after advent of the sulfonamides.

Death from hemorrhage and shock occurred in 35 patients during the first period and in 13 during the second. Two factors of apparent importance in this decrease were the blood bank, with liberal use of transfusion preoperatively, during surgery and postoperatively, and better organization of the gynecologic service, with sufficient residents and interns for adequate pre- and postoperative care.

Pneumonia and atelectasis caused 18 deaths (8.5 per cent of the total mortality) in the first series, whereas they caused only 4 deaths (5.8 per cent) in the second. Early ambulation plus use of penicillin and sulfonamides were probably responsible. Early postoperative ambulation was also primarily responsible for a decrease in deaths due to pulmonary embolism from 18 in the first series to 2 in the more recent group. Although malignancy as a cause of death showed an apparent increase (from 7.5 to 20 per cent), this was due to a decrease in the total number of deaths. Better supervision and more frequent consultations with the medical staff were believed responsible for a decrease from 12 to 6 deaths due to myocardial failure.

[Nearly all hospitals can show a pronounced lowering of the death rate following gynecologic operations during the past 20 years. There are many reasons for this.—Ed.]

**Anticoagulant Therapy in Gynecologic Surgery** is discussed by Benjamin E. Urdan and Marvin Wagner<sup>2</sup> (Milwaukee). Of 900 consecutive patients who underwent major gynecologic procedures, 450 were given dicumarol<sup>®</sup> routinely to prevent complications from intravascular clotting. Early ambulation was used as routine.

Dicumarol,<sup>®</sup> which lengthens clotting time by decreasing the blood prothrombin level, should be used only when frequent determinations of prothrombin time are possible. The authors used the simplified bedside test described by Ziffren and associates, results of which are expressed in percentage in reference to a normal control; the only reagent required is

(2) *Am. J. Obst. & Gynec.* 61:982-989, May, 1951.

thromboplastin. Individualization is essential in dicumarol<sup>®</sup> therapy since some patients are resistant and others sensitive to the drug.

A prothrombin deficiency of 30-40 per cent of normal was maintained until the patient had been totally ambulatory for three days. The only hazard encountered was bleeding, which was readily controlled by administration of 72 mg. hykinone<sup>®</sup> intravenously and 30 mg. synkayvite<sup>®</sup> intramuscularly three times at four hour intervals.

Absolute contraindications to dicumarol<sup>®</sup> therapy are subacute bacterial endocarditis, hemorrhagic disease, significant liver disease, moderate to severe renal disease and conditions requiring tube drainage. Relative contraindications are dietary deficiency states, especially of vitamin K; fever; salicylate or sulfonamide therapy, and operation on the brain or spinal cord.

Of the 450 patients who did not receive dicumarol<sup>®</sup>, 7 had phlebothrombosis, 11 thrombophlebitis, 9 pulmonary embolism with infarction and 4 fatal pulmonary embolism. Of the 450 patients who did receive dicumarol<sup>®</sup>, 1 had a vascular complication and 1 who was refractory to dicumarol<sup>®</sup> had phlebothrombosis. This illustrates that in a private or general hospital, where there is always variance in treatment of surgical patients, use of dicumarol<sup>®</sup> prophylactically can be safe and will decrease the incidence of, or entirely eliminate, intravascular clotting and its sequelae.

**Puncture of Ovarian Cysts and Cystography.** L. Portes, A. Granjon and A. M. Beau<sup>3</sup> (Paris) have had good results with injection of an opaque fluid, which permits cystographic definition of the form and dimensions of the cyst. It is better tolerated than peritoneal injection, is harmless and allows evaluation of later puncture to evacuate the cyst. Puncture may be made through the vagina or the abdomen. The liquid removed should be examined from cytologic, chemical and biologic points of view. Puncture always has diagnostic and sometimes therapeutic value, especially in follicular cysts, which have thus been cured without surgery. Value of new products injected is still under study.

[I cannot see the need for injecting an iodized oil preparation in ovarian cysts and then taking roentgenograms. When an ovarian cyst is

(3) *Gynéc. et obst.* 49:422-431, April, 1950.

large, a laparotomy should be performed. If an ovarian cyst is small, I prefer to wait and re-examine the patient at two or three month intervals. If the cyst grows, I would remove it; otherwise I would leave it alone. If the cyst feels doughy and there is a suspicion of a dermoid or a teratoma, a roentgenogram will often help to determine this. In all cases of doubt, and certainly when the cyst is more than 5 cm. in diameter, the neoplasm should be removed. Usually when the cyst is benign, a portion of the ovary can be retained in situ.

McCutchen and Kinder (J. South Carolina M. A. 47:1, January, 1951) report on 18 proved cases and 1 suspected case of bilateral polycystic ovaries. Sterility was the complaint of nine patients; only three of them conceived and had normal babies after operation.—Ed.]

**Acute Abdominal Symptoms from Bleeding Ovary: Analysis of 84 Proved Cases.** Richard Finley Grise and Charles Bruce Morton<sup>4</sup> (Univ. of Virginia) observed 172 patients with signs and symptoms believed to be due to rupture of a graafian follicle, graafian follicle cyst or corpus luteum among 183,761 patients hospitalized in 17 years. In only 84 was the diagnosis verified by surgery; 88 were either not operated on or the ovary could not be adequately visualized.

The 84 patients were aged 14-44, the majority being 17-23. Pain occurred in all, appearing suddenly in 33 per cent, gradually intensifying in 26 per cent and not specified in the rest. In 55 per cent it was localized in the right lower abdominal quadrant. In 30 per cent pain was constant and in 35 per cent intermittent and cramping. It was severe in 39 per cent and moderate or mild in 34 per cent. Nausea was present in 79 per cent, accompanied by vomiting in 26 per cent. Previous similar attacks were reported by 27 per cent. Eighty-eight per cent had tenderness on the right side; 70 per cent, adnexal tenderness. Leukocyte count was 4,000-21,000/cc. blood.

Preoperative diagnosis was correct in only a few patients; the majority were thought to have appendicitis. In 20 per cent symptoms were thought to be due to a ruptured follicle. Other diagnoses included ectopic pregnancy, ovarian cyst and pelvic inflammation.

Laparotomy was performed under spinal anesthesia in all cases. A McBurney incision was used in 67, a paramedian in 16 and a left midline in 1. A ruptured follicle or corpus hemorrhagicum or corpus luteum of the ovary was found on the right in 79 patients and on the left in 5. Blood-tinged fluid amounting to 1,500 cc. was found in one patient but in others there was only a negligible quantity. The appendix was re-

(4) Surgery 29:117-123, January, 1951.

moved from all patients who had not had an appendectomy. Treatment of the ovary was inspection alone in 45, suture of the bleeding area in 32, excision and suture of the defect in 5 and expression of a clot in 2. Radical surgery is never indicated. Occasionally, suture for hemostasis may be necessary, but rarely oophorectomy. In every patient as much ovarian tissue as possible should be left.

There were in general more instances of bleeding near the middle of the intermenstrual phase of the cycle than at other times. Bleeding from the ovary not associated with ovulation is due to ruptured corpus hemorrhagicum, corpus luteum or retention cyst, but the ovary may also be the site of endometriosis.

Despite the vast experience of many years, incidence of correct diagnoses of bleeding ovary has improved little and unnecessary operations are still common.

[The authors are to be commended on their most conservative stand regarding treatment of bleeding ovaries. As they emphasize, it is rarely necessary to remove an ovary because of hemorrhage. All that need be done in most cases is to suture bleeding points. Even this is often unnecessary. In many cases after the abdomen has been opened to be certain that the acute condition which may have been diagnosed acute appendicitis or a ruptured ectopic pregnancy, there was nothing more than a bleeding ovary.

Rautureau and Mardrus (*Compt. rend. Soc. Franç. gynéc.* 21:36, January, 1951) report 17 cases of ovarian hemorrhage due to rupture of corpus luteum cysts. The ruptured cyst was removed 15 times and the ovary twice. The appendix was also removed in 15 cases.—Ed.]

**Trauma to Urinary Bladder in Gynecologic Surgery: Analysis of 61 Injuries** (0.3 per cent) in the course of 22,250 gynecologic procedures was made by Abe Golden and Leo Abraham<sup>5</sup> (New Orleans) to determine what happened to patients as a result of the injury and to analyze the methods of repair and use of the retention catheter, irrigations and chemotherapy. Such trauma was noted in every type of procedure and, in most, the accident was immediately noticed and repaired. However, 17 vesicovaginal fistulas developed when the trauma was apparently not recognized. The only consistent finding indicating the injury was hematuria. Suprapubic tenderness, frequency, urinary retention, dysuria, loin pain and signs of peritonitis were no more frequent than in uncomplicated cases.

Most fistulas developed within two weeks, with a range of

---

(5) *South. M. J.* 43:783-787, September, 1950.

one day to six months postoperatively. Compared with uncomplicated cases, little difference in morbidity was found, but this series averaged longer hospital stays due generally to prolonged indwelling of catheters (5-14 days). Catheters were used in all recognized bladder injuries and in all vaginal hysterectomies with later fistulas. Various irrigation solutions were used.

Chromic catgut sutures (00 and 000) were used in all repairs. In the case in which the fistula developed six months later, cotton sutures had inadvertently been placed into the bladder and were removed just before fistula formation. Vesicovaginal fistulas healed spontaneously in two patients and were successfully repaired in the others.

From the data available, all the fistulas formed as a result of sutures taken into the bladder or from damage to the blood supply. No fistula formed if the bladder injury was recognized. The mode of repair seemed unimportant as long as the continuity of the bladder was restored. The retention catheter was important and was used in every case, five to seven days being adequate. Bladder irrigations, though done in every case, appear unnecessary as long as the catheter drains; it would seem more rational not to stimulate or irritate the bladder during the healing process. Chemotherapy was not well evaluated but seemed of value.

[Urinary tract injuries are not infrequent, especially during gynecologic operations by surgeons with limited experience. Most of the injuries occur during total abdominal and vaginal hysterectomy. Injury to the bladder or ureter is extremely rare during a supravaginal hysterectomy. Whenever a bladder or ureteral injury is detected at the time it occurs, an attempt should be made to correct it immediately. If the surgeon is unable to do so, he should immediately call someone capable of repairing it. This is one reason why all residents in gynecology should be trained as well in urologic and intestinal surgery. Everyone who performs gynecologic surgery sooner or later has a bladder or intestinal injury and must be able to correct such damage. Some gynecologists instill methylene blue or other colored substance into the bladder before every radical Wertheim operation, and even ordinary hysterectomies, so that injury to the bladder will be manifested by spill of the colored solution. I see no need for this.

If methylene blue is not instilled in the bladder, no laparotomy should ever be started until the bladder has been emptied by catheter, even though the patient voided just before being taken to the operating room. A midline incision in the peritoneum should always be opened at the very upper edge of the incision near the umbilicus. When cutting the peritoneum to expose the peritoneal cavity one must always be alert for adhesions and also for the top of the bladder. If the bladder is high up, the lower part of the peritoneal incision should be directed to either the

right or the left side of the bladder. If, when the abdomen is opened the bladder is found to be full, time should be taken to have the bladder catheterized. When there is very little bladder peritoneum or the bladder is adherent to the uterus, great care must be exercised in separating the bladder from the uterus. The bladder should be freed to the sides in the direction of the broad ligaments only as far as necessary for the particular operation. For supravaginal hysterectomy, not much lateral separation of the bladder is necessary. For total hysterectomy, the bladder must be separated not only off the cervix and upper part of the vagina but also laterally for at least 2 cm. to expose the cardinal (Kocks) ligaments. This separation also displaces the ureters laterally. For radical hysterectomy, downward and lateral stripping of the bladder must be much more extensive, and here bleeding is nearly always encountered. No structure should ever be clamped, cut or ligated until it has been definitely identified, regardless of the location.

If a bladder injury consists simply of laceration of the muscle wall, a few interrupted surgical gut sutures are inserted and the raw area covered by a piece of free omentum. When the entire bladder wall and the mucosa are torn or cut, bladder damage is easily repaired and quickly heals. If a ureter is accidentally cut or a portion of it is removed and the damage is discovered during the operation, a ureterovesical or ureteroureteral anastomosis is done. However, usually when a piece of ureter has been removed, it is impossible to unite the remaining portions. Strange as it may seem, sometimes when a ureteral catheter is inserted through both portions of the ureter and the cut ends of the ureter drawn together as much as possible with sutures to shorten the gap, the two ends of the ureter unite and a functioning ureter results. The exposed surface should be covered with peritoneum as much as possible or with a free omental transplant. If the gap between two cut portions of the ureter is more than 1 cm. this outcome is hardly likely and one must usually resort to permanent ligation of the ureter with silk or to temporary fixation of the kidney end of the ureter into the abdominal wound followed by a nephrectomy.

If both ureters are cut or tied, permanent ligation is out of the question. The preferred procedure is implantation of the ureters into the bowel by the Coffey method. This is a long operation, so if the patient's condition is not too good it is best to bring the kidney ends of both ureters out through the abdomen for drainage of urine. After the patient recovers the ureters should be implanted into the bowel.

What is to be done when ureteral damage is not discovered until after operation? There are two groups of cases: (1) both ureters have been ligated, causing distressing symptoms, and (2) one or both ureters have been cut and diagnosis is made because of leakage of urine. It is surprising how often symptoms are absent when one ureter is ligated. Diagnosis of ligated ureter can usually be made if a woman who has had a pelvic operation complains of pain in the kidney region on the third or fourth day and the kidney is enlarged, palpable and tender. Failure in an attempt to pass a ureteral catheter make the diagnosis certain. It is difficult to deligate a ureter after the abdomen has been closed. A ureter which has been tied off with catgut will usually function normally in six to eight weeks. However, during these weeks the kidney must be protected by drainage of urine, so a nephrostomy should be done without delay. After the ligated ureter heals in several weeks the nephrostomy incision is closed.

If both ureters have been tied, the situation is usually discovered 24 hours because no urine is passed nor is any obtained from the bladder.

by catheter. Treatment may be by bilateral nephrostomy, removal of ligatures from the ureters, ureterovesical or ureteroureteral anastomosis or transplantation of the ureters into the bowel. The best results are obtained by bilateral nephrostomy. The corrective operation should be performed as soon as a diagnosis is made.—Ed.]

**Partial and Complete Pelvic Exenteration: Progress Report Based on First 100 Operations** is given by Alexander Brunschwig and Virginia K. Pierce<sup>6</sup> (New York City). All patients had some form of advanced pelvic cancer involving bladder and vagina-uterus, or the latter and the rectum, or all three. Primary growths included carcinomas and sarcomas. Most growths were primary in the cervix; some were primary in the vagina, corpus, pelvic colon and vulva. A wet colostomy was performed in all except three patients with complete exenteration; one patient had unilateral cutaneous ureterostomy and sigmoid ureterostomy and two had bilateral cutaneous ureterostomy. Thirty-five received partial and 65 complete pelvic exenteration. There were 8 surgical deaths (within 30 days of operation regardless of cause) in the former group, 12 in the latter. Uremia and pyelonephritis were the major cause of 11 of the 20 deaths. Urinary tract complications may not be considered simply as the hazard of implantation of ureters into colon, since a certain degree of urinary tract infection and ureteral obstruction due to advanced pelvic cancer was present before operation. Forty-nine patients survived one to eight months (short term survivors); of these 35 died of metastases. Thus, 69 operations (20 immediate surgical deaths and 49 short term survivors) must be recognized as failures.

Nine patients survived at least one year (effective palliation), returned to fairly normal activity, yet succumbed eventually to metastases. Included are patients living more than one year but with evidence of recurrences or metastases.

Twelve patients (long term survivors) survived at least one year and five months, returned to normal activity and have no evidence of recurrences although a five year period has not yet elapsed. Thus effective palliation was achieved by partial or complete pelvic exenteration in 21 per cent.

It is apparent that radical surgery has something to offer patients in advanced stages of pelvic cancer in whom radiology and more conservative surgery have failed.

(6) *Cancer* 3:972-974, November, 1950.



[The operation known as partial or complete pelvic exenteration, popularized by Brunschwig, should be performed only by highly experienced surgeons who work in well equipped hospitals with well trained personnel, ample equipment and a huge supply of blood available for blood transfusions.—Ed.]

---

## INFECTIONS

**Leukorrhoea** literally means a white discharge, but H. H. Fouracre Barns<sup>7</sup> (London) notes that the term is often applied to abnormal vaginal discharge, not blood stained. This is usually yellow but may appear brown when dried, in which case presence of altered blood must be ruled out. A normal amount of discharge will not soil garments.

Causes of increase of uterine secretion are endometrial polyps or fibroids (occasionally); inflammation of the endometrium from infection or trauma (discharge usually purulent, possibly blood stained); pyometra (periodic discharge); adenocarcinoma of body of uterus (discharge watery becoming blood stained); neoplasm of fallopian tube (if malignant, discharge becomes blood stained).

Most leukorrhoea is due to excessive cervical secretion (clear and mucoid) from stimulation of the cervical glands, as by administration of estrogens or at ovulation. Other causes of increased secretion are hypertrophy of cervical glands during pregnancy, exposure of cervical canal mucosa by laceration during delivery, cervicitis due to gonococci or other pathogenic organisms (mucopurulent discharge), cervical carcinoma (mucopurulent discharge becoming blood stained). Hypertrophy of cervical glands with enlargement of cervix may accompany leukorrhoea due to stimulation of cervical glands; the cervical canal mucosa may proliferate to form a cervical mucous polyp. Cervical erosion due to continual exposure of external os epithelium to discharge may be cleared by curing leukorrhoea.

Increase in the vaginal transudate, usually due to infection of the mucosa, is the other common cause of leukorrhoea. *Trichomonas vaginalis* flourishing in the abundant glycogen in normal vaginal epithelium and in the relatively alkaline condition at menstruation is most commonly responsible. The

---

(7) Practitioner 166:583-587, June, 1951.

yellowish gray watery discharge, occasionally frothy, is irritating to the skin of the vulva. Small raised red spots appear on the vaginal wall. Vaginitis is also caused by *Monilia albicans* which requires an acid medium and is often associated with glycosuria. The discharge is white, less fluid than most, and irritating to the vulval skin. White patches appear on the vaginal wall. Vulvovaginitis of infancy (often due to gonococci) and senile vaginitis (due to pyogenic organisms) also occur. Other causes of increased vaginal transudate are secondary vaginitis from pessaries, inflammation from douches, vaginal carcinoma (purulent discharge becoming blood stained) and temporary Bartholin gland secretion resulting only from sexual excitement.

Physical examination, history and study of smears differentiate vaginal lesions. Vulvovaginitis of infancy and senile vaginitis are helped by estrogens orally or locally. Sulfonamides or penicillin also are used for gonococcic vulvovaginitis of children. Stovarsol or picragol<sup>®</sup> suppositories are used for senile and trichomonas vaginitis, over two or three periods in the latter. Monilial vaginitis responds to mycil suppositories or daily vaginal application of 2 per cent gentian violet or mersogel fungicide jelly.

If, after cleansing, the cervix appears inflamed, with mucopurulent exudate from the cervical canal, smears are taken to exclude gonococcic infection. Gonococcic cervicitis, not a common cause of leukorrhea, is soon controlled with sulfonamides and penicillin. More often there is a clear cervical mucus with no inflammation; this is treated by application of electric cautery to the cervical canal; operative removal or repair of the vaginal portion of the cervix is not necessary. With active infection of the cervix, however, electric cautery should be avoided as it may cause extension of infection.

When leukorrhea results from a uterine condition, the discharge is watery and other symptoms of the uterine lesion usually exist. Diagnostic curettage is helpful. Treatment varies with the lesion found.

**Bacteriologic Studies in Salpingitis with Special Reference to Gonococcus Viability** were made by J. Mason Hundley, Jr., William K. Diehl and Joseph W. Baggott<sup>8</sup> (Univ. of Maryland) on 80 patients. No chemotherapy or antibiotics

(8) *Am. J. Obst. & Gynec.* 60:977-984, November, 1950.

were used preoperatively. Uterine myomas were present in 51 instances and varying degrees of salpingitis in 73.

Smears and cultures were obtained from the urethra, cervix and tubal lumen. Sections of tubal wall were macerated and cultures made. Positive gonococcic infection of the urethra and cervix was noted in 33 cases (41.25 per cent) and of the fallopian tubes in 5 (6.25 per cent). Every tubal infection was associated with cervical and urethral infection. The fallopian tubes were sterile in 76.1 per cent, the cervix in 2.5 per cent and the urethra in 3.75 per cent.

Preliminary observations on pH determinations of the urethra, cervix and tubes showed no conclusive relation with longevity of the gonococcus. Readings in general showed slight acidity, many nearly neutral and a few alkalinity.

No evidence of tuberculosis was found in this bacteriologic study. In 19 of 1,069 patients, salpingitis was due to tubercle bacilli.

Persistent viable gonococcic infection is a disease of the lower generative tract. Reinfection comes not from the fallopian tube but from the cervix and Bartholin's glands, probably during menstruation and ovulation. Gonococcic infection of the tubes is short lived.

[These studies by Hundley and his associates verify what Curtis showed many years ago, namely, that gonococcic infections of the tubes are short-lived and that repeated attacks of salpingitis are due to reinfection from the lower generative tract. Damage from the gonococcus formerly observed in the tubes and ovaries will probably become increasingly rare owing to the extensive use of antibiotics early in gonorrheal infections. It is interesting that in this series tuberculosis of the tubes was found in 1.7 per cent of the 1,069 patients with tubal disease. In some series the incidence of tuberculous salpingitis is as high as 7 per cent.—Ed.]

**Nongonorrheal Vulvovaginitis Due to Gram-negative Intracellular Diplococci.** Thorough gynecologic examinations including bacteriologic cultures were done on 1,014 mentally deficient children by John Dale Weaver<sup>9</sup> (Univ. of Texas). Differential diagnosis of gram-negative intracellular diplococci was based on bacteriologic cultures on proteose peptone hemoglobin agar followed by fermentation reactions, *Neisseria gonorrhoeae* fermenting glucose and no other sugar, whereas *N. sicca* ferments all sugars except mannitol.

(9) Am. J. Obst. & Gynec. 60:257-260, August, 1950.

Four children had gonorrhoea and 12 vulvovaginitis in which gram-negative intra- and extracellular diplococci were found that proved to be *N. sicca*. Degree of inflammatory changes in the 12 varied, but all had hyperemia and edema of the mucosa with superficial desquamation and vaginal discharge. Although some investigators contend that *N. sicca* is nonpathogenic, Weaver points out that all these cases were in youngsters, whose vaginal epithelium was therefore of an undifferentiated, more or less round-celled type which offered little resistance to invasion. This micro-organism may be the cause of epidemics of vulvovaginitis not affected by penicillin which are misdiagnosed as gonorrhoea. In these cases the tissues grossly and the stained bacterial smears appeared the same as those of gonorrhoea.

In the discussion, John W. Huffman pointed out the desirability of demonstrating *N. sicca* as a pathogen in these cases by inoculation of others with this micro-organism to see whether vulvovaginitis can be reproduced.

[Some physicians still attribute practically all vaginal discharges in young girls to gonorrhoea regardless of whether or not smears show gram-negative intracellular and extracellular diplococci. In private practice few of the vulvovaginal discharges we see are due to gonorrhoea. Whenever a young girl has a vaginal discharge, a rectal examination should be made to rule out a foreign body in the vagina. Small foreign bodies, such as a safety pin, a piece of pencil or a small marble, are found much more often than is usually believed.]

Gonorrhoeal vulvovaginitis is easily treated with sulfadiazine, sulfathiazole or penicillin. Generally 0.5-0.75 gr. sulfadiazine or sulfathiazole per lb. body weight is given every 24 hours in four daily doses. The dose should not exceed 20 gr./day and there should be no reduction in the fluid intake. Spectacular results can be obtained with penicillin. The dose varies with the age; e.g., the dose intramuscularly for a child of 3 is 25,000 units and for a child of 8, 50,000 units.

Waters and Wager (*Am. J. Obst. & Gynec.* 60:885, October, 1950) consider gentian violet the most consistently effective therapy for vaginal mycosis and describe a jelly packed in a single dose disposable applicator which eliminates the disadvantages of other gentian violet applicators. In 191 pregnant women, cure was obtained in 78 per cent, improvement in 15 per cent and failure in 7 per cent.

Cooke (*Brit. M. J.* 2:1241, 1950) reported the case of a woman found dead on the bathroom floor with a Higginson syringe lying between her legs. This was a death following a vaginal douche. The douche water contained soap. Douching during pregnancy with a fountain syringe is not dangerous, but one form of therapy is very risky, i.e., insufflation of substances into the vagina by a blower or syringe. No substance should ever be blown into the vagina of a pregnant woman except through an open speculum. This applies to treatment of trichomonas vaginitis or any other condition.—Ed.]

**Method of Diagnosing and Treating Functional Pelvic Disease.** Frank R. Lock and Harold M. Sluder<sup>1</sup> (Bowman Gray School of Med.) obtain a complete medical history and physical examination at the preliminary interview, with further diagnostic studies and consultations as indicated. A frank appraisal of the problem is presented to the patient. If pelvic disease is present, its character and consequences of conservative and operative treatment are explained, as is the mechanism responsible for production of pain in functional disease. Many patients, accepting diagnosis of pelvic disease, recognize their problems and obtain good results. Psychiatric assistance is suggested for patients who do not recognize or acknowledge the emotional problem.

Of 2,315 patients studied, 73.7 per cent (group 1) had organic disease sufficient to explain their complaints, 17.2 per cent (group 2) had symptoms in excess of demonstrable lesion and 9.1 per cent (group 3) had pelvic symptoms without abnormal changes. In group 2, 30 per cent required special diagnostic studies to eliminate organic disease. The majority had emotional problems solvable by simple psychotherapy. Of the 195 patients followed by the authors, 85 per cent obtained complete relief from symptoms despite persistence of organic disease in 108.

Special diagnostic studies proved the absence of organic disease in 73 patients in group 3. Of 86 patients followed, 53 per cent were relieved of symptoms after simple office treatment; 59 were treated by a psychiatrist. Results of treatment in group 3 were least satisfactory. In groups 2 and 3, 13 operations were performed; 51 operations had been recommended elsewhere and 141 done without relief.

Diagnosis of functional pelvic disease depends on absence of an organic lesion sufficient to explain the patient's complaints and presence of a distinct emotional problem. Most patients recognize their own emotional problems after proper explanation; the rest require professional psychiatric care.

**Treatment of Pelvic Inflammatory Disease in Women with Chloramphenicol.** Charles S. Stevenson, Nicholas J. Kohlerman, Edwin F. Snider and S. S. Schlingman<sup>2</sup> (Detroit) report results in 34 patients. In all cases cultures were obtained from

(1) *Am. J. Obst. & Gynec.* 60:1121-1134, November, 1950.

(2) *Ibid.* 61:498-513, March, 1951.

the uterine cavity or by aspiration from the culdesac or a pelvic abscess. *Escherichia coli*, nonhemolytic streptococci and *Aerobacter aerogenes* were the usual pathogens, and all fell well within the spectrum of chloramphenicol activity. Also found were *Staphylococcus aureus* or *albus*, alpha and gamma streptococcus, gram-negative streptococcus, beta hemolytic streptococcus, *Alcaligenes fecalis* and *Proteus vulgaris*. Most infections were mixed.

Dosage was 0.5 Gm. chloramphenicol given enterally every six hours for 10 days, with additional supportive therapy. Patients unable to swallow received the drug by intestinal tube. Some required several 10 day courses of treatment. Of 15 patients with culdesac abscesses, 14 responded to chloramphenicol; one with a *Staph. albus* infection responded only to penicillin. In all cases improvement was apparent within 24-96 hours. In five patients with nonpuerperal subacute salpingitis without abscess, response to chloramphenicol was rapid. Of nine patients with postabortal sepsis, eight were successfully treated and one died. Three with postpartum sepsis and two with pelvic peritonitis due to ruptured appendix were also successfully treated with this drug. Of these 34 patients, 21 had previous treatment with penicillin, streptomycin and/or sulfadiazine; only 2 showed good response. Recovery of 14 moribund patients was attributed to chloramphenicol therapy. Laparotomy, when indicated, could usually be performed within three to four weeks because of the rapid disappearance of peritonitis and regression of tubo-ovarian inflammatory masses. Patients with large pelvic abscesses improved so rapidly that posterior colpotomy was unnecessary.

[The antibiotics chloramphenicol, aureomycin hydrochloride and terramycin hydrochloride are highly bacteriostatic for many bacteria. Susceptible bacteria are suppressed and monilia and other yeastlike organisms may replace the normal or abnormal bacterial flora. This most frequently occurs in the large bowel and is of little consequence. When these drugs are prescribed and women complain of pruritus vulvae and/or ani, the first thought should be of monilia. Patients should be warned about this possibility.—Ed.]

**Treatment of Chronic Female Pelvic Sepsis by Short Wave Diathermy: Review of 50 Cases.** T. W. Burgess<sup>3</sup> (Sidney) used the abdominovaginal method with a surgical circuit of 6 mm. wavelength. The vaginal electrode (Corbus and O'Connor type) was placed under and behind the cervix, and

(3) *M. J. Australia* 2:285-287, Aug. 19, 1950.

the dispersive electrode was placed over the lower part of the abdomen. Intensity and duration are gradually increased during the course of treatments which are given three times a week to a total number varying with the type and severity of the condition. Maximal temperatures of 106-110 F. are reached, and duration is up to 30 minutes. Both electrodes may be applied externally, but, since greater temperature can be concentrated in the pelvis by the method described, it is more efficient in most cases.

Conditions treated are broadly classified as chronic salpingitis and salpingo-ovaritis, blocked fallopian tubes, chronic cervicitis and endocervicitis, chronic parametritis and postoperative adhesions. Treatment was given to relieve pain of pelvic sepsis in 34 patients, 29 of whom were cured or relieved. Patency was obtained in four of nine patients with blocked fallopian tubes. Of seven with cervicitis causing defective sperm invasion, all were clinically cured, although the sterility was not affected since treatment resulted in drying of cervical mucus in 50 per cent.

**Trichomonas Vaginalis Vaginitis: Treatment with New Surface-Active Trichomonacide** was successful in 94 of 100 clinic patients studied by J. Mason Hundley, Jr., William K. Diehl, Herman A. Shelanski and Robert L. Stone<sup>4</sup> (Univ. of Maryland). Results of laboratory tests were negative in 73 within one week and in 90 within two weeks.

Tetronyl is a mixture of two quaternary ammonium compounds (1 per cent) in a vehicle of sodium carboxymethylcellulose (99 per cent). The quaternary ammonium compounds apparently make the organism's cell membrane permeable so that the protozoan imbibes fluid from the surrounding medium and swells until finally the cell membrane ruptures (Figs. 103-106). Tetronyl, effective in a pH range of 3.2-10, acts against *Monilia albicans* and other bacteria that often complicate trichomonad infestations. For effective treatment, coexisting disease must be corrected and trichomonad infection eradicated. The husband should also be examined to guard against reinfection.

Therapy, consisting of one physician-administered treatment weekly with tetronyl powder and two daily patient-administered treatments with tetronyl jelly for up to four

(4) Am. J. Obst. & Gynec. 60:843-850, October, 1950.

weeks, should be continued during the menstrual period. The technic requires only a speculum, eliminates need for "ballooning" insufflation and preparatory washing and drying of the vagina; soaps or other detergents leave a residue that may inactivate tetronyl. The powder is "puffed" from a disposable single treatment container.

Tetronyl is simple and convenient to use, is an efficient de-

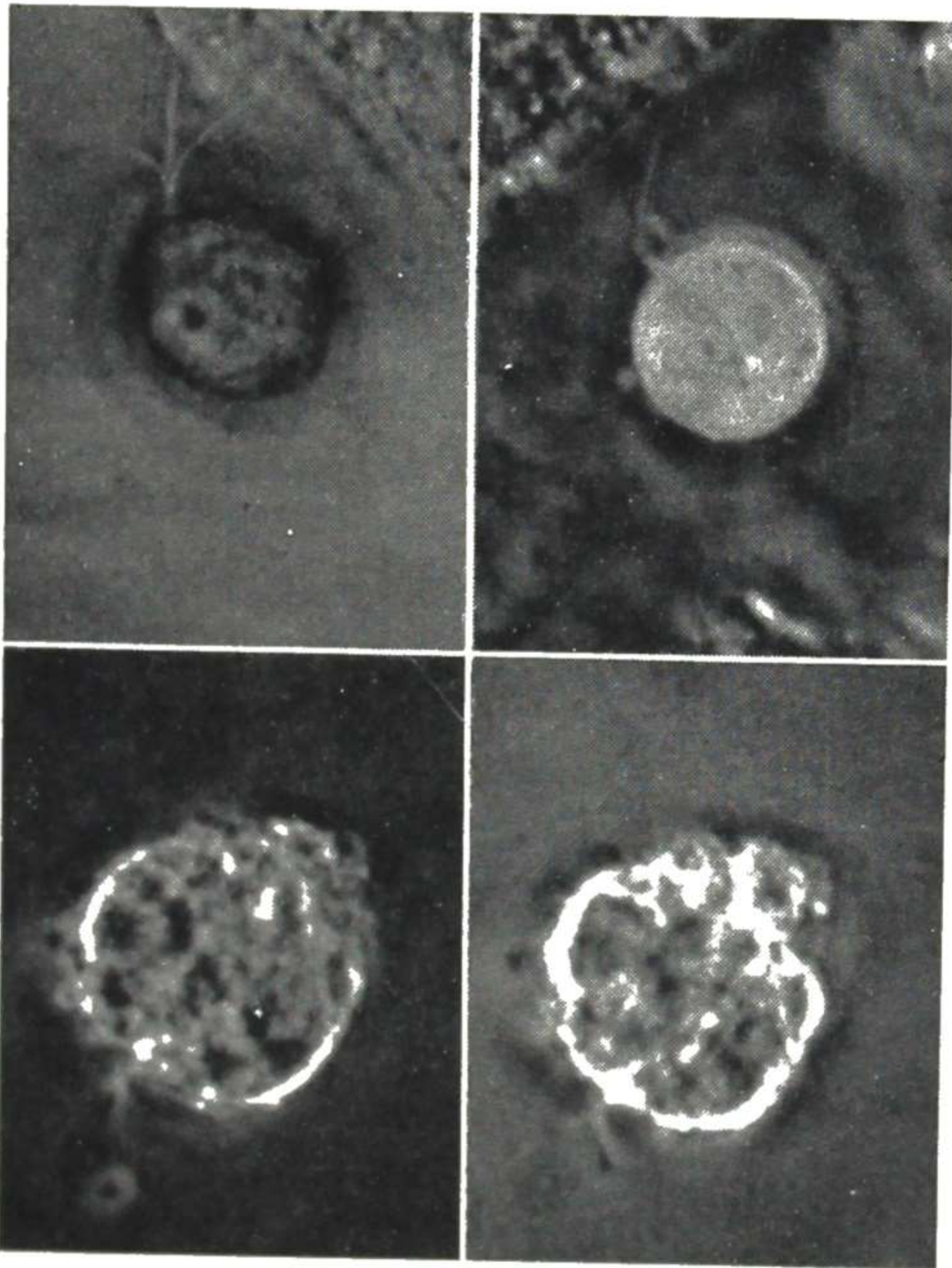


Fig. 103 (top left).—Living trichomonad, showing three flagella.

Fig. 104 (top right).—Immediate effect of trichomonacide, in 1:10,000 dilution—a "balling up" of the organism.

Fig. 105 (bottom left).—Organism 30 seconds after contact; note rupturing cell membrane.

Fig. 106 (bottom right).—Same organism one minute later, with cytoplasmic contents escaping through ruptured cell wall.

(Courtesy of Hundley, J. M., Jr., *et al.*: *Am. J. Obst. & Gynec.* 60:843-850, October, 1950.)

odorizer, will not stain clothing and requires no pads or tampons. Its wide therapeutic activity, self-spreading action, prolonged retention, lack of toxicity, and sensitizing power are advantageous.

[As the years go on, more and more new treatments for trichomoniasis



are recommended. I sincerely hope that soon we will have a specific therapy, because all of us are plagued with recurrences. Hundley and his group obtained successful results in 94 of 100 patients, but I should like to know how many remained cured several months after therapy was stopped. We must bear in mind that pruritus vulvae may be due to aureomycin.

Karnaky (Am. J. Obst. & Gynec. 61:229, January, 1951) has taken issue with Shelanski concerning the treatment of *Trichomonas vaginalis* infections. He was particularly upset because Shelanski stated that since *T. vaginalis* grows luxuriantly in acid secretions, efforts to maintain an acid reaction of the vagina are not of great value, whereas Karnaky believes he has proved that *T. vaginalis* will not grow in a pH below 5.0.—Ed.]

**Morphologic and Cytochemical Vaginal Smear Study: Effect of Topical Penicillin in Treatment of Focal Infections of Vaginal Tract** is discussed by W. Burton Ayre, Robert Favreau and J. Ernest Ayre<sup>5</sup> (McGill Univ.). Suppositories containing 100,000 units of calcium penicillin in a cocoa butter base were used daily at bedtime for 7-10 days by 15 women with chronic cervicitis and leukorrhea. Prompt symptomatic improvement was achieved and maintained in most cases. Two mild reactions were encountered; symptoms did not appear until after 10 days of treatment and disappeared when suppositories were discontinued. Vaginal smears were studied before and during treatment and glycogen index (G.I.), cornification index (C.I.) and clarity as regards presence of bacteria and leukocytes recorded. Three effects were observed after treatment. (1) Visible bacteria and leukocytes, initially prominent, disappeared. (2) Epithelial cells during and after therapy usually had a G.I. of 50 per cent or more, whereas vaginal smears before therapy were glycopenic (G.I., 0-30 per cent). (3) When suppositories were used in either the follicular or luteal phase of the normal menstrual cycle, the number of cornified epithelial cells increased noticeably. Thus the usual pattern of changes in vaginal cornification was altered.

Results suggest that in combating focal vaginal infections, penicillin acts as an antibacterial agent and reinforces the physiologic mechanism (vaginal glycogen) for the continued control of the vaginal flora and in some manner epithelial cornification is stimulated, apparently increasing the resistance of the epithelium to bacterial invasion. Thus, a synergistic relation is established between the antibiotic and the physiologic defense mechanisms of the vaginal tract.

(5) Am. J. Obst. & Gynec. 60:798-805, October, 1950.

Penicillin therapy resulting in a G.I. of 50 per cent or more apparently restores physiologic conditions. Vaginal smear-glycogen study may provide an objective guide to this type of therapy.

**Relative Infrequency of Unsuspected Genital Tuberculosis as Cause of Tubal Occlusion** is discussed by S. Leon Israel and David R. Meranze<sup>6</sup> (Mount Sinai Hosp., Philadelphia). It is believed that the endometrium may harbor occult tuberculosis for a long time. Average incidence of such subclinical tuberculosis has been reported as less than 1 per cent but reaches 5 per cent in some parts of the world. Halbrecht reported an incidence in Israel of 37.5 per cent among sterile women with tubal occlusion.

Endometrial findings in 177 voluntarily barren women who had undergone transuterine insufflation (Rubin's test) and uterine curettage at the same time were reviewed. In 104 (58.8 per cent) there was normal tubal patency, in 40 (22.6 per cent) complete occlusion and in 33 (18.6 per cent) some degree of tubal stricture. Histologic examination revealed no tuberculous endometritis.

It was concluded that unsuspected genital tuberculosis is not a universally frequent cause of tubal occlusion. High incidence in the Israeli series may be historically conditioned. The relation of unsuspected genital tuberculosis and tubal occlusion may well vary with the geographic (the endemic) incidence of tuberculosis.

[The incidence of tuberculosis of the endometrium varies considerably in different parts of the world. It is common in Israel and in Glasgow. Whereas the authors failed to find a single instance of tuberculosis of the endometrium among 177 sterile women, Rabau found genital tuberculosis in 3.5 per cent of 2,000 sterile women.—Ed.]

**Genital Tuberculosis** as reported by Hernando Amaya León<sup>7</sup> represents about 2 per cent of all gynecologic conditions and 0.6 per cent of all illnesses. It usually appears with generalized tuberculous peritonitis. Most patients with this form of tuberculosis are under age 36.

Diagnosis of genital peritoneal tuberculosis is complex. Often syndromes of nonspecific flow, intermittent pain, indefinite sensation to touch and amenorrhea or menorrhagia without apparent cause suggest bacillary invasion. Though

(6) *Fertil. & Steril.* 1:523-526, November, 1950.

(7) *Rev. colomb. obst. y ginec.* 1:227-251, Oct.-Nov., 1950.

laparotomy is a good adjunct in treatment of genital peritoneal tuberculosis, pneumoperitoneum is often better because it is less hazardous.

In 13 cases of genital tuberculosis studied, the tubes were involved in all, the ovaries in half and the uterus in a third. Hysterectomy with salpingectomy gives the best results in such cases. Since this form of tuberculosis evolves silently, all measures should be used to locate other sites of infection.

Of 40 patients with pulmonary tuberculosis, 2 were found to have tuberculous endometritis. Probably the incidence is greater, but lesions are latent and asymptomatic and hence go undetected. Endometritis due to tuberculosis usually results from extensive destruction of the mucosa. Most patients are in poor physical condition with advanced lesions and poor prognosis. In addition to general medical treatment, radiotherapy and/or surgery may be used. Curettage is strictly contraindicated because of the possibility of dissemination of the disease.

Amenorrhea is the most common gynecologic symptom in pulmonary tuberculosis, occurring in about 40 per cent of cases. When a woman has amenorrhea without cause, extragenital tuberculosis should be considered. If amenorrhea is prolonged in a patient with pulmonary tuberculosis, prognosis is poor. However, return of the menses is a favorable sign, as is continuation of the menses without change. When a woman presents clinical symptomatology of tuberculosis together with amenorrhea, extragenital lesions, especially in the lungs, should be suspected.

**Symptomatology and Pathology of Tuberculous Endometritis.** F. Nogales and E. Vilar<sup>8</sup> (Madrid) do not consider endometritis a cause of sterility per se, since many women with this condition have conceived and gone to term. In 55 cases, a fresh corpus luteum was found in the ovaries of 2 women after hysterectomy, although 90 per cent of the women were sterile. Normal tubes were found in 40 per cent. However, in all of 24 cases in which material was available for study the tubes were involved, while the uterus was involved in 85 per cent and the ovaries in 20 per cent.

Tuberculous endometritis may be secondary to a distant extragenital lesion and transmitted through the circulator.

(8) Acta ginec. 1:189-200, 1950.

system, may be an extension of a previous tubal tuberculosis, or lymphatic transmission of pelvic or abdominal tuberculosis. Much uterine tuberculosis originates in infancy or near puberty without manifesting itself. Hypoplastic uterus predisposes to the fixation of Koch bacillus in the endometrium, or if tuberculosis predates puberty, fixation of the bacillus produces uterine hypoplasia. Sterility is caused by inability of the endometrium to implant a fertilized ovum, loss of the functional capacity of the parenchyma, tubal obstruction, monophasic cycles and caseous destruction of the uterine mucosa.

There are two forms of endometrial tuberculosis, miliary and ulcerocaseous with thickened and polypous mucosa. Symptomatology is scant and confusing; in this series, 50 per cent had normal menses, while the rest had monophasic cycles with afunctional mucosa, anovulation, persistent follicles and thickened polycystic ovaries. There is little pain. Diagnosis is facilitated if a hypoplastic uterus is found with tubal inflammation. Endometrial biopsy is not contraindicated and has revealed some cancers which otherwise would have gone undetected.

Treatment includes adequate diet, large doses of vitamin D, calcium, streptomycin and para-aminosalicylic acid. By this means, endometrial function may be restored and sterility occasionally cured. Bacilli were no longer found in the endometrium after 45 Gm. streptomycin, 1 Gm. daily. Biopsy controls were done at the 20, 30 and 45 Gm. stages of treatment. Intrauterine radium therapy is contraindicated.

With severe tubal lesions as well as tuberculous endometritis, the tubal lesions are treated first. Roentgen therapy and streptomycin give good results. Surgery is reserved for severe cases.

[Most of the considerable recent literature on tuberculosis of the female pelvic organs has dealt with tuberculous endometritis. Generally, diagnosis has been made during biopsy for sterility. Tuberculosis is an infrequent cause of sterility, although in some parts of the world 5-6 per cent of all the endometrial biopsies performed on infertile women show tuberculosis. Formerly nearly all cures in cases of pelvic tuberculosis were achieved by surgery. Now conservative therapy is promising through use of streptomycin. Operations can be avoided in many cases, and occasionally streptomycin cures the condition so that pregnancy will follow. In a number of cases, after streptomycin therapy tuberculosis of the endometrium was shown to be completely healed. Even when operation is necessary, preliminary treatment with streptomycin may allow

a more conservative operation. Additional proof of the value of streptomycin is offered by Halbrecht, who treated six patients with latent genital tuberculosis with streptomycin. Five responded. In five women, endometrial tuberculosis was found at the time of biopsy for sterility. In the sixth, *Mycobacterium tuberculosis* was found on culture of menstrual discharge. Total dosage varied between 40 and 45 Gm. in five cases and was 75 Gm. in one case; daily dosage was 1 Gm. These results encourage the belief that streptomycin, even in the fairly low total dosage 40-45 Gm., is effective in such cases. One advantage of this therapy is that the endometrium is preserved so that the remote chance of subsequent pregnancy is not completely removed.

In an extensive monograph, Jedberg (*Acta obst. et gynec. scandinav.*, vol. 31, supp. 1, 1950) analyzed 186 cases of surgically treated genital tuberculosis from various hospitals in Sweden during the years 1942-45. In this series, 56 per cent had a history of tuberculosis elsewhere in the body and 36 per cent had coexistent tuberculous lesions elsewhere. Definite diagnosis of pelvic tuberculosis is difficult but can be made by biopsy of uterine endometrium, culture of menstrual blood and cervical mucus on Löwenstein's medium, guinea pig inoculation and hysterosalpingography. Treatment should be conservative, using para-aminosalicylic acid and streptomycin. Surgery should be reserved for women who do not respond to conservative treatment. Patients should receive pre- and postoperative antibiotic therapy and also sanatorium care before and after operation. Schut and Teenstra (*Nederl. tijdschr. verlosk. en gynaec.* 51:48, 1951) studied the endometrium of women patients in a sanatorium for bone and joint disease. Menstrual blood was cultured on Löwenstein's medium and injected into guinea pigs. Of the 66 patients examined, 20 (30 per cent) had positive results. On the other hand, culture of the menstrual blood of 59 female patients in a sanatorium for pulmonary disease failed to give a single positive result.—Ed.]

**Female Genital Tuberculosis.** Daniel Ribeiro<sup>9</sup> (Belo Horizonte) reports on 35 cases, 28 confirmed histologically and 7 diagnosed from symptoms and macroscopic findings. In the confirmed cases the lesion was found in the endometrium in six, peritoneum in five and tubes in four; in the rest, multiple lesions were present. In six of the unconfirmed cases peritoneal lesions involved surrounding tissue, perimetrium and intestinal loops; in the seventh, there were exudative peritonitis and active pulmonary tuberculosis.

Laparotomy was done in 13 cases, hysterectomy in 9 (with salpingo-oophorectomy in 7), salpingo-oophorectomy alone in 4 and curettage in 2. In eight cases, ultraviolet or x-ray therapy followed surgery. One patient had diathermy and six, symptomatic treatment. Of the group, 16 were cured, 8 improved, 3 unimproved and 8 died.

**Genital Tuberculosis of the Female and Sterility.** According to Erwin Rabau<sup>1</sup> (Petah Tiqva, Palestine), among 2,000

(9) *An. brasil. ginec.* 30:227-232, September, 1950.

(1) *Fertil. & Steril.* 1:517-522, November, 1950.

patients with sterility, genital tuberculosis has been established in 3.5 per cent. Tubercle bacilli may reach the genital system via the blood stream or by direct penetration from the tubes. Tubal tuberculosis is two to three times as frequent as endometrial involvement. Genital tuberculosis is, as a rule, the only symptom, the patients feeling well and having no history of tuberculous infection. When there is tubal obstruction, the reason for sterility is obvious; but in 25 per cent of Rabau's endometrial cases the tubes were patent although pregnancy had not occurred, suggesting that endometrial tuberculosis is an absolute reason for sterility.

A definite diagnosis of genital tuberculosis can be made by histologic and bacteriologic examination of the endometrium, uterine secretions and menstrual blood. In most cases it is only detected incidentally during routine examination because of sterility.

Prognosis for life is not unfavorable provided therapy is started in time. Streptomycin should be considered, although thus far it has not relieved the sterility. Tuberculous pyosalpinx indicates surgery as early as possible, before further spread can take place. This avoids later x-ray treatment which, although effective, usually implies destruction of ovarian function.

**Tuberculosis of Uterus.** In 100 cases studied by F. Nogales Ortiz<sup>2</sup>. (Madrid), the uterus was normal in 50, hypoplastic in 40 and enlarged in 10 (only 4 of these were intrinsically enlarged; the other 6 were myomatous). Distinction must be made between tuberculosis of the cervix and of the portio vaginalis. In many cases, both are extensions of the same process, although tuberculosis of the cervix is harder to diagnose.

Demonstration of the specific elements of tuberculosis was prerequisite to diagnosis of tuberculosis of the cervix or the uterus. In 60 cases, Ortiz found that uterine dystrophy with giant cells was a result rather than a cause of endometrial tuberculosis. In 56 cases, the mucosa in the proliferative or secretory state was well developed; in 44, monophasic cycles and hyperplasias were seen. Twelve of 36 hysterectomy sections showed abundant tuberculous adnexitis. In only 14 cases were the adnexa apparently normal. Secondary altera-

(2) , Acta ginec. 2:13-28, 1951.

tion of ovarian rhythm was noted in some cases and complete lack of function in others. Pseudoerosions did not heal spontaneously, and many curious effects followed radiation.

**Roentgen Diagnosis of Tuberculous Salpingitis.** Kristina Ekengren and Åke B. V. Rydén<sup>3</sup> (Karolinska Inst.) state that tuberculosis of the genital organs is commoner than it was once thought to be. It is frequently impossible to recognize the tuberculous nature of adnexal changes during laparotomy; when the microscope reveals tuberculosis, it is often an unexpected surprise.

Salpingographic records of 75 cases of tubal tuberculosis occurring in nine years were studied. There were no subjective complaints in 55 and no genital disturbances in 64. The cases were divided into seven groups according to roentgen findings. Group 1 patients had slightly dilated club-shaped tubes with even contour and no mucous membrane relief which were obstructed at the beginning of the ampulla or at the isthmus. This picture was due to connective tissue in the wall of the tube occluding the lumen. Eighteen patients had bilateral and 11 unilateral lesions of this type. In group 2 the tubes were closed at the isthmus or beginning of the ampulla and showed irregular, ragged contours at the point of occlusion. This was due to dense connective tissue scars; it occurred bilaterally in four patients and unilaterally in one. Group 3 had tubes with multiple strictures near the isthmus or ampulla, the result of longitudinal ridges formed from hypertrophic villi. There were 7 bilateral and 14 unilateral cases. In group 4 the tubes were moderately dilated, with mucous membrane relief in the ampulla. This picture was due to gaps in the contrast material caused by isolated groups of hypertrophic villi and partial obstruction of the villous structure. The condition was unilateral in four of five patients. The tubes in group 5 were dilated, with hypertrophic longitudinal ridges and irregular mucous membrane relief in the ampulla; this occurred bilaterally in 17 of 21 patients. Group 6 showed dilated tubes with irregular hypertrophic mucous membrane relief in the ampulla and stricture proximal to the ostium. In six of nine patients involvement was bilateral. The 10 patients in group 7 had moderately dilated tubes with

(3) Acta radiol. 34:193-214, September, 1950.

ragged, irregular contour and contrast defects in the ampulla. This was due to tuberculous changes and was present bilaterally in six patients.

Comparison with 95 control subjects showed that salpingograms of the type described are commoner in patients with tuberculous salpingitis than in normal patients. Pronounced hypertrophic ridges of mucous membrane, calcifications in the region of the tubes or ovaries, fistula formation and intramural abscesses were found only in tuberculosis. Another sign suggestive of tuberculosis were differences between the changes in the two ovaries. Duration of the disease was 5-15 years. Tuberculous peritonitis had preceded salpingography in 17 patients and skeletal or renal infection in 4.

Salpingography does not entail risk of activation or spread of the infectious process. The only complication was mild fever in one patient. A water-soluble contrast medium was used. Permeability of the tubes with passage of contrast medium into the peritoneal cavity or into walled-off spaces occurred in 39 of the 75 patients.

[Diagnosis of tuberculosis by salpingography is especially important because of possible improvement by streptomycin. Diagnosis should always be proved before claims are made for streptomycin in tuberculosis. If more roentgenologists and gynecologists will become familiar with the roentgen findings in the tubes of women with genital tuberculosis, some laparotomies will be avoided when there are no abscesses or material from which to make smears or guinea pig inoculations. If the endometrium is involved, gentle curettage will yield material for diagnosis. However, the uterus is involved in not more than about 70 per cent of cases of tuberculosis of the tubes. In nearly all cases of genital tuberculosis, except of the cervix and vagina, the tubes are involved bilaterally.]

Murray (*Obst. y ginec. latino-am.* 8:223, 1950) reports on 65 cases of genital tuberculosis, 44 in the tubes, 13 in the endometrium and 8 in the cervix. Cervical involvement was unusually high. Among the women who came for advice about sterility, 1.59 per cent had endometrial tuberculosis. Correct diagnosis was made in only 20.5 per cent. Uterine and vaginal smears were negative for Koch bacillus in all cases. Tubal insufflation and hysterosalpingography were used when absence of symptoms did not permit diagnosis. Tubal insufflation revealed bilateral tubal closure in 41.65 per cent and hysterosalpingography in 67.8 per cent. Murray believes genital tuberculosis should be treated as a disease of the whole organism and should include sunshine, proper general regimen, calcium, vitamins and streptomycin. For the genital lesions, Murray advises deep x-ray therapy in stimulating doses. Surgery can be resorted to when this conservative plan fails or in the presence of pyosalpinx. Pregnancy occurred later in 6 per cent of cases, but in only one case did it go to term, ectopic tubal pregnancy or spontaneous interruption occurring in the rest.—Ed.]



**Clinical Study of Granuloma Inguinale with Routine for Diagnosis of Lesions of Vulva.** According to Walter L. Thomas<sup>4</sup> (Duke Univ.), granuloma inguinale is a specific, chronic, supposedly infectious, granulomatous disease caused by the gram-negative bacillus, *Donovania granulomatis* or Donovan body. Diagnosis is based on demonstration of morphologically typical intracellular bacilli in tissue smears. The disease must be differentiated from syphilis, carcinoma, lymphopathia venereum, chancroid, tuberculosis, blastomycosis, condyloma acuminatum and other granulomatous diseases.

Tissue smear examination revealed typical Donovan bodies in 79 patients. Biopsy gave a positive diagnosis in 9 of 37 of these patients. Thirty-two also had syphilis, 18 secondary fusospirochetosis, 9 chancroid, 6 lymphopathia venereum, 3 condyloma acuminatum and 1 vulvar carcinoma. Racial distribution was 77 Negroes, 1 Filipino and 1 Caucasian. Mortality was 2.5 per cent.

Treatment ranged from prolonged intravenous therapy with tartar emetic, with or without partial or total vulvectomy, to streptomycin. The last seven patients received an average total dose of 20 Gm. streptomycin. It was followed by rapid, complete healing of the lesions and no recurrences. Recent reports indicate that aureomycin and chloramphenicol are equally effective.

---

## BENIGN TUMORS AND ENDOMETRIOSIS

**Management of Fibromyomata Uteri.** In review of 4,077 white gynecologic patients, C. H. Mauzy, F. R. Lock and J. F. Donnelly<sup>5</sup> (Bowman Gray School of Med.) found 253 (6 per cent) with fibroids. Conservative measures such as observation or expectant treatment, myomectomy and irradiation were used in 186 cases; hysterectomy was done or recommended in 67. Among 153 patients in the observation group, 88 were followed and required no radical surgery. Improvement was noted in 82 cases. Myomectomies were performed in 12 cases, 10 abdominal and 2 vaginal. Only eight patients received irradiation therapy; the authors avoid its use whe

(4) *Am. J. Obst. & Gynec.* 61:790-800, April, 1951.

(5) *Ibid.*, pp. 32-40, January, 1951.

ever possible since it does not always control bleeding and works by suppression of ovarian function. In addition, early carcinoma of the endometrium may be overlooked by operator or pathologist. Of 12 gravid patients with fibroids, 6 were delivered vaginally and 6 referred for interruption of pregnancy. In 67 patients treated radically, hysterectomy was done for tumor alone in 55, for tumor and malignancy in 3 and for tumor and pregnancy in 1; 8 were sent back to the referring physician for hysterectomy for large fibroids with associated symptoms. Critical review of findings and symptomatology of the operative group suggested that in 26 cases surgery was not wholly justified. Exclusion of these cases would reduce the incidence of surgery from 26.4 to 16 per cent. Neither size of tumor nor age of patient need be considered in expectant treatment, as most tumors regress in the postmenopausal period. Rapid growth, bleeding, pain and pronounced pressure symptoms are the most reliable indications for surgery.

[I fully approve of this conservatism in treatment of fibromyomas of the uterus. Not more than one in three women with fibromyomas ever require surgery. Follow-up will show that over a period of years no harm is done in permitting asymptomatic small and moderate-sized fibromyomas to remain until the change of life. After this, nearly all tumors up to 10 cm. shrink. The risk of fatal malignancy in fibromyomas is almost negligible. Far too many fibromyomatous uteri are removed when no symptoms are present. The chief reason for removing a uterus with fibromyomas should be excessive bleeding, not the presence of myomas. When there is no profuse bleeding and no pain on palpation of the uterus, and especially when growth of the neoplasm is not rapid, there is no justification for surgery.—Ed.]

**Fertility in Etiology of Endometriosis.** William V. Cavanagh<sup>6</sup> (Columbia Univ.) reports observations in 646 histologically proved cases, excluding those of internal endometriosis or adenomyosis. In 82 per cent one or both ovaries were replaced by hemorrhagic endometrioma with or without further pelvic dissemination. The median age of patients was 37.9 years. Forty-three per cent were ward and 57 per cent private patients. Over-all incidence of endometriosis in patients undergoing laparotomy for pelvic disease was 7.5 per cent (4.1 per cent in Negro and 6.2 per cent in white ward patients and 10.6 per cent in private patients). Because incidence of pelvic inflammatory disease and fibroids is lower in private than in ward patients, incidence of endometriosis is approximately

(6) *Am. J. Obst. & Gynec.* 61:539-547, March, 1951.

the same in both groups. It was slightly higher in unmarried patients over 30.

Fertility patterns in these patients, compared with those in a control series of 600 pneumonia patients of similar age and social status, showed a much lower pregnancy rate in endometriosis patients, regardless of age at marriage. The disease was associated with infertility in twice the normal expected frequency in women marrying before 30 and nine times the expected frequency thereafter. Patients destined to have endometriosis showed no greater tendency to postpone marriage or delay pregnancy after marriage than did controls. These observations fail to support the thesis that endometriosis results from voluntary delay of pregnancy or is related to economic conditions.

**Endometriosis, Clinical Aspects and Therapeutic Considerations.** Among 2,000 private patients, Samuel L. Siegler and Joseph R. Bisaccio<sup>7</sup> (Brooklyn) found 162 cases of endometriosis (88 proved by surgery and 74 clinical). About 80 per cent of the patients with proved external endometriosis were 26-40 and 75 per cent of those with internal endometriosis 36-45. Menorrhagia, metrorrhagia, dysmenorrhea, lower abdominal pain aggravated during menses, jarring of pelvis, intercourse, pelvic examination, prolonged standing and backache were the dominant symptoms. The most frequent physical observations were culdesac tenderness and irregularity, palpable enlarged ovaries, tender adnexa with or without induration, and uterine enlargement almost invariably due to coexisting fibromas.

Prolonged childlessness was frequent in all types. Of 67 surgical patients with external endometriosis, 45 were childless for five years; of the 74 with clinically suspected cases, 30 were childless for five years, and of the 21 with internal endometriosis, 16 were childless for over five years.

The most frequent sites in the surgically proved cases were the ovary (51), posterior culdesac (38) and rectosigmoid (11). The most frequent associated findings were myom and retrodisplacement.

Early marriage, frequent childbearing, balanced diet, dilatation of the cervix for stenosis and meticulous care in instrumentation reduce incidence of endometriosis. Expectant an

(7) Am. J. Obst. & Gynec. 61:99-108, January, 1951.

conservative treatment, especially in young women, was used to preserve the ovarian and gestational functions. In young patients, surgery was done only when symptoms were uncontrollably progressive; in older women there was no hesitancy about radical procedures. Diethylstilbestrol was used in 11 patients, with no relief in 5 who eventually came to surgery. There was one pregnancy after a year; two patients had definite lessening of induration in the culdesac, four became amenorrheic, and one menstruated regularly with normal biphasic basal temperature. Greenblatt postulates that the endometriosis may be derived from celomic epithelium or some other embryonic cells which are easily destroyed by large and continuous doses of estrogen.

Androgens were of only temporary value. To avoid masculinization, not more than 400 mg. was administered, intermittently. Only young patients with minimal changes definitely related to the menstrual cycle received androgens. Complete relief was seen in 7 patients, 4 of whom became pregnant; there were 33 failures and 6 with partial relief who were later treated with sedatives, thyroid, antispasmodics and benzedrine.<sup>®</sup>

Conservative surgery with preservation of ovary and uterus gave good results since reoperation for exacerbation of symptoms was only 5-6 per cent. Conservative surgery in 32 resulted in complete relief in 19, partial relief in 8 and 5 failures; there were 9 pregnancies. In women over 40, panhysterectomy was done when possible. Watchful waiting and observation should be used in young patients. In the clinically suspected group, 9 of 27 became pregnant without treatment and 8 of 47 with medical treatment.

[During the last few years Karnaky has advocated diethylstilbestrol treatment of endometriosis. Siegler and Bisaccio used diethylstilbestrol in 11 patients, 1 of whom required 2,500 cc. blood before operation because of severe hemorrhage induced by the drug. Four patients became amenorrheic. As a result of their experience in these 11 cases, the authors say: "At present the mode of action of stilbestrol can only be conjectured *and its use should be cautiously and judiciously individualized*" (authors' italics).—Ed.]

**Pregnancy after Conservative Surgery for Endometriosis.** G. E. Norwood<sup>8</sup> (San Marino, Calif.) presents results in 43 patients, 28 of whom had conservative surgery for endometriosis and associated conditions, 15 for endometriosis alone.

(8) *Ann. West. Med. & Surg.* 5:181-187, March, 1951.

All patients were followed at least a year. All had attempted to become pregnant before and following surgery and were under routine sterility care; no sterility factor was present in male partners.

Thirty-two patients became pregnant following surgery. There were no ectopic pregnancies after surgery, whereas 2 of the 17 pregnancies before surgery were ectopic. There was no significant difference in number of abortions before and after surgery. Of 11 patients who did not become pregnant, in 6 the time elapsed since operation was less than 2½ years, the average time before a living infant was born in the other 32. All but 2 of these 11 patients underwent operations for associated pathologic conditions in addition to endometriosis. Surgery for endometriosis alone thus gave better results, measured by increase in fertility from 27 per cent preoperatively to 87 per cent after surgery.

[The occurrence of pregnancy with full term babies after conservative operations for endometriosis is gratifying and is the best argument for conservative surgical therapy in young women.—Ed.]

**Experimental Endometriosis** was studied in the female *Macacus rhesus* monkey by Richard W. TeLinde and Roger B. Scott<sup>9</sup> (Johns Hopkins Univ.) to determine whether cast-off endometrium is viable or dead. This laboratory animal was chosen since its menstrual cycle resembles that of the human female. In previous observations, extensive endometriosis (Fig. 107) was found two to four years after hysterotomies on pregnant monkeys.

In seven monkeys undesquamated endometrium was excised from the uterine lining and autogenously transplanted throughout the pelvic organs, intestines and abdominal wall. Six animals had at least one take. The time of transplantation relative to the day in the menstrual cycle or pregnancy did not seem to affect development of transplants; preoperative implantation of estrone pellets in two instances also had no apparent effect.

Experiments with desquamated endometrium were carried out. Ten monkeys were surgically treated to permit them to menstruate into the abdominal cavity (Fig. 108). In no instance was intact endometrium instrumented or traumatized. Five monkeys had extensive adhesions of the bowel to the

(9) Am. J. Obst. & Gynec. 60:1147-1173, November, 1950.

turned cervix, and the intervening fibrous tissue revealed endometrial tissue. In one of these five animals typical endometriosis lesions also developed on the bowel wall and pelvic peritoneum at some distance from the turned cervix. In five of the surgically altered monkeys there was no external endometriosis; these showed one or a combination of hematometra, hematocervix, cervicointestinal fistula, hydroureter and



Fig. 107.—Extensive endometriosis involving intestines and lower abdomen of monkey three years after hysterotomy to recover early embryo. (Courtesy of TeLinde, R. W., and Scott, R. B.: *Am. J. Obst. & Gynec.* 60:1147-1173, November, 1950.)

hydronephrosis, peritonitis and extensive tuberculosis. Another monkey was so surgically altered that it menstruated via the cervical canal into the abdominal wall, and subsequently endometriosis developed in the abdominal wall scar tissue.

In two human patients, histologically viable endometrium was found in vaginal menstrual discharge or in the tubes (Fig. 109).

Heteroplasia of the pelvic peritoneum or endocervix, di-

rect extensions from the intact endometrium and venous or lymphatic spread are not feasible explanations from the gross and microscopic studies. These experiments indicate that in adult female monkeys, cast-off menstrual endometrium is apparently viable and capable of growing to produce lesions

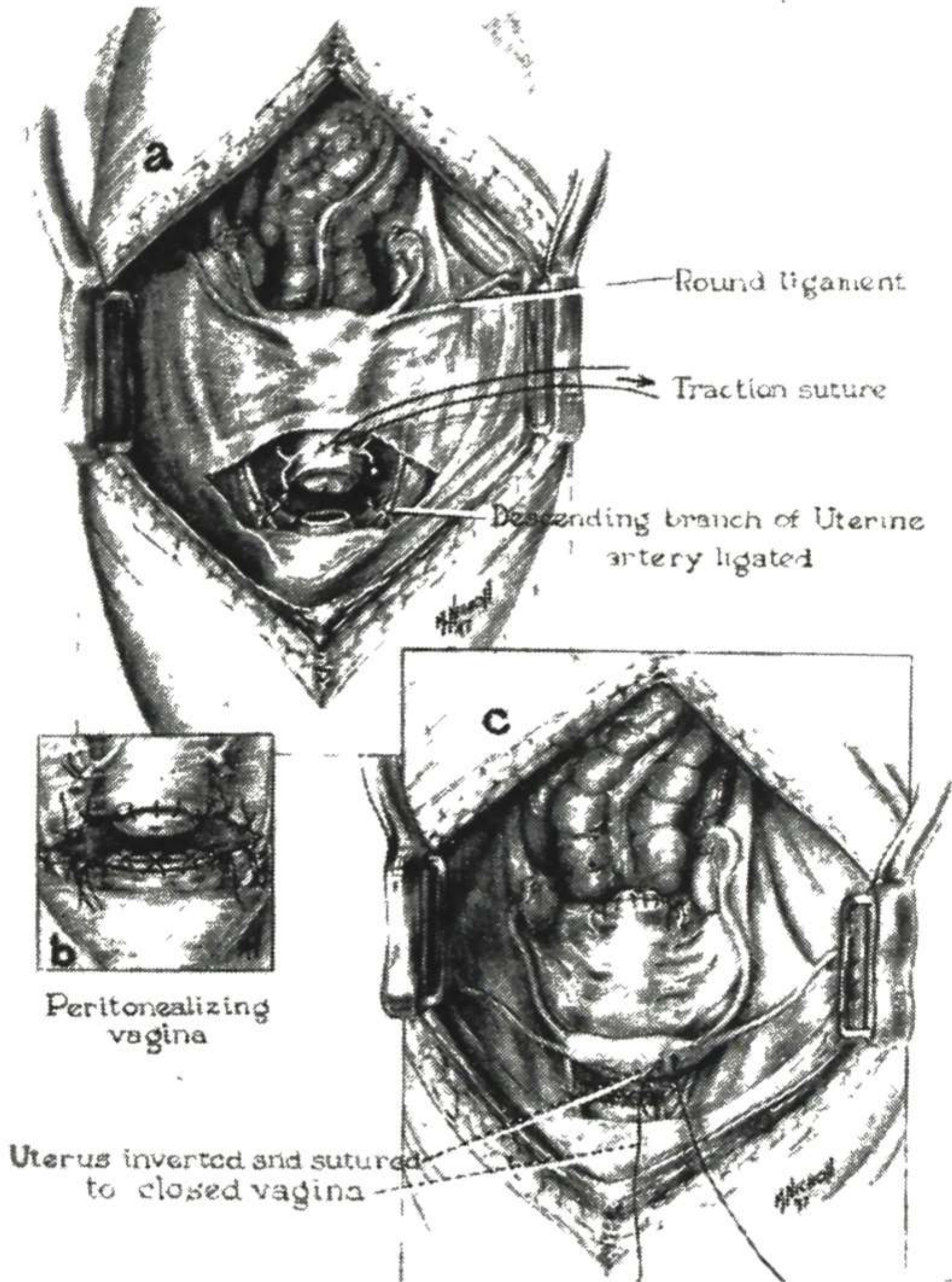


Fig. 108.—To allow intra-abdominal menstruation, entire uterus, separated from vagina, was turned through 180 degrees. (Courtesy of TeLinde, R. W., and Scott, R. B.: *Am. J. Obst. & Gynec.* 60:1147-1173, November, 1950.)

in the pelvic area similar to the lesions in human endometriosis.

[Scott and TeLinde (*Ann. Surg.* 131:697, May, 1950) reported that 516 patients with external endometriosis were operated upon at Johns Hopkins Hospital. External endometriosis was encountered in 2.7 per cent of the gynecologic abdominal operations in Negroes, in 3.2 per cent of the white charity patients and in 15.9 per cent of the private patients. Hence the condition seems to be more frequent in the higher economic levels of society. Adenomyomas and adenomyosis were found in 63 (12.2 per cent). Everyone agrees that surgery is advisable but that child-bearing function

should, if possible, be preserved. In the Hopkins series, 38 subsequent pregnancies in 26 patients of the 64 followed was the reward for preserving child-bearing function. Presacral neurectomy is useful when the uterus is not removed and dysmenorrhea is a major preoperative complaint.

Fallon (A. M. A. Arch. Surg. 62:412, March, 1951) has shown that there is a definite pattern to the distribution of endometriosis. This pattern is compatible with the concept of distribution of some active agent by gravity but not with the theories of origin from embryonic rests, lymphatic or vascular distribution, metaplasia, heterotopia or extension in continuity from tube or uterus. That the pattern is so clear is a surprise. The author asks, "Does the path start from the tube, from the ovary, or from both?"



Fig. 109.—Unattached fragment of endometrium found in isthmus portion of removed human tube;  $\times 100$ . (Courtesy of TeLinde, R. W., and Scott, R. B.: Am. J. Obst. & Gynec. 60:1147-1173, November, 1950.)

Presumably many of the peritoneal lesions are started by droppings from ovarian endometriomas, but what source supplies the peritoneal lesions in cases in which there was no visible endometriosis? The evidence of the gravity pattern points to the tube.

According to Benjamin and Beaver (Am. J. Clin. Path. 21:212, March, 1951), salpingitis isthmica nodosa appears to be an acquired lesion similar in all respects to uterine adenomyosis, with the tubal epithelium penetrating the tubal musculature just as the endometrium penetrates the myometrium. Subsequent transformation of the penetrating glands from tubal to endometrial type is probably due to metaplastic transformation such as occurs in endometriosis in certain other anatomic situations or to a further differentiation of müllerian epithelium from tubal to endometrial type. The myosalpinx undergoes hypertrophic and hyperplastic changes as does the myometrium in similar conditions. Tubal inflammation is not a proved common factor in the pathogenesis of the lesion but appears to be secondary and coincidental.

In treatment of endometriosis associated with sterility, Simmons (Chicago M. Soc. Bull., p. 525, Dec. 30, 1950) maintains that the recommended massive doses of methyl testosterone, usually 300 mg./month, are



far too large and may have masculinizing effects as well as prevent ovulation. He administers 5 mg. methyl testosterone sublingually daily for 100 days, followed by a month's rest. In none of his cases was ovulation suppressed and five patients became pregnant during treatment.

Keettell and Stein (*Am. J. Obst. & Gynec.* 61:440, February, 1951) found that cast-off endometrium obtained from menstrual fluid can be grown in tissue cultures.

Klüver and Bartelmez (*Surg., Gynec. & Obs.* 92:650, June, 1951) reported spontaneous pelvic endometriosis in a rhesus monkey which had been subjected to four lobectomies. Following the operations, severe dysmenorrhea appeared and the authors believe that the endometriosis resulted from the endocrine dyscrasia produced by the lobectomies. This case can best be explained on the basis of metaplasia of the pelvic peritoneum.

Blinik and Merendino (*Am. J. Surg.* 81:635, June, 1951) found that among 4,477 laparotomies performed at Harlem Hospital, where the vast majority of the patients are Negroes, endometriosis had the almost incredibly low incidence of 0.11 per cent. My experience at the Cook County Hospital confirms the rarity of endometriosis among Negro women.—Ed.]

**Treatment of Kraurosis Vulvae.** Although actual etiology is unknown, kraurosis vulvae may be associated with or follow chronic vulvovaginal infection, avitaminosis or estrogen deficiency. Robert B. Greenblatt<sup>1</sup> (Med. College of Georgia) believes that if pruritus is controlled in early cases, thus avoiding constant trauma, irritation and infection, carcinomatous degeneration will not develop. None of 23 patients observed 10 years or more, had epithelioma.

Topical application of antihistamines and estrogenic ointments gave most relief from pruritus. Oral administration of antihistamines was a valuable adjunct. When denuded or ulcerated areas are present, antihistaminic or estrogenic ointments may aggravate the vulval dermatitis. In such instances soothing ointments should first be used and antihistamines and estrogens given orally. Estrogen therapy may often cause yeastlike infections in the vagina owing to glycogen deposits in the vaginal mucosa and increased acidity of vaginal secretions. Usually, instillations of vaginal propionate jelly will clear the infection, and alkaline (soda) douches will hasten the result and prevent recurrences. Administration of dilute hydrochloric acid, cod liver oil, vitamins A and B may be used empirically. Therapy of complications, such as intertriginous dermatitis, trichomoniasis, moniliasis and trichophyton infections should not be overlooked; signs of avitaminosis must be sought and estrogen deficiency adequately treated.

Though kraurosis vulvae may be completely arrested and

(1) *Postgrad. Med.* 8:471-478, December, 1950.

the vulva restored to normal in early cases, lesions of long duration are irreversible. Surgery is unnecessary if proper therapy is begun early in the disease.

[Any conservative treatment that will eliminate the necessity for operation for kraurosis vulvae is extremely welcome. It is generally believed that in about 50 per cent of cases carcinoma will develop in the kraurosis lesions. Greenblatt has followed some of his patients for 10 or more years, which is a long time. However, we do not know the final outcome as long as these patients are alive. Nevertheless, in early cases of kraurosis vulvae conservative therapy along the lines suggested by Greenblatt should be tried. However, when a patient has had kraurosis for a long time and itching is intractable, vulvectomy should be done without delay.—Ed.]

**Behavior of Pseudomucinous Cystadenoma.** Clayton T. Beecham<sup>2</sup> studied 30 cases. The terms pseudomucinous and serous were originally suggested by Pfannenstiel to describe the cyst contents of the two ovarian tumors which are so much alike externally. Although the pseudomucinous cystadenoma is now a distinct clinical and pathologic entity, the literature contains few statistics and much confusion regarding incidence, histogenesis and benign or malignant spread. From review of the literature and his experience, Beecham believes that this tumor is less common than it is usually thought to be.

In 10 years, 332 primary ovarian tumors were removed at Temple University. Nine per cent were pseudomucinous cysts, 7.8 per cent were serous and the most frequently encountered benign tumor was the dermoid which accounted for 21.3 per cent. The principal pathology textbooks state that incidence of pseudomucinous and serous cysts are equal and indicate that together they constitute the commonest ovarian neoplasms. Allan and Hertig found 1,740 primary ovarian tumors over 43 years, of which 21 per cent were pseudomucinous cysts.

Figures concerning malignant change in these tumors show equally wide variation. Beecham found that 2 of the 332 tumors showed such change. Meyer found a 5 per cent incidence of malignant degeneration, whereas Goodall believes malignancy is a common change. Beecham believes the tumor possesses a bizarre and unpredictable clinical pattern, and reports one case showing wide dissemination with benign cellular pattern.

(2) *Am. J. Obst. & Gynec.* 61:755-765, April, 1951.

## SPECIAL OVARIAN TUMORS

### **Granulosa Cell Tumor of Ovary: Analysis of 40 Cases.**

In a 17 year survey of clinical and pathologic material, Magnus Haines and Ian Jackson<sup>3</sup> (Chelsea Hosp. for Women, London) found 40 cases of granulosa cell tumors. Chief symptoms were uterine bleeding (21), pain (14), swelling of the abdomen (8) and amenorrhea (5). In six patients the chief complaint was ascites and in four free fluid was found in the peritoneal cavity at operation. Torsion of the pedicle occurred four times and required immediate operation in two cases. Over half the patients were past 40. The cases are divided into four groups: prepuberal, reproductive, menopausal and postmenopausal. A single case belonged in the prepuberal group and was not followed. Nine patients in the second group, 11 in the third and 19 in the fourth had menstrual irregularities. The tumors were bilateral in 7, of the right ovary in 18 and the left in 13; the location was not indicated in 2. They were freely movable and measured 2.5-27 cm. in diameter. The surface was generally smooth and glistening and the mass soft. On cross section some lesions were solid, others had areas of softening, and five resembled a cyst. The pattern of the endometrium was strongly positive for estrogen in seven of nine cases. No case of cancer of the ovary or body of the uterus was found.

Mortality for the 30 patients followed was high: 13 died, and 3 others had local recurrences. The malignant nature of this disease is apparent from these figures and the fatal outcome is related to the stage which the disease had reached when operation was undertaken.

In young women only, the affected ovary should be extirpated, and when both ovaries are involved a small section of one should be conserved unless there is local metastasis. In women over 40, both ovaries should be removed and total hysterectomy performed. The value of radiotherapy in this disease has not been established and it has not definitely been determined that these tumors are radiosensitive.

[Granulosa cell tumors have been proved to be much more malignant than we formerly thought. When women operated on for granulosa cell

(3) J. Obst. & Gynaec. Brit. Emp. 57:737-746, October, 1950.

tumors are followed up for many years, we find that both recurrence and death rates are high because recurrences are common long after operation. The authors emphasize that recurrence can take place at all ages and is related not to the type of operation but to the stage of the disease at which the operation is performed. The death rate of 45 per cent is the highest I have seen in any sizable series.—Ed.]

**Malignant Lesions of Uterus Associated with Estrogen-Producing Ovarian Tumors.** Malcolm B. Dockerty and Elizabeth Mussey<sup>4</sup> (Mayo Clinic) in a study of 87 granulosa cell and theca cell tumors found 15 associated uterine cancers. Three patients had mammary cancer. Association of uterine and ovarian lesions was 15 per cent in all patients and 27 per cent in women over 50. Carcinogenic influence of estrogen is suggested as a possible cause. Carcinoma-like lesions have been induced in cervixes of mice receiving estrogens and metastasizing fundal carcinomas have been produced in old multiparous rabbits in which impaired livers prevented breakdown of circulating estrogens.

Uterine as well as mammary carcinomas are rarely observed clinically after oophorectomy; there is high incidence of fundal carcinoma in cirrhosis of the liver. Vaginal smear in a group of women with malignant uterine lesions showed sustained estrogen activity; patients with such lesions have a late menopause with mild symptoms. Development of uterine cancer has been reported in a woman who received 12,000,000 R.U. of estrogen for eight years.

Association with mammary cancer in three cases is further evidence for the role of estrogen in production of uterine tumors. The incidence of coexisting mammary and uterine cancer has been found to be 2.4 times as great as would be expected on the basis of chance alone.

[I agree fully with Dockerty and Mussey that 16 cases of feminizing ovarian tumors associated with carcinoma is a much higher incidence than can be explained on the basis of chance alone. Giardini (*Obst. y ginec. latino-am.* 7:501, 1949) reported two cases of thecoma with adenocarcinoma of the endometrium. From Ingram and Novak's study it appears that thecomas, more than granulosa cell carcinomas, are associated with endometrial carcinomas, although thecomas are far less common than granulosa cell tumors. There seems to be a definite relation between excessive estrogen production from feminizing tumors and hyperplasia of the endometrium and carcinoma of the endometrium.

Crossen and Suntzeff (*Arch. Path.* 50:721, December, 1950) administered 120 mg. estradiol benzoate by implantation plus 1,630 mg. progesterone by mouth to an aged female monkey in three years. In addition to pronounced cystic hyperplasia of the endometrium, a large hemor-

(4) *Am. J. Obst. & Gynec.* 61:147-153, January, 1951.

rhagic endometrial polyp was produced. Crossen has long maintained that endometrial carcinoma is four times as common in women who menstruate past 50 as in women who have the menopause before 50. This opinion has not been universally accepted.—Ed.]

**Endometrial Carcinoma Associated with Feminizing Ovarian Tumors** is discussed by James M. Ingram, Jr., and Emil Novak.<sup>5</sup> The term feminizing mesenchymoma of the ovary includes luteoma, thecoma and granulosa cell tumors, because of the common histogenesis of the cell types and their frequent coexistence. Thecoma and granulosa cells are thought to originate in the undifferentiated cells of the ovarian mesenchyme; the luteoma is thought to represent the complete or partial luteinization of the thecoma or granulosa cell tumor. The authors call the combination of feminizing ovarian tumor with uterine carcinoma a combined tumor.

Review of the literature, 1920-49, revealed 50 cases of combined tumor, the ovarian components consisting of 28 thecomas and 22 granulosa cell tumors. Since granulosa cell tumors are in general about 10 times as common as thecal cell tumors, the incidence found in combined tumors suggested that granulosa tumors have less carcinogenic capacity, presumably due to a lower degree of estrogen production. It has been suggested that the estrogenic effects of granulosa cell tumors are due to admixtures of thecal elements. The uterine components consisted of 54 endometrial and 2 cervical carcinomas. Uterine myomas occurred with 45 per cent of the feminizing tumors. Two instances of cervical squamous metaplasia and one of adenomyosis were described. Adenocarcinoma was the commonest type, and almost all patients were postmenopausal. Postmenopausal bleeding was the presenting symptom of 85 per cent of the patients, and bleeding was of much longer duration than that which is seen with endometrial carcinoma alone.

Of 66 consecutive cases of feminizing ovarian tumor at Johns Hopkins Hospital, 4 were combined with endometrial adenocarcinoma, all occurring in postmenopausal women. Sixteen had endometrial hyperplasia, 7 proliferative or atrophic endometrium and 1 secretory endometrium. In one patient, adenocanthoma invading the myometrium was combined with granulosa cell carcinoma of the ovary (Fig. 110). A woman, 64, whose presenting complaint was postmeno-

(5) Am. J. Obst. & Gynec. 61:774-789, April, 1951.



Fig. 110 (top).—Cylindromatous granulosa cell carcinoma. Note dark-staining nestomosing cylinders of granulosa cells separated by light-staining trabeculae of connective tissue.

Fig. 111 (bottom). Endometrial carcinoma.

(Courtesy of Ingram, J. M., Jr., and Novak, E.: *Am. J. Obst. & Gynec.* 61: 774-789, April, 1951.)

pausal bleeding, had endometrial carcinoma with granulosa cell ovarian carcinoma (Fig. 111).

Dockerty found that 27 per cent of postmenopausal women with feminizing tumors also had endometrial carcinoma, the

incidence of which was estimated to be 100 times greater in the presence of feminizing tumors. Hertig estimated that 18-20 per cent of granulosa cell tumors are accompanied by uterine carcinoma; of 33 postmenopausal women with feminizing tumors, 12 per cent had uterine carcinoma. That the combined tumor does not appear until such a late age supports the theory that tissues must remain under estrogenic influence for a long time before a carcinogenic effect is exerted. Because of the frequent coexistence of endometrial hyperplasia and endometrial carcinoma, and the prolonged postmenopausal bleeding observed with carcinoma, it is postulated that endometrial hyperplasia is capable of transformation into endometrial carcinoma.

Five of the 66 patients with feminizing tumors had received pelvic irradiation. Although no causal relationship can be established, the possibility offers interesting speculation. Estrogen inactivation by the liver and resulting rise in pituitary gonadotrophins have been believed to stimulate growth of luteomas and granulosa cell tumors in spleen-implanted ovaries.

Hyperestrogenism appears to be the initiating carcinogenic factor in women predisposed to cancer. The authors concluded that investigation of combined tumors by hormone assays and specific stains should yield valuable information with regard to the cause of endometrial carcinoma.

[The authors make the following significant statements: "As expected, the presenting symptom was postmenopausal bleeding, this being noted in 85 per cent of the patients. This bleeding was of much longer duration than is seen with endometrial carcinoma alone. Seventy per cent of the twenty patients in whom bleeding was described had bled intermittently for from two to ten years. . . . It seems logical to suspect that many of these patients had bled from a hyperplasia for years before the appearance of carcinoma." Rigo, Scipiades and Vaczy (*Oncologia* 3:232, 1950) followed up 240 patients who had glandular cystic hyperplasia. In 19 (7.9 per cent) the hyperplasia was followed by a genital carcinoma. Based on their observations, the authors urge strict control of patients with hyperplasia. Winter (*Zentralbl. Gynäk.* 72:880, 1950) followed 763 cases of glandular hyperplasia and found 7 cases of carcinoma (1.44 per cent). He could not find a transition from glandular hyperplasia to carcinoma. Nevertheless he too believes that all women with hyperplasia should be carefully controlled.—Ed.]

**Arrhenoblastoma: Incidence of Malignancy and Relationship to Pregnancy, to Sterility and to Treatment** were assessed by Cart T. Javert and William F. Finn<sup>6</sup> (Cornell

(6) *Cancer* 4:60-77, January, 1951.

Univ.) by an analysis of cases adequately described in the literature and follow-up data obtained from a questionnaire sent to the authors. In 80 of the 122 known cases data were adequate for analysis.

The tumor is more often on the right side and only 5 per cent of tumors were bilateral. Amenorrhea is a common symptom, but masculinization is rare and, when present, does not necessarily correlate with histologic type of tumor. Normal as well as high ketosteroid values have been reported. Of the 122 tumors, 27 were clinically malignant (22 per cent) and 5 showed carcinoma histologically. No patient with the clinically malignant type has been known to survive or be free from recurrence. Since malignancy is usually evident at operation, conservation of uterus and opposite ovary is indicated in grossly benign cases; most patients are in the second or third decade. Subsequent histologic detection of malignancy requires further extirpation. Radical surgery is also indicated in cases with ascites, rapid growth of tumor, adhesions, bilateral tumors or evidence of invasion. Pregnancy occurred before appearance of tumor in 38 patients, after conservative removal in 25 and concomitant with arrhenoblastoma in 5.

[The 26 per cent incidence of malignancy arrived at by these authors is about what most of us have cited as the incidence of malignancy for this tumor. However, perhaps in 10 years, after many more patients have been followed up, the percentage of malignancy will be raised, just as it has been for granulosa cell tumors.—Ed.]

**Dysgerminoma of Ovary: Analysis of 17 Cases with Special Reference to Histogenesis and Therapy** is presented by Paul Pedowitz and David M. Grayzel<sup>7</sup> (Brooklyn). Dysgerminoma is an epithelial neoplasm, identical in structure to testicular seminoma. It is usually unilateral, varying in size from 3 to 5 cm. to a mass filling the pelvis (Fig. 112). Its fibrous capsule disappears in later stages when perforation has occurred. The cells are large, round or polygonal, with abundant clear cytoplasm and a large centrally placed nucleus (Figs. 113 and 114). They are arranged in alveoli. Mitoses are not uncommon. Areas of degeneration and hemorrhage are common, and Langhans type giant cells are seen in the former. Spread occurs through the lymphatics and by direct continuity and may be generalized. In this series there was

(7) *Am. J. Obst. & Gynec.* 61:1243-1252, June, 1951.



one case of choriocarcinoma within a dysgerminoma. Pregnancy tests were positive.

The cell of origin has not been determined but is thought by some to be either a sexually undifferentiated cell (similar tumors in testes) or a totipotent cell in the sex cell series close to the ovum (explaining the association of other teratomas with some of these tumors). The authors believe that these tumors arise from totipotent cells, since chorionepithelioma has been found in metastases without being noted in the original tumor.

Dysgerminomas have been reported less often than granu-



Fig. 112.—Autopsy specimen of uterus and other ovary containing metastatic tumor. Note that ovary is encapsulated and retains its general shape. At operation three months previously ovary was normal in size and appearance. (Courtesy of Pedowitz, P., and Grayzel, D. M.: *Am. J. Obst. & Gynec.* 61:1243-1252, June, 1951.)

losa cell tumors, but in the present series they were twice as frequent. The youngest patient was 6, the oldest 78. There were no sexual or menstrual abnormalities and no characteristic symptoms. Abdominal pain and enlargement were the most frequent complaints, associated with recurrent attacks of nausea and vomiting. Often, the tumors outgrow the blood supply with resultant necrosis and peritoneal irritation. Torsion of a pedicle with acute pain occurred in two patients. In six, ascites was present; in four the fluid was hemorrhagic, indicating a poor prognosis. Metastases were noted at operation in six patients, in three generalized.

The Aschheim-Zondek reaction, if positive, may help in diagnosis. An abdominal x-ray will aid in excluding pregnancies over 14 weeks.

Two patients were alive five years or more and three others from 1 to 2½ years. The death rate was 70.6 per cent and five year survival rate 12.5 per cent.

Radical surgery is advocated in all cases regardless of age,

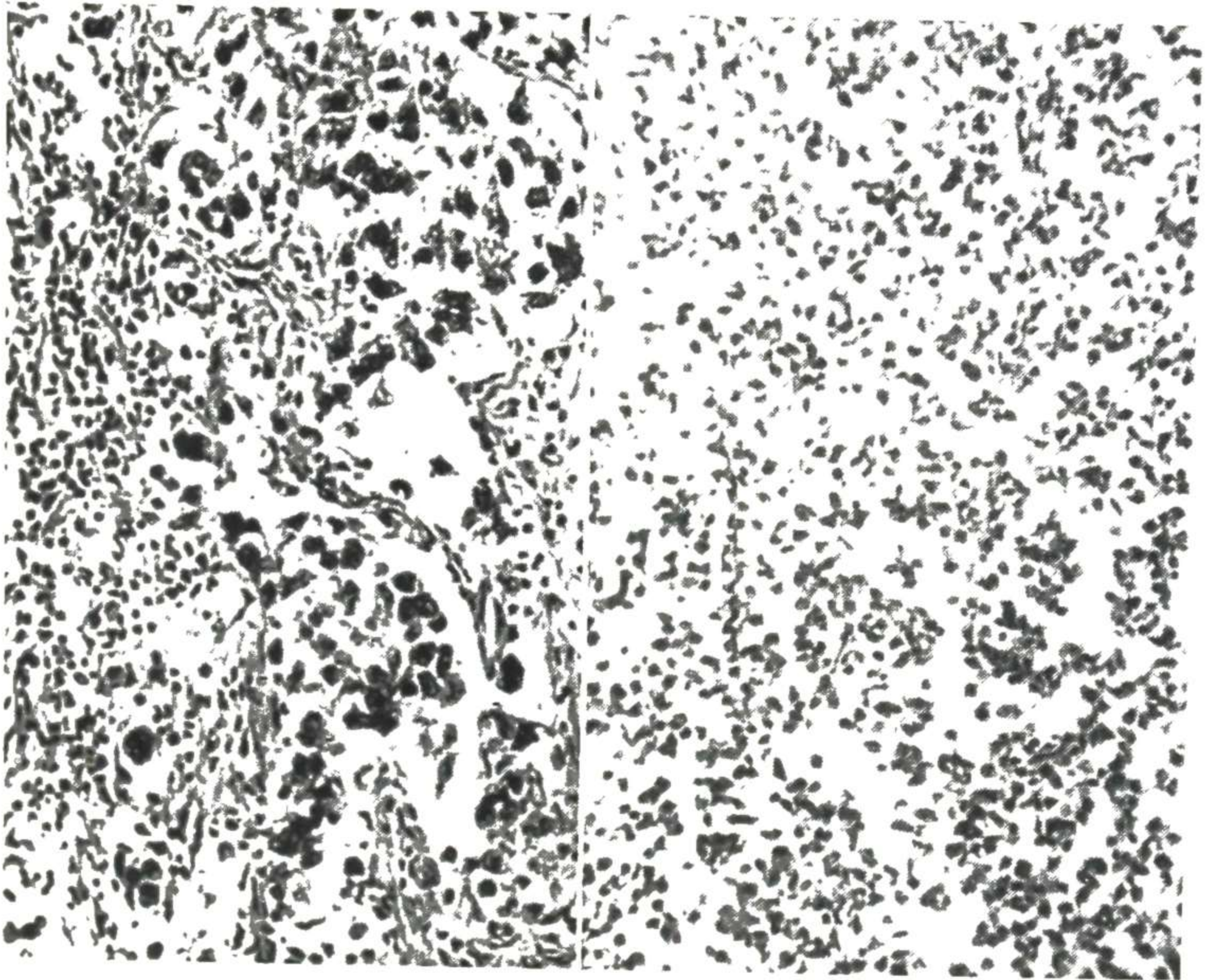


Fig. 113 (left).—Tumor section showing alveolar pattern and lymphocytic infiltration of stroma.

Fig. 114 (right).—Sections showing more pronounced cellularity and scanty stroma.

(Courtesy of Pedowitz, P., and Grayzel, D. M.: *Am. J. Obst. & Gynec.* 61:1243-1252, June, 1951.)

tumor size or degree of encapsulation, because broad ligament lymphatic metastasis is often recognized only histologically. Surgery should be followed by x-ray therapy. Of eight patients in whom no metastases were demonstrable at operation and only salpingo-oophorectomy was done, four had metastases within six months and two others died within this period.

## MALIGNANT TUMORS

**Relation of Hormones to Female Genital Cancer.** Emil Novak<sup>8</sup> (Johns Hopkins Univ.) states that for many years steroid hormones, especially ovarian estrogens, have been suspected of complicity in cancerogenesis. In mice ovarian hormone has been associated with cancer in the genital tract and mammary glands, tissues under physiologic control of the ovaries. Mammary cancer has been produced in male mice of a strain of which only the females were susceptible to mammary cancer; the prolonged use of estrogens needed to give this result made total dosage very large. Later investigations suggest that prolonged exposure rather than large doses for a short time may lead to cancer. Whereas histologically, cancer-like breast lesions have been produced experimentally in monkeys, metastasis and death typical of true clinical cancer do not occur. Genuine carcinoma of the cervix has been produced in mice by Gardner and Li and others.

Indications are that prolonged exposure of the endometrium to estrogens may contribute to development of carcinoma in predisposed subjects. Postmenopausal production of estrogen presumably by the adrenal cortex and not infrequently expressed by endometrial hyperplasia is not uncommon in uteri, the seat of endometrial carcinoma. The endometrium is under the influence of estrogens throughout reproductive life, but there are a monthly sweeping-off and an apparently protective effect from progesterone, so far not suspected as a carcinogen; prolonged exposure of the aging endometrium to even small amounts of estrogen without this protection conceivably could predispose to cancer. Additional evidence is that late menopause appears to influence development of endometrial cancer and that at times estrogen-induced benign hyperplasia, atypical adenomatous hyperplasia and unquestioned adenocarcinoma can all be found in a single endometrium.

Clinical use of estrogens is still widely abused; they are often given without justification especially in treatment of genuine or supposedly menopausal symptoms. Histologic

(8) Am. J. Surg. 82:149-151, July, 1951.

studies in some cases suggest a hazard of cancer from excessive or prolonged estrogen therapy. Also for other reasons, estrogens should never be used continuously, in most women not at all, at the menopause. For the small proportion with severe vasomotor symptoms the interrupted use of estrogens is justified. However it is safest to avoid their use for women with history of precancerous lesion or cancer treatment surgically or radiologically or with strong family history of cancer; testosterone will satisfactorily relieve the vasomotor symptoms. Paradoxically, large doses of estrogens now used in the palliative treatment of advanced cancer of the breast are usually effective. Novak believes androgenic hormone is of even greater value.

**Of What Value Is Male Hormone in Management of Genital Cancer in the Female?** Norman F. Miller, George Thompson and Walter Johnson<sup>9</sup> (Univ. of Michigan) conducted a three year study of patients given customary radium and x-ray therapy plus male hormones. Results were compared with a control group treated by irradiation alone. The male hormone was usually administered as 75 mg. pellets implanted subcutaneously; initial dose was 6-8 pellets. Patients were observed at three month intervals and additional hormone therapy given if significant signs of virilism did not appear. Because of varying individual requirements, total dosage was 450-5,250 mg.

Of 66 patients with carcinoma of the cervix, absolute three year survival rate was 34.9 per cent; survival rate was 69 per cent in 71 controls. These results raise an important question: Does testosterone enhance neoplastic growth in female genital cancer? Treated patients who had evidence of virilism had a much higher three year survival rate than those without virilism. Because virilism usually did not become apparent until seven months after the initial testosterone implant, this difference is explained by early death in the latter group. Comparison of survival rates in study and control patients on the basis of clinical stage of cancer indicated that testosterone, in the dosage used, does not delay growth of cervix cancer. Comparison of 13 study and 17 control patients with endometrial carcinoma showed no benefit from supplemental testosterone therapy. Localized abscesses de-

(9) *Am. J. Obst. & Gynec.* 61:582-588, March, 1951.

veloped at the site of implantation in 7 of 91 treated patients (7.6 per cent). It was impossible to determine the number of pellets lost, but five patients later showed signs of virilism.

Results indicate that testosterone does not prolong life in cervix or endometrial carcinoma.

**Early Diagnosis of Cancer in Women** is best accomplished by periodic complete physical health examinations. At the Strang prevention clinics of the New York Infirmary and of the Memorial Hospital, 26,076 examinations of seemingly healthy women revealed a cancer incidence in various organs of 2.1 per cent and 1.3 per cent, respectively. Although cancers of the breast and pelvic organs produce the highest mortality of this disease, Elise Strang L'Esperance<sup>1</sup> emphasizes that the wide distribution of cancer in women in these series is conclusive proof of the importance of complete examination. Among 258 cases at the Memorial Hospital, there were 5 of lymphatic disease, 2 of multiple myeloma, 23 rectosigmoid cancers, 39 cancers of the skin, 3 silent cancers of the lung and 4 cancers of the kidney and bladder.

Among diagnostic procedures available to the general practitioner, the cytologic diagnosis of tissue obtained by aspiration or by direct smears of surface tissue deserves first place in neoplasms of the female genital tract. The Papanicolaou smear test is easily performed and should be a routine procedure in doctor's office or clinic, although the prepared smear must be sent to a laboratory for diagnosis. A positive result must be confirmed by punch biopsy. The Schiller iodine test may be helpful in locating the lesion. Excellent results have been obtained by examination of sedimented urine by the Papanicolaou smear method and examinations of sputum and rectal washings, but surgical biopsy affords the most accurate diagnosis. It is readily available for extrinsic lesions. In deeper structures, such as the breast, this type of biopsy becomes a surgical procedure and requires hospitalization. X-ray examination is the most valuable diagnostic aid for intrinsic tumors of the gastrointestinal and genitourinary tracts and lungs. However, this can be supplemented by Papanicolaou smear examinations of secretions. Proctosigmoidoscopic examination for rectal and colon disease gives the most accurate information as to conditions of the lower bowel and

(1) Bull. New York Acad. Med. 26:703-720, November, 1950.

should be routine procedure. When there is evidence of disease, either polyp or other manifestation of pathologic change, a barium enema is advisable, with air contrast. These special tests are all valuable, but in diagnosis of early cancer they are secondary to complete periodic physical examination of apparently healthy women.

[I believe all doctors are convinced of the great importance of periodic examinations particular emphasis must be placed on the breasts and a year and those past 40 should have two examinations a year. In all examinations particular emphasis must be placed on the breasts and external and internal pelvic organs. Rectal examination should also be made. No examination is complete without the use of a speculum. In indicated cases vaginal and cervical smears should be made. Today women are being bombarded with information and misinformation about cancer and many of them are unduly alarmed. These women should be set straight by the physician concerning cancer and the importance of periodic examinations. Among the things women should be told is that a large proportion of cancers are definitely curable, especially if detected early and properly treated.

Palmer, Knarr and Eccleston (*Am. J. Obst. & Gynec.* 60:671, September, 1950) maintain that aspiration curettage is an entirely safe office procedure and applicable to almost all patients examined, despite the conviction of others that aspiration curettage is not satisfactory for diagnosis of endometrial malignancy. These authors found diagnostic accuracy of the office method equal to that of conventional dilatation and curettage. I cannot see how aspiration curettage can be as thorough as that under anesthesia in a hospital. When cancer is suspected, the curettage must be systematic and thorough. The authors found aspiration curettage invaluable in diagnosing recurrent activity in postradiation, inoperable patients.

In an effort to improve the five year survival rate for cancer of the cervix, a number of patients who formerly would have been considered to have a nonsurgical condition are now being evaluated from the standpoint of the surgical risk of a radical Wertheim hysterectomy. This changing view in the past 15 years is indicated by the fact that an increasing number of the patients who have undergone this operation have also had preoperative irradiation. Thus, according to Pratt and Foust (*S. Clin. North America* 30:125, August, 1950), at the Mayo Clinic in 1949, of 17 patients with squamous cell epithelioma and 3 with adenocarcinoma who were treated by Wertheim hysterectomy, 12 had had full courses of radium and some of the 12 had had, in addition, roentgen therapy preoperatively. Caution must be exercised in selection of patients for extensive surgery, and only those for whom the risk is considered reasonable should be accepted. There should be no contraindication to operation, such as renal or cardiac disease. Physiologically, but not necessarily chronologically, the patients should not be past the middle fifties. Preferably they should not be overweight; the short obese patient particularly is not a good candidate. By observance of the foregoing points the mortality rate can be kept at a reasonable figure; there were no deaths at the Mayo Clinic in the 90 cases since 1943.

The first report from an individual physician of cancer detection in office practice is that of Siddall (*J. A. M. A.* 145: 314, Feb. 3, 1951). During the preceding six years in rural practice 1,650 examinations

were made on 950 presumably well women. Among them, 13 malignant conditions were discovered: 1 of the fundus uteri, 4 of the breast, 3 of the bowel, 3 of the skin, 1 of the blood (leukemia) and 1 of the lymph nodes (Hodgkin's disease).—Ed.]

**Diagnosis of Early Carcinoma of Cervix.** Clinically recognizable cancer of the cervix is usually not difficult to detect. The problem has been to detect the lesion at a stage permitting adequate treatment by radiation or surgery. The proportion of stage I cancer of the cervix even in most efficiently conducted gynecologic clinics rarely rises above 10 per cent. Newer knowledge suggests that cervical cancer may exist, sometimes for a long period, as a lesion confined to the covering epithelium, with rapid and violent progress likely only in the terminal stage. Review of the literature reveals average age of patients with preinvasive carcinoma to be 38-40; the incidence approaches but does not exceed that of clinically recognizable invasive cancer (1.6 per cent).

Gordon Watkins Douglas and William E. Studdiford<sup>2</sup> (New York Univ.) suggest that a group comprising these cases be added to the present classification of clinical carcinoma. In April 1947 they began an intensive effort to recognize more of these preinvasive lesions. By greatly increasing the number of biopsies, especially of the cervix which was abnormal at the squamocolumnar junction, and by cytologic studies, 16 such cases were discovered by January 1950. Thirteen were intraepithelial and 3 showed early invasion, all detected before treatment. Six patients gave a history of irregular or intermenstrual bleeding. This emphasizes the fact that women over 30 with intermenstrual bleeding, particularly when related to trauma, demand careful investigation of the cervix, both canal and portio, no matter how normal the organ may be to sight and touch. The remaining 10 patients had no symptoms referable to the cervix. Palpation and inspection of the cervix revealed evidence of malignancy in only one patient, who exhibited a small papillomatous mass. Five had reddish zones varying in symmetry about the external os, uniformly interpreted as "erosions." No cystic cervicitis or marked evidence of inflammation was seen.

Biopsy and cell smear are necessary to detect these sub-clinical lesions. Since the lesion may be small and is usually asymmetrical, multiple biopsies are recommended. Because

(2) Surg., Gynec. & Obst. 91:728-741, December, 1950.

deep excision of the squamocolumnar junction may lead to stricture, specimens were taken from four quadrants of the external os with a square-nosed, sharp Schubert punch. Since a supposed intraepithelial lesion found on biopsy may be the margin of an invasive cancer, the cervical canal should be carefully curetted to rule out this possibility. Hospitalization is desirable, since bleeding may require control by suturing. Positive biopsies were obtained in 15 patients. Ayre's wooden spatula was used to obtain cell smears directly from the cervix in 13 patients; 11 were regarded as positive. This method should pick up even the smallest lesions if they are not located high in the canal. Chief disadvantages are time required for proper study of each slide and need for training and experience in interpretation of findings. It is concluded that knowledge of the lesions, use of smears to detect their presence and of biopsy and curettage to define their character and extent, when applied on a large scale, should change the present end results of cervical carcinoma.

[Each year the number of articles on carcinoma of the uterus increases. There are three distinct groups of articles. One group deals with smear methods of detecting carcinoma of the cervix and corpus before clinical signs and symptoms appear. The second deals with intraepithelial carcinoma or carcinoma in situ, and its detection and treatment, and the third group deals with treatment, an increasing portion of which concerns surgery. Almost a complete Year Book could be devoted to each of these three aspects of cancer of the uterus.

Nearly all observers agree that smears of the vaginal contents and cervical and uterine secretions are distinctly helpful in detection of carcinoma before the physician can detect its presence. Many large series of thousands of cases have proved that not infrequently cancer is detected by this means long before any symptoms appear.

As to intraepithelial carcinoma or carcinoma in situ, there is almost general agreement that it can be dangerous and that it should be treated, with one exception. The kind of therapy recommended is by no means uniform. Some gynecologists amputate the cervix, others perform a simple total hysterectomy and still others favor a radical panhysterectomy. Galvin and TeLinde pointed out that in many cases with a diagnosis of intraepithelial carcinoma, serial sections of the cervix after a Wertheim operation, show that invasion definitely exists. In fact, in 55 of their 75 cases diagnosed as carcinoma in situ, microscopic invasion was found. Therefore these women properly were candidates for radical hysterectomy with removal of the lymph nodes. The question of what to do when carcinoma in situ is found in the presence of pregnancy is important and controversial. One group of gynecologists favor a radical Wertheim operation in the presence of pregnancy regardless of the patient's age, but there is a conservative group who do nothing but make repeated smears and biopsies not only during the pregnancy but after delivery. I belong to this group. In an occasional case, carcinoma in situ is diagnosed one or more times during pregnancy but smears fail to show carcinoma after



pregnancy. These women should be followed up closely for the rest of their lives. Several women who have shown carcinoma in situ during and after pregnancy and have refused operation have gone on for a few years with no change in the local condition, but in a few definite invasive carcinoma has developed with disastrous results. Hence, in all nonpregnant women some form of surgical treatment should be used, preferably a modified radical (Wertheim) operation. In pregnancy, on the other hand, it is often difficult to be certain that the cell changes are definitely carcinomatous and not reversible, so one should wait until after delivery for more studies.

Now as regards treatment of carcinoma of the uterine cervix. I have received the sixth volume of *Statements of Results Obtained in 1943 and Previous Years*, sponsored by the British Empire Cancer Campaign, London, Donner Foundation, Philadelphia, Cancerföreningen, Stockholm, and the World Health Organization. The committee consists of Heyman of Stockholm, Donaldson of London and Meigs of Boston. The report includes statements from 37 radiotherapeutic institutions in 11 countries. To avoid confusion the term "fundus" is used throughout the report to indicate that part of the uterus which lies above a line joining the points of entrance of the uterine tubes—the "anatomical fundus." The terms "endocervical" and "corporeal" mucosa are used instead of endometrium of the cervix and corpus, respectively. Since there is no general agreement concerning the exact meaning of the word cancer, the committee decided to use the term carcinoma. In accordance with the procedure adopted by the Subcommittee on the Registration of Cases of Cancer As Well As Their Statistical Presentation, the term "cure rate" has been exchanged for "apparent recovery rate." Similarly, the term "alive but not cured" has been replaced by "alive with carcinoma present."

This report includes the new classification accepted last year and reprinted in the 1950 YEAR BOOK, page 483. The report deals with 41,046 patients who underwent treatment. Of this number, 31.8 per cent were alive with no evidence of disease after five years, 1.5 per cent were alive with carcinoma present, 62.4 per cent had died of carcinoma, 1.9 per cent had been lost sight of, and 2.4 per cent had died of an intercurrent disease.

The five year results of treatment calculated for each of the four stages follow. Relative apparent recovery rate of stage I was 61.0 per cent, of stage II 40.6 per cent, of stage III 22.0 per cent and of stage IV 6.5 per cent. Relative apparent cure recovery rate for the entire 41,046 was 31.8 per cent. This is the highest rate recorded in any of the six reports. The improvement in recovery rate from 26.7 in Volume II to 31.8 per cent is due both to a reduced proportion of advanced cases and to an increased apparent recovery rate in stages I, II and IV.

For the first time in these reports surgical cases have been included. Only 215 such cases relating to the period 1939-43 are presented and the conclusion drawn from the results is: "It is obvious that figures . . . do not justify conclusions being drawn as to the value of a more extensive use of surgery." Of course, since 1943 hundreds more patients have been operated on, and with improvements in operative technics and anesthesia, use of antibiotics and for other reasons, the results of surgery have been considerably improved, so perhaps the next report will be more optimistic about the results of surgery.—Ed.]

**Total Uterine Sampling: Proposed Aid in Early Cytologic Detection of Cancer** is presented by Joseph Bernard Doyle<sup>3</sup>

(3) New England J. Med. 243:121-124, July 27, 1950.

(Tufts College). With this simple, inexpensive method substantial samplings of exfoliative endometrium and scraped endocervical and stratocolumnar-junction tissue are obtained in the office at the onset of menstruation.

TECHNIC.—The cervical spoon of Lucite is designed to fit the posterior vaginal fornix beneath the cervix. It can be anchored to the perineum with cellophane tape. With the labia spread by one hand, the spoon is inserted by pressure on its shaft beneath the cervix with the other index finger (Fig. 115). The spoon may be

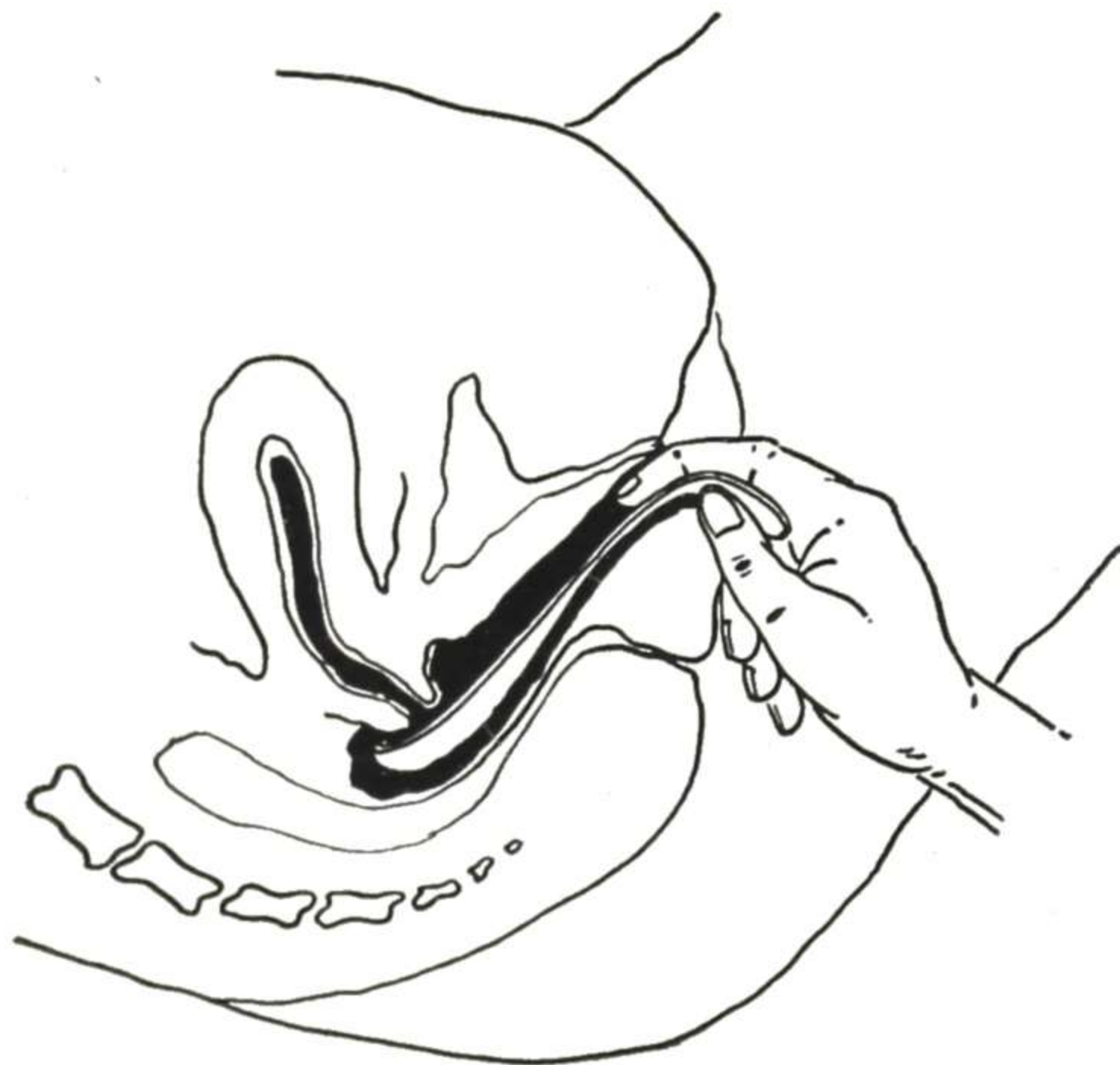


Fig. 115.—Insertion of spoon in cervical canal. (Courtesy of Doyle, J. B.: *New England J. Med.* 243:121-124, July 27, 1950.)

worn through the day after insertion of a tampon in the introitus to absorb menstrual fluid. In the 4 cc. cup of the spoon endometrial exfoliative fragments will collect without necrosis from vaginal acidity. Tampon may be changed hourly and endometrial fragments swirled off in physiologic saline. After standing 10 minutes the supernatant saline solution with suspended red cells is decanted. Residual endometrial fragments are then deposited in 10 per cent Formalin for the usual cell block studies. When blood loss is minimal, fragments can be placed directly in Formalin. Ample cytologic samples may be obtained during the first 12-24 hours of flow. In the office, scrapings can be made of endocervical areas and squamocolumnar junction, and scrapings swirled from the spoon directly into Formalin or smeared on glass slides.

In the postmenopausal patient with dubious smears and biopsies, continuous overnight collection is possible. The

spoon's contents are immersed directly in Formalin for cell block study. Positive cervical or vaginal smear, however, does not constitute a diagnosis of cancer. Surface biopsy as well as endocervical and endometrial curettage must supplement smears before final diagnosis and therapy.

[Doyle's spoon should permit one to obtain far more cytologic material than scrapings for the detection of cancer cells. Of course, both scrapings and Doyle's spoon can be used together.

Kulcsar (*Am. J. Clin. Path.* 20:958, October, 1950) found that almost 50 per cent of cases of early stage of carcinoma of the cervix may be missed by the vaginal pool smear technic. He studied 100 vaginal pool smears and 100 cervical surface scrapings taken concurrently from 24 patients with intraepithelial carcinoma. Neoplastic cells were not found in 45 per cent of the vaginal smears and in 7 per cent of the cervical smears. Only 10 per cent of the vaginal smears contained more than 4 atypical cells or groups of cells, in contrast with 74 per cent of the cervical smears. Therefore, the smears of cervical surface scrapings appear to give a better chance of discovering early carcinoma in this region.

Maloney (*Am. J. Obst. & Gynec.* 60:533, September, 1950) followed up 13 patients with stages I and II carcinoma of the cervix with vaginal smears throughout radiologic treatment. In all cases in which the initial smears were positive, correlation existed with the clinical course. In 41 cases of stages III and IV, when a positive initial diagnosis of carcinoma was made by this method, correlation existed in 66 per cent of the cases. Based on this small number, there is some evidence that vaginal smears have value in assessing the radiosensitivity of a tumor of the cervix. If this is so, tumors which show evidence of radioresistance early in radiologic treatment could be selected and treated surgically.

Gladstone and Selzer (*Am. J. Surg.* 81:307, March, 1951) used sponge biopsy, which was devised for diagnosis of cancer in inaccessible sites, in a study of the cervix uteri of 641 patients. Cancer was found in 16, in 7 of which there was complete absence of signs and symptoms of cancer. Sponge biopsy of the cervix indicated cancer in all cases in which cancer was demonstrated in specimens obtained subsequently by surgical biopsy or at operation.—Ed.]

**Exfoliative Dyskaryotic Cells Associated with Atypical Cervical Lesions.** Louis S. Lapid and Morris A. Goldberger<sup>4</sup> (Mount Sinai Hosp., New York City) attempted to evaluate the significance of such cells in a vaginal smear with regard to atypical cervical lesions and cervical carcinoma. The term dyskaryosis refers to those nuclear changes which are sufficient atypical to suggest malignant origin. Superficial dyskaryosis refers to atypical cells derived from the outer layers of squamous epithelium. Intermediate or navicular dyskaryosis and parabasal cell dyskaryosis are the terms used when the abnormal cells are derived from deeper epithelial layers. Such cells may show such nuclear abnormalities as enlarge-

(4) *Am. J. Obst. & Gynec.* 61:1324-1328, June, 1951.

ment, hyperchromatism and multiple nuclei. Perinuclear vacuoles, cornification and acidophilic staining have been noted in such cells.

Of 2,000 patients studied by vaginal smears, 12 gave dyskaryotic smears but not in conjunction with cancer. Over 9-48 months, one or more cervical biopsies were done in these and all revealed a uniform microscopic lesion, characterized by varying degrees of cellular proliferation, anaplasia, cell atypism, slight and localized basal cell hyperactivity with intact basement membrane, and occasional mitoses. Cellular stratification was occasionally partially disrupted.

The minimal criteria necessary for diagnosis of intraepithelial carcinoma were not present, nor was invasiveness noted. The histologic changes, however, were definitely more than normal variations. In one case in which the original cervical biopsy report was greatly increased cellular proliferation without mitosis, a positive smear was found two years later. Cervical biopsy at this time revealed immature squamous cell carcinoma. In two others the original dyskaryotic smears were associated with biopsies revealing hyperchromatic basal cells and cellular atypism with mitosis. Over 1½ years, these changes proved reversible, repeated smears and biopsy specimens being normal. In the remaining nine cases no change was noted in subsequent smears or biopsy specimens. Thus, nine cases remained unchanged, two reversed to normal and one progressed to unequivocal carcinoma.

Because of a relatively short follow-up, 556 consecutive cervical biopsy specimens taken 4-10 years ago were re-studied. Thirteen showed the same degree of atypism as described. Investigation revealed that three of these women had died of unrelated causes, nine had remained well and in one squamous cell carcinoma of the cervix had developed six years after initial biopsy.

Whether finding of a dyskaryotic smear and an atypical biopsy specimen is related to future development of a true malignancy is speculative. An 8 per cent incidence, two and six years after biopsy, is suggestive. Repeated smears and biopsies are certainly indicated.

**Contribution to Study of Etiology and Prevention of Cancer of Cervix of Uterus.** Postulating that, if cervicitis is the basis of cervical cancer, this cancer should not exist among

women such as nuns whose social state and mode of life protect them from the usual causes of cervicitis or chronic irritative lesions. Fabien Gagnon<sup>5</sup> (Laval Univ., Quebec) surveyed medical files on an annual average of 13,000 nuns covering 20 years. He found 14 cases of carcinoma of the corpus uteri recorded and not a single case of carcinoma of the cervix uteri, whereas Meigs' index of frequency for general civilian population was 1 case of cancer of the corpus uteri to every 6 of cancer of the cervix uteri. A similar survey of pathologic records from numerous laboratories disclosed 19 cases of carcinoma of the corpus uteri in nuns and only 3 of carcinoma of the cervix uteri—also the reverse of what would be expected on the basis of Meigs' index of frequency.

Gagnon concludes that chronic cervicitis is important in the genesis of carcinoma of the cervix although he does not minimize other contributory factors such as heredity, acquired constitutional states, viruses, enzymes, deficiencies and biochemical and hormonal influences. Furthermore, in over 4,000 patients with cervicitis treated systematically in 17 years, Gagnon has not seen a carcinoma of the cervix. It is therefore recommended that cervicitis be systematically treated until eradicated as an efficient method of bringing about the disappearance of cancer of the cervix.

McKelvey, in discussion, agreed that the findings were startling but felt that the conclusion drawn was not fully warranted since (1) no one has yet demonstrated the transitional stages between erosion healing and cancer and (2) the absence of squamous cell carcinoma of the cervix in Jewish women is not explained.

[It is startling to note complete absence of carcinoma of the cervix in nuns. Gagnon attributes this to absence of cervicitis, just as he does the absence of carcinoma in his 4,000 patients treated for cervicitis. I do not believe that the absence of cancer of the cervix in nuns or after treatment of the cervix is proof that cervicitis is the cause of cancer. It is well known that cancer of the cervix is rare among Jewish women and they surely have as much cervicitis as other women.]

Lombard and Potter (Cancer 3:960, November, 1950) emphasize that the strong correlation between cancer of the cervix and marriage before age 20, divorce or separation at any age, unrepaired lacerations, birth of the last child before the woman is 25 and syphilis indicates that these variables have etiologic significance.—Ed.]

**Coning Biopsy in Detection of Early Cancer of Cervix: Survey of 500 Normal Women over 35, selected from a gen-**

(5) Am. J. Obst. & Gynec. 60:516-522, September, 1950.

eral hospital diagnostic clinic by exclusion of those with any menstrual abnormality, history of abnormal uterine bleeding or any lesion suggestive of cancer on pelvic examination, is reported by S. B. Gusberg<sup>6</sup> (Columbia Univ.).

Since the trigger site of most early intraepithelial cervical carcinoma is the histologic external os, biopsy of the squa-

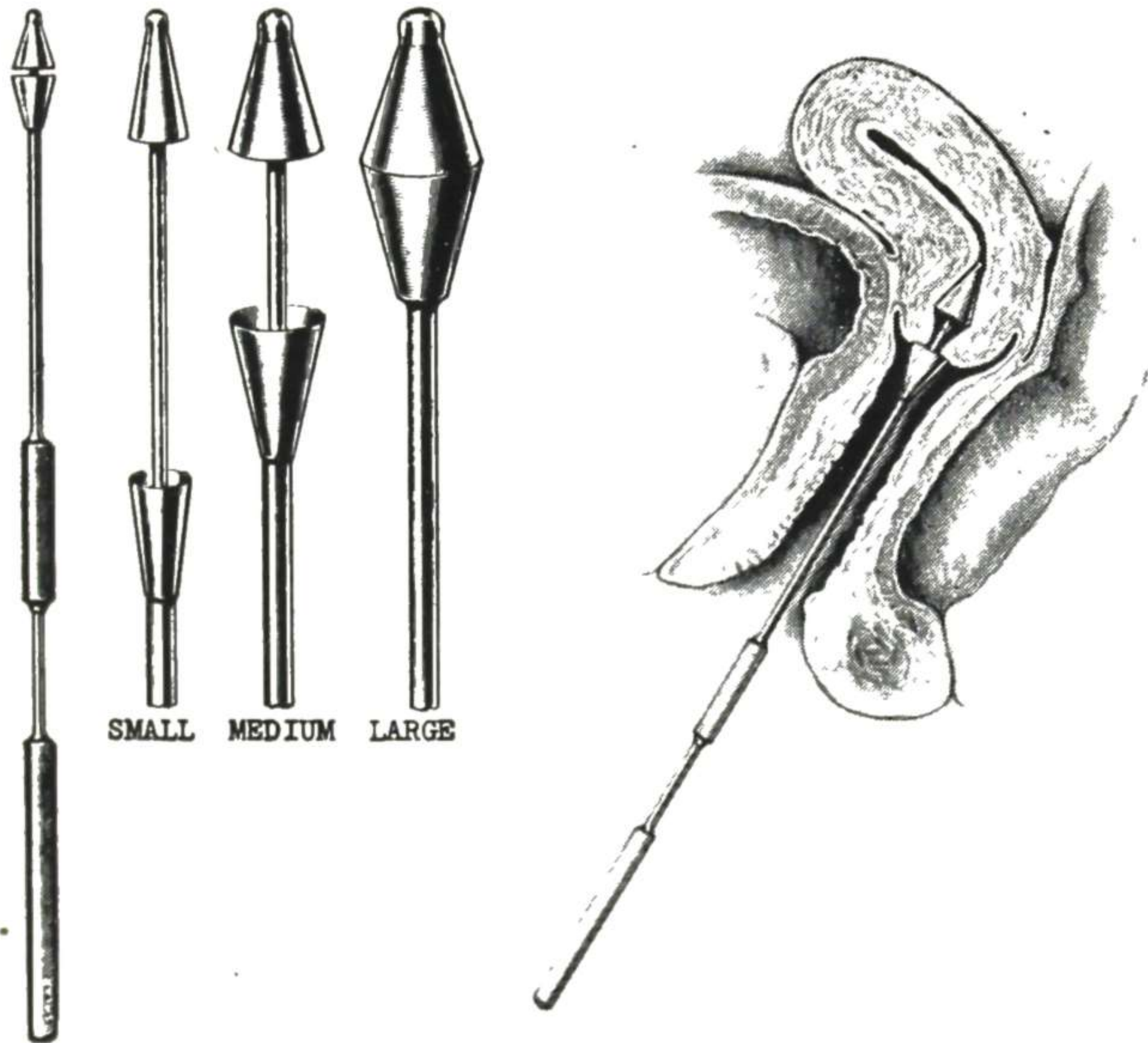


Fig. 116 (left).—Endocervical biopsy curets. Note open and closed positions of cutting cups.

Fig. 117 (right).—Curet in cervical canal.

(Courtesy of Gusberg, S. B.: *Am. J. Obst. & Gynec.* 61:276-288, February, 1951.)

mous-columnar junction is vital to early detection. Cytologic study of cervical smears helps bring early cases under surveillance, but therapy should not be undertaken until biopsy specimens have been examined histologically to learn the exact nature of the lesion and its geographic limits. Punch biopsy technics are inadequate for obtaining a general sample of the normal-appearing cervix, and cervical scrapers or scalpels seem to obtain samples which lie midway between smear and biopsy. An anesthetic agent is necessary to obtain

(6) *Am. J. Obst. & Gynec.* 61:276-288, February, 1951.

a proper segment by these methods, which limits their use as screening or outpatient procedures.

With the endocervical coning biopsy curet (Figs. 116 and 117), a circumferential sample can be taken from the squamous-columnar junction of the relatively normal cervix without a well defined lesion. An anesthetic agent is unnecessary and the procedure may be done on an outpatient basis. Undue bleeding is rare; however, it can be controlled by use of a gauze tampon or pledget of oxidized cellulose gauze.

Of the 500 women, 10 were found to have intraepithelial cancer and 10 basal cell hyperplasia. No sections with debatable minimal disorganization such as is occasionally seen in squamous metaplasia were included in the results reported. Cervical cancer detection rate was 2 per cent. This rate is lower than that obtained by multiple sectioning of apparently benign hysterectomy specimens, but the present concept that these lesions are truly malignant necessitates adjusting diagnostic methods to prevent these lesions from progressing to a stage where treatment is complex and often fails.

Gusberg concluded that this method, as a histologic corollary to cytologic technics and as a primary scouting method, may be clinically useful and also teach more about the evolution of intraepithelial cervical carcinoma.

**Validity of Vaginal Smear Diagnosis in Carcinoma in Situ of Cervix: Report of 60 Cases**, found during a 3½ year study which included examination of 11,871 vaginal smears from 9,748 gynecologic patients, is presented by Rachel R. Achenbach, Robert E. Johnstone and Arthur T. Hertig<sup>7</sup> (Brookline, Mass.). This study was made to determine the ability of the vaginal smear to reveal early malignancy, technical accuracy in discovering malignant cells and usefulness of the technic in an outpatient clinic. Therefore in 42 cases the smear was examined before histologic diagnosis was made, and in 18 cases, although histologic diagnosis preceded obtaining of the initial smear, smears were examined without knowledge of the diagnosis whenever possible.

To determine the highest possible accuracy of cytologic diagnoses, all smears originally diagnosed as benign were reviewed and tissue diagnoses were correlated with initial cytologic diagnoses. Results indicated that routine examina-

(7) Am. J. Obst. & Gynec. 61:385-392, February, 1951.

tion of smears gave a diagnosis of malignancy in 42 cases, but re-examination of the 18 false negative smears revealed malignant cells in 7 others.

By the first smear examination, malignancy was diagnosed in 54 per cent of the cases which had only surface changes and in 81 per cent of those in which tumor extended into the glands. In seven cases, repeated examination did not reveal malignant cells.

Of the 60 cases, 12 were unsuspected clinically and were thus discovered by vaginal smears. In 11, complete hysterectomy or trachelectomy was eventually done. In the presence of a doubtful vaginal smear, or whenever possible, smears of endocervical or endometrial secretions should also be studied.

As a routine screening procedure and as a follow-up method for patients with questionable early malignancy of the cervix, vaginal smears were useful. With few exceptions, presence of malignant cells indicates carcinoma in the genital tract. However a positive smear alone does not always justify definitive cancer treatment. Ten patients showed disappearance of malignant cells from vaginal smears after cervical biopsy, cauterization or conization, or during pregnancy.

Because simple procedures were apparently curative in this series, because false positive diagnoses are possible and because this diagnostic method is still being evaluated in regard to early lesions, the authors believe it is unwise and therapeutically unnecessary to destroy such early tumors before their extent and nature are established. A positive smear should never be considered conclusive evidence of disease, but every effort should be made to confirm the diagnosis and to locate the lesion before the patient is treated.

**Studies of Early Uterine Carcinomas Discovered by Cytologic Examination of Vaginal Contents** are reported by Edward L. Burns, Walter H. Hartung, Jr., and Elizabeth Brittingham<sup>8</sup> (Toledo, O.). The Toledo program for early detection of uterine cancer embodies an area-wide plan for pelvic and cytologic examination of the vaginal contents of every woman at regular intervals of six months to one year. The plan gives continuity to the detection program, a primary requirement for early detection.

Of 6,437 women surveyed at one hospital, 74 (1.14 per

(8) Arch. Path. 50:699-708, December, 1950.



cent) were proved to have uterine carcinoma. Age range was 26-81, average 48. There were 20 adenocarcinomas of the fundus, and 54 squamous cell carcinomas of the cervix, all demonstrated by histologic examination. There were 36 known errors in examination of the 9,205 smears made from the 6,437 patients. Eighteen were false negative diagnoses, of which 10 were fundal and 8 cervical carcinoma. False negative diagnoses were more common in cases of advanced carcinoma, suggesting that ulcerations and infection of late stages may alter or destroy neoplastic cells.

Of the 74 women shown to have uterine carcinoma, 22 were not suspected of having it from clinical symptoms or results of pelvic examination. Age range of patients with unsuspected fundus carcinoma was 49-71, average 61, with peak between 70 and 79. In the "suspected" cases, age range was 48-81, average 66.3, with peak incidence between 60 and 69. In the "unsuspected" cases of cervical carcinoma, age range was 26-61, average 39.8, with peak incidence between 30 and 39. In "suspected" cases, age range was 27-73, average 50.4, with peak incidence between 40 and 49.

It is possible that early carcinoma of the cervix for a time grows slowly and perhaps remains localized to the epithelium. In three cases, neoplastic cells were found in smears several months before carcinoma could be histologically demonstrated.

Histologic studies on nine uteri removed for early carcinoma of the cervix showed, in some, multiple widely separated foci of atypical hyperplasia of the stratified squamous epithelium, suggesting that generalized disturbances of growth processes may take place in the cervix before neoplasia develops. Whether invasion proceeds from many or few such areas of altered epithelium is still to be studied. These observations suggest that carcinoma may develop in the vaginal cuff after total hysterectomy, thereby emphasizing the need for follow-up.

**Subclinical Carcinoma of Cervix Uteri: Evaluation of Endocervical Curettage in Detection and Differential Diagnosis of Preinvasive and Covert Invasive Carcinoma.** Edgar R. Pund and Joe M. Echols<sup>9</sup> (Univ. of Georgia) state that when cells suggestive of cancer are found in smears, diagnosis must

(9) J. A. M. A. 143:1226-1228, Aug. 5, 1950.

be confirmed by histologic study. Multiple biopsies of the squamocolumnar junction are necessary in order not to miss a small focus. Preinvasive should be differentiated from invasive carcinoma; the latter may be surrounded by preinvasive borders. Because invasion often begins in the endocervical canal, cervical biopsies may fail to disclose it. Histologic study of endocervical curettings minimizes the possibility of false diagnosis of preinvasive cancer.

In 71 cases of subclinical carcinoma, endocervical curettage was performed. In 44 of 55 patients who also had cervical biopsies, neoplasms were found in the biopsied specimens. Four patients with negative biopsies received radium treatment; in two of five subjected to hysterectomy, remains of preinvasive carcinoma were found.

In 25 (16 without biopsy and 9 with negative biopsies) of the 71 patients diagnosis was made by examination of endocervical curettings; 13 displayed preinvasive carcinoma and 3, invasive carcinoma. Diagnosis of preinvasive carcinoma was confirmed on hysterectomy in six of seven patients; in the seventh superficial invasion had occurred. Diagnosis of invasive carcinoma was confirmed in two; the third was treated with radium. In two patients diagnosis was missed both by biopsy and curettage.

In 25 patients, cancer was observed in both the biopsy specimen and curettings. Biopsies revealed no evidence of invasion, but slight invasion was observed in two specimens of endocervical scrapings. Hysterectomy was performed on all. Carcinoma was preinvasive in 21 of 23 cases diagnosed as such and invasive in 2 diagnosed invasive; in 2 others slight invasion was observed. In 19 patients with positive smears, preinvasive carcinoma was found in biopsy specimens but not in curettings. Invasion was not seen in specimens obtained at hysterectomy.

In 272 cases of preinvasive carcinoma of the cervix, diagnosis was made from cervical biopsy and curettage in 162 and from routine examination of surgically removed uteri in 110. Routine study of exfoliative cells should be made before hysterectomy. Conservative methods of therapy, such as cautery conization, are recommended in patients under 35 when invasion has been excluded by multiple cervical biopsies and endocervical curettage.

**Carcinoma of Cervix in Jewish Women** was compared with its frequency in non-Jewish women by Irwin Weiner, Louis Burke and Morris A. Goldberger<sup>1</sup> (Mount Sinai Hosp., New York City). From Jan. 1, 1928 to Dec. 31, 1948, 323 patients with cervical carcinoma were treated, 93 per cent of whom had squamous cell carcinoma and 7 per cent adenocarcinoma. Twenty-five per cent were Jewish, 95 per cent having squamous cell carcinoma. The 75 per cent classified as non-Jewish included 14 from whom a definite statement of religion was not obtainable.

In eight Jewish patients, cervical carcinoma developed after subtotal hysterectomy; seven had squamous cell carcinoma, which appeared in six patients four or more years after surgery. One had squamous cell carcinoma six months after hysterectomy and one adenocarcinoma two years after operation.

During this period, 98,996 women were admitted to all services. An estimated 58.5 per cent were Jewish. Incidence of cervical carcinoma was therefore 0.86/1,000 Jewish women and 4.6/1,000 non-Jewish women. Thus, cervical carcinoma was about a fifth as common in Jewish as in non-Jewish women.

The incidence found in this study is similar to that estimated by Davidsohn in 1939 at Mount Sinai Hospital, Chicago, whereas Rubin, on the basis of 85 cases in 1909-18, reported an incidence 12.5 times greater in non-Jewish than in Jewish women at Mount Sinai Hospital, New York City. These figures seem to indicate an increasing occurrence of cervical carcinoma in Jewish women. This apparently supports the theory that limitation of cohabitation during menstruation as imposed by Mosaic laws is an important factor in production of cervical carcinoma since Jewish women today do not adhere as meticulously to Mosaic laws as they did at the turn of the century. Davidsohn believes that the difference in incidence may be explained by the practice of circumcision, a theory which is supported by demonstration of the carcinogenic action of smegma. Hereditary immunity probably plays a role.

[Most likely the relative infrequency of carcinoma of the cervix in Jewish women is related to circumcision, because carcinoma of the peni

(1) Am. J. Obst. & Gynec. 61:418-422, February, 1951.

occurs almost exclusively in uncircumcised males. Horse smegma has produced carcinoma in mice (see the 1947 YEAR BOOK, p. 484).—Ed.]

**Carcinoma in Situ of Cervix: Survey of Treatment in United States and Canada** was made by means of questionnaires sent to 79 medical schools by Randolph H. Hoge<sup>2</sup> (Med. College of Virginia). The previous literature contains no concise evaluation of the indicated treatment for intra-epithelial cancer of the cervix. Suggested therapy has ranged from cauterization to radical panhysterectomy.

Replies on the questionnaire were received from 77 schools which indicated their preferred and alternate methods from the following selection: cauterization, conization or amputation of the cervix, simple or radical total hysterectomy, radium alone or with x-rays, or other procedures.

Cauterization was checked by two schools as being used in conjunction with other methods. Conization was used exclusively in two schools and in conjunction with other procedures in three others. Amputation was the sole treatment at one and was used with other forms of therapy at eight. Simple total hysterectomy was used at 36 schools, being the only procedure at 14. Radical panhysterectomy was used at 31 institutions, exclusively at 13. Two schools used radium but not as a sole procedure. Radium and x-rays were used at 18 schools, being the only treatment at 12. Surgery and irradiation were combined at six schools, four using no other treatment. One school recognized none of the above but chose to follow with repeated biopsies and Papanicolaou smears. In 14 schools the more radical procedures were elected in the older patients. Hoge prefers total hysterectomy, with preservation of ovarian function in the young but points out that this treatment is inadequate in invading carcinoma.

[Hoge (Surg., Gynec. & Obst. 89:521, December, 1949) reviewed the literature on treatment of carcinoma of the cervix and also polled the 79 accredited four-year medical schools in the United States and Canada concerning treatment and received replies from 77. Eighty-two per cent of the schools used the League of Nations Classification exclusively or in combination with others and 16 per cent used the Schmitz classification. As usual treatment of stage I, 66 per cent of the schools used radiation alone, 19.5 per cent combined radiation and surgery, 1.3 per cent used surgery alone and 13 per cent listed multiple methods. For stage II, the routine was radiation alone by 90.9 per cent and a combination by 9.1 per cent. For stages III and IV, radiation alone was the usual treatment in all schools. Therefore irradiation is the most widely used method in each and all stages. However, surgery is being used increasingly in the

(2) Obst. & Gynec. Surv. 5:621-628, October, 1950.

early stages, especially in combination with irradiation. Surgery alone is little used except in highly selected early cases or for special study.—Ed.]

**Technic of Radical Hysterectomy for Carcinoma of Cervix**, described by Gray H. Twombly<sup>3</sup> (Columbia Univ.), was evolved with the intent constantly in mind of (1) gentle, complete dissection of lymph nodes draining the cervix, (2) minimum of cutting across of lymphatics or direct extensions from the tumor toward the nodes, (3) minimum of rough squeezing and kneading of the cancer. Thoroughness is most important, four hours or more is not too long to do a proper job. Ideally, radical surgery is done in the thin patient with a stage I or II lesion (League of Nations). Obesity is a contraindication, although the difficulties of inadequate exposure may be overcome somewhat by a transverse incision cutting rectus muscles just above their insertions. Though old age in itself is not a serious contraindication, severe hypertension or history of cardiac decompensation is a hazard to radical surgery.

Most important is preoperative study of the genitourinary tract, first by cystoscopy and pelvic examination with the cystoscope in the bladder and then by intravenous pyelography. Preoperative cystometric examination is valuable in dealing with the commonest postoperative complication, a difficulty in voiding and large residual urine. Nonprotein nitrogen and blood urea nitrogen determinations should be done. Usually, simple rectal palpation indicates posterior extent of tumor invasion. Other studies include chest x-ray, ECG, prothrombin time, blood count and determination of blood volume. In patients with normal blood count and hemoglobin but greatly reduced blood volume, use of multiple transfusions have made it possible to restore red cell mass to normal levels before surgery. A red cell mass of 34 ml./kg. is considered normal for most women with cervical cancer.

**TECHNIC.**—Good lighting and exposure and proper anesthesia are essential. Continuous spinal anesthesia, supplemented by pentothal,<sup>®</sup> is most likely to give proper relaxation throughout operation. A moderate Trendelenburg position is recommended. A midline incision is made from the symphysis to a few centimeters above the umbilicus; skin, fat, fascia and muscles are separated down to the symphysis. In the obese patient, a transverse incision through all layers improves exposure. The rectus fascia is divided as in the classic Pfannenstiel incision, but rectus muscles are cut from their insertions at the pubic rami. Wound edges are held apart with a

(3) Cancer 3:975-991, November, 1950.

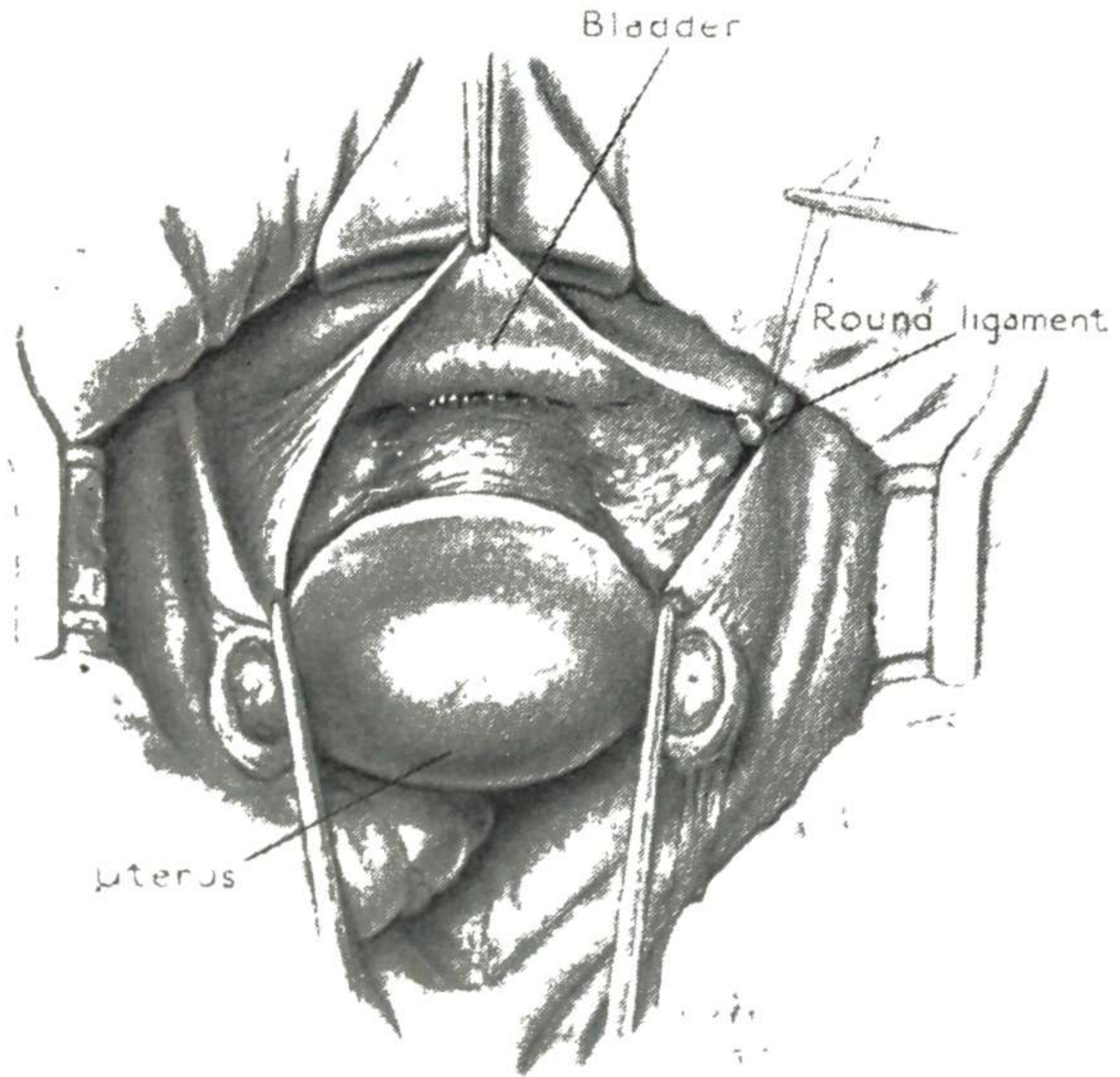
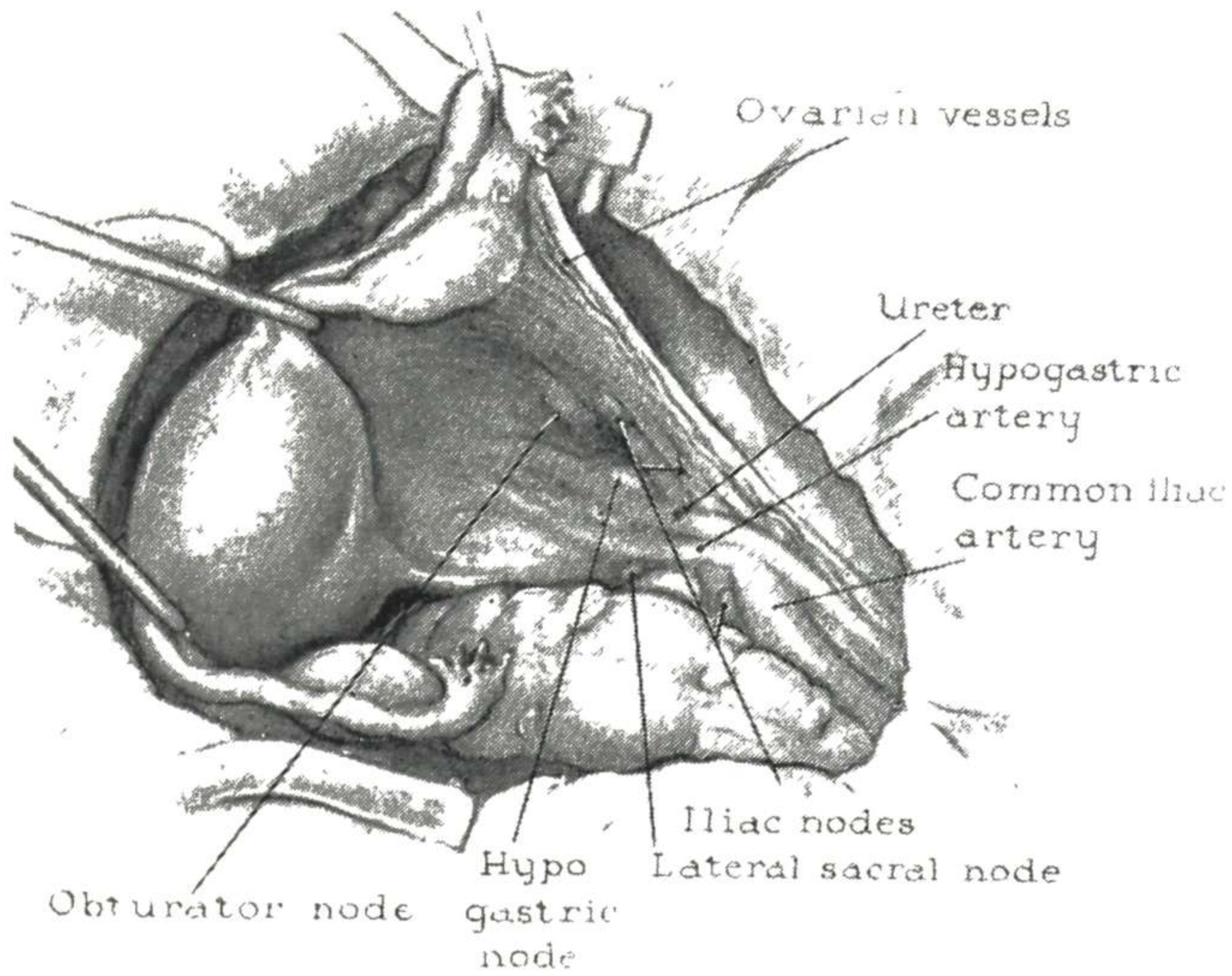
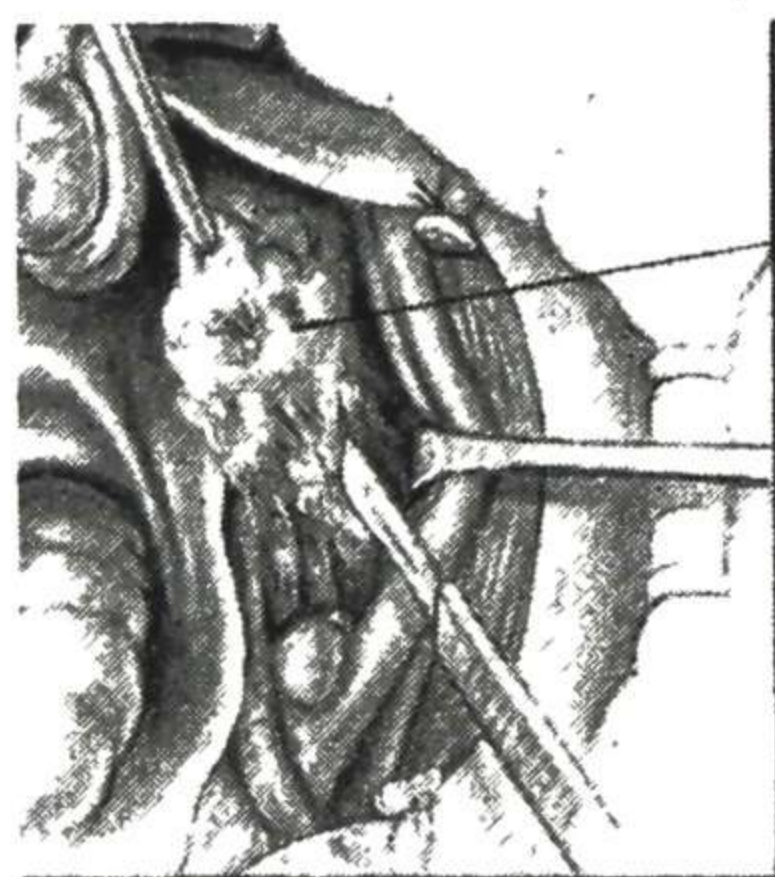
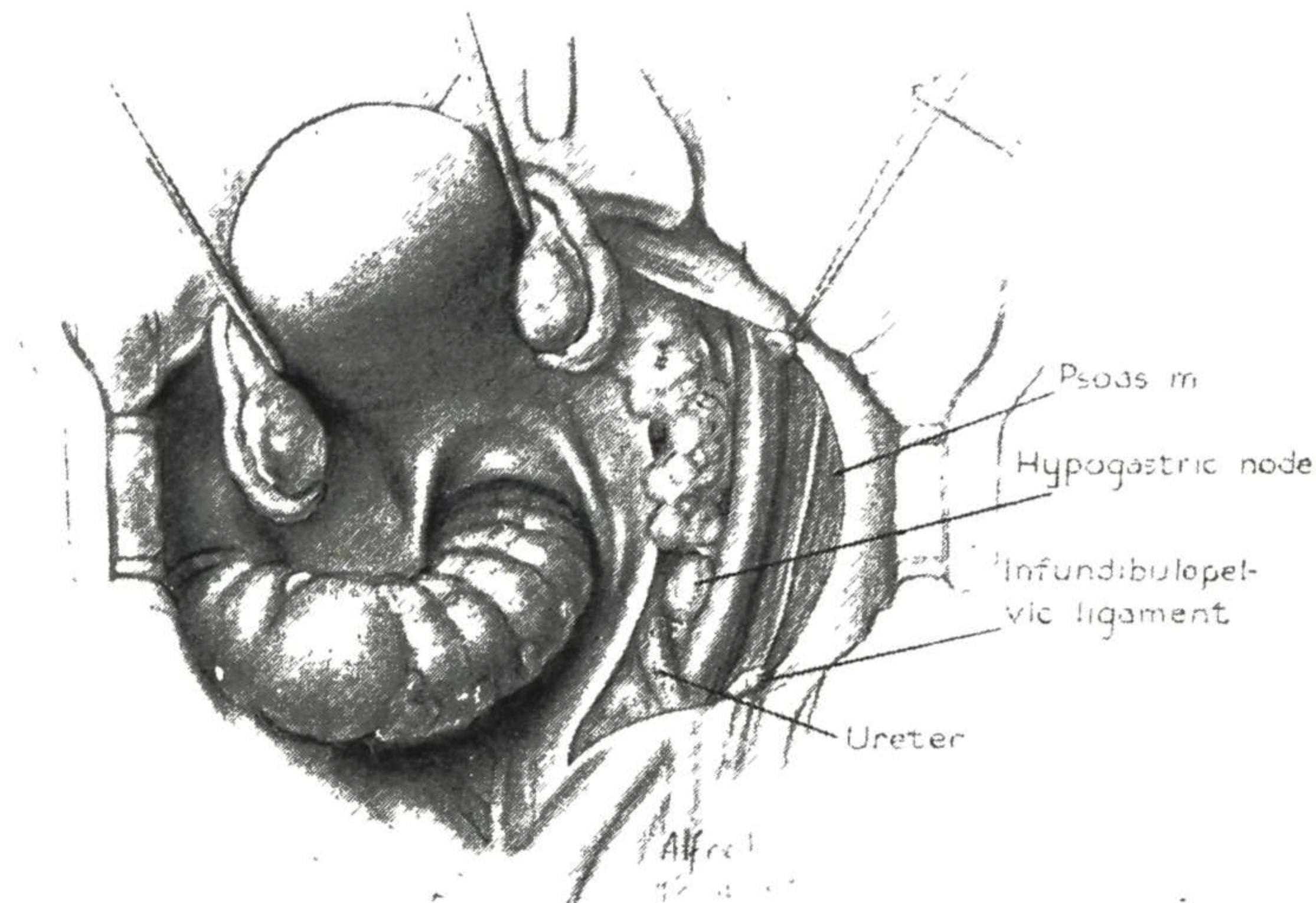


Fig. 118 (top).—Pelvic organs viewed from patient's left side at start of radical hysterectomy. Uterus is drawn forward and out of pelvis by straight clamps placed across round ligaments and tubes.  
 Fig. 119 (bottom).—Peritoneum cut between round ligaments and cervix and trigone separated by blunt dissection. Carcinoma infiltrating base of bladder precludes carrying the procedure further.  
 (Courtesy of Twombly, G. H.: *Cancer* 3:975-991, November, 1950.)



Obturator nodes

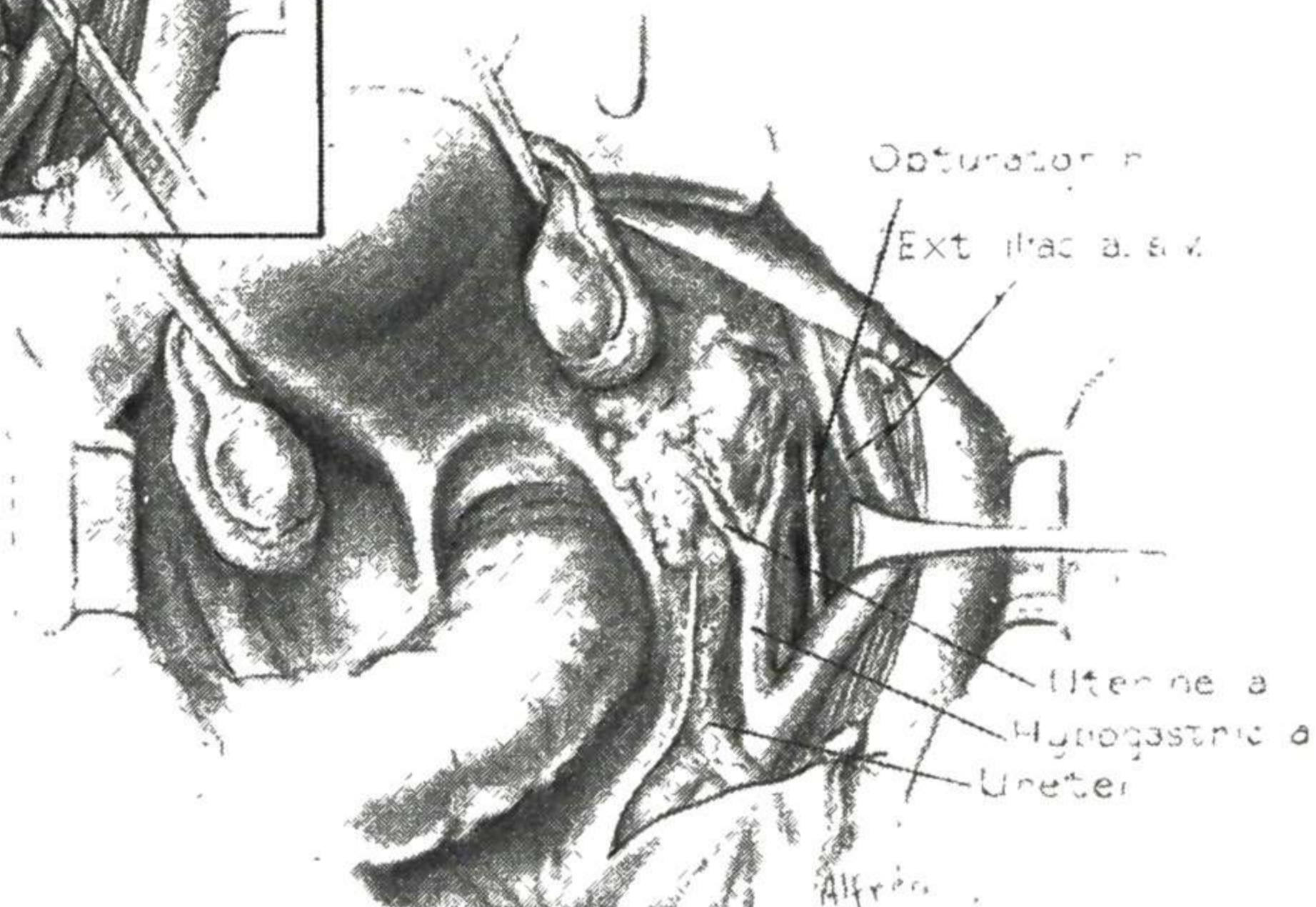


Fig. 120 (top).—After ligation of infundibulopelvic ligament, peritoneum between it and round ligament is cut to expose areolar and fatty tissue and lymph nodes and these are dissected off the psoas muscle and external iliac artery.

Fig. 121 (bottom).—Inset shows dissection of nodes, fat and areolar tissue around external iliac vessels, exposing contents of obturator fossa and the hypogastric node. Then obturator fossa is dissected out completely, exposing obturator nerve; the hypogastric nerve is dissected free, exposing hypogastric and uterine

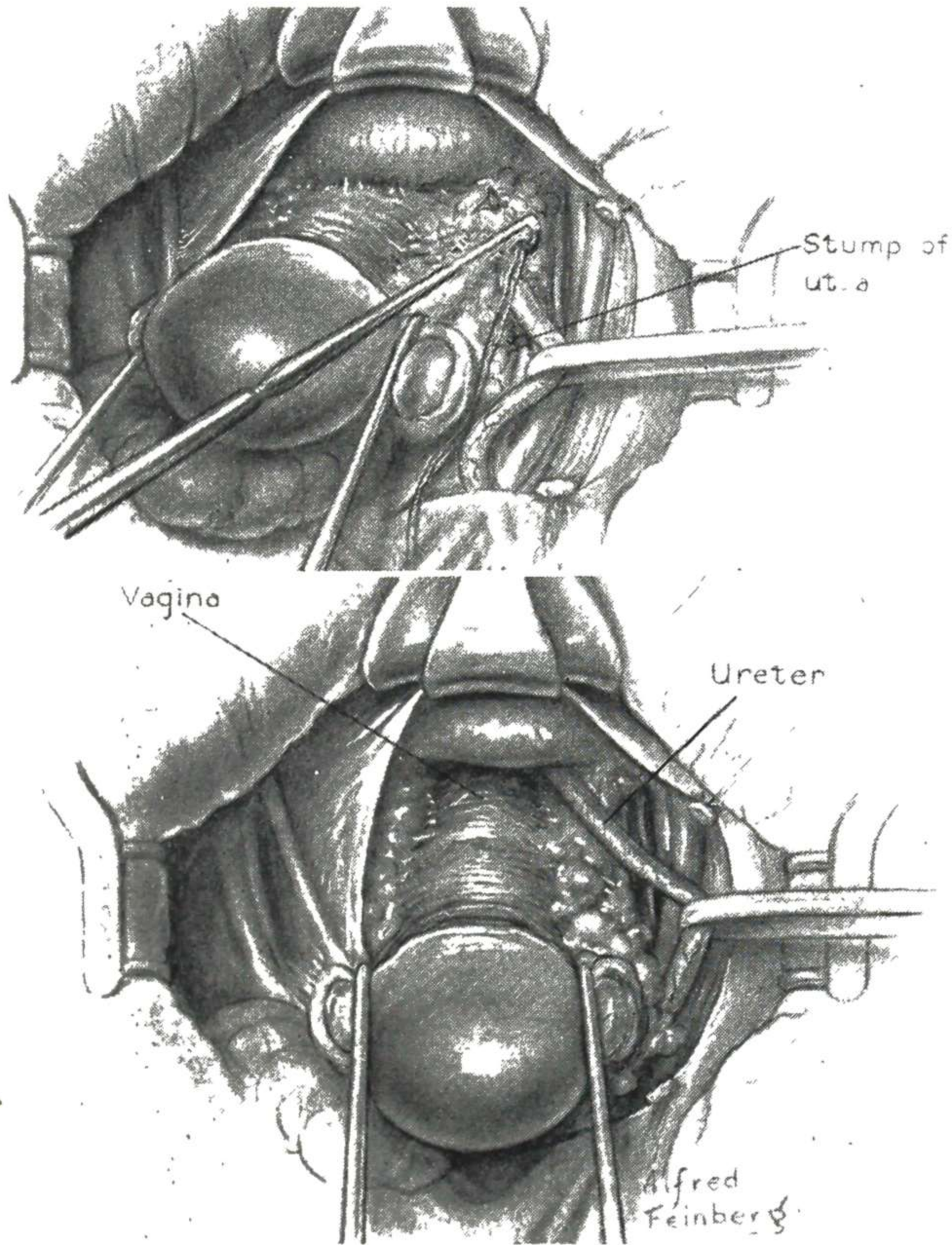


Fig. 122 (top).—Middle third of ureter has been freed and retracted with Penrose drain. Uterine artery has been ligated and cut and uterine veins are being ligated.

Fig. 123 (bottom).—Ureter freed completely from 3 cm. below pelvic brim to trigone. Parametrium and pelvic nodes are seen attached to site of uterus.

(Courtesy of Twombly, G. H.: *Cancer* 3:975-991, November, 1950.)

self-retaining retractor and covered with saline-soaked gauze pads (Fig. 118). Large wet abdominal gauze pads, rolled to form cylinders  $6 \times 2\frac{1}{2}$  in., are placed under the abdominal wall, one transversely in the midline to hold up the small bowel, one to the right to push up the cecum and one on the left behind which are packed any redundant loops of sigmoid.

With operator at patient's left, the right pelvis is dissected first. After palpation of uterus and pelvic walls, the uterus is picked up

arteries. All nodes on right pelvic wall are gently dissected free and reflected toward midline. Ureter is adherent to medial leaf of peritoneum.

(Courtesy of Twombly, G. H.: *Cancer* 3:975-991, November, 1950.)



with straight Péan hysterectomy clamps. The bladder flap of peritoneum is then cut across from side to side (Fig. 119). By gentle blunt dissection, cervix and vagina are separated from underside of the bladder, the forefinger pushed down to about 2 cm. below the cervix in the midline. If no carcinoma is found, the right round ligament is ligated close to the abdominal wall and cut. The infundibulopelvic ligament is picked up where it crosses the pelvic brim and doubly ligated and cut; care is taken to avoid the ureter. The peritoneum between the infundibular and round ligaments is incised, exposing fat, lymph nodes and areolar tissue over the right external iliac artery (Fig. 120). These structures are dissected as a sheet starting from the lateral side to the midline, exposing psoas muscle and the bare arterial wall. Further dissection around the artery exposes the external iliac vein and base of the hypogastric artery; the hypogastric node, frequently found nestled in bifurcation of common iliac artery, somewhat medial to the vein (Fig. 121), should be removed by careful dissection. Clean dissection is made from the round ligament to bifurcation of the common iliac artery, taking enlarged nodes lying just above the pelvic brim along the artery. Dissection is adequate if all iliac nodes below the bifurcation, hypogastric nodes and nodes in the obturator fossa are removed cleanly and en bloc (Fig. 121).

The uterine artery is freed at its origin from the hypogastric, doubly ligated with 00 silk and cut. A clamp on the distal cut end serves as both guide and retractor in subsequent dissection of the ureter. Catheterization of ureters is unnecessary. Any two of the three small arteries which supply the ureter may be safely cut. The ureter should never be picked up with forceps; tension may be supplied by picking up the areolar tissue around it or by gentle retraction with a piece of empty Penrose rubber tubing. The ureter must be carefully exposed and freed from its bed to where it disappears into the trigone. Dissection from the uterine veins is best done by passing a threaded ligature carrier along the course of the ureter a little at a time and cutting between the suture and a clamp placed on the uterine side (Fig. 122). When all lymph nodes have been dissected from the right pelvic wall and the ureter freed (Fig. 123), the same procedure is carried out on the other side.

With both sides of the pelvis completely dissected, the uterus is drawn upward and forward, stretching the peritoneum. Peritoneal incision is made in the extreme bottom of the posterior culdesac well below the uterosacral ligaments. If the peritoneum is incised where rectum and vagina meet, the two may be separated bloodlessly by gentle blunt dissection. Separation for 5-6 cm. in the midline reveals strong fibrous bands holding the cervix in the pelvis and surrounding the rectum on either side. These uterosacral ligaments are clamped (Fig. 125) and severed, freeing the uterus, cervix and vagina which can be pulled forward and up out of the pelvis. Lateral to the uterosacral ligaments lie the pararectal spaces; anterior to these, lie structures known as cardinal or Mackenrodt's

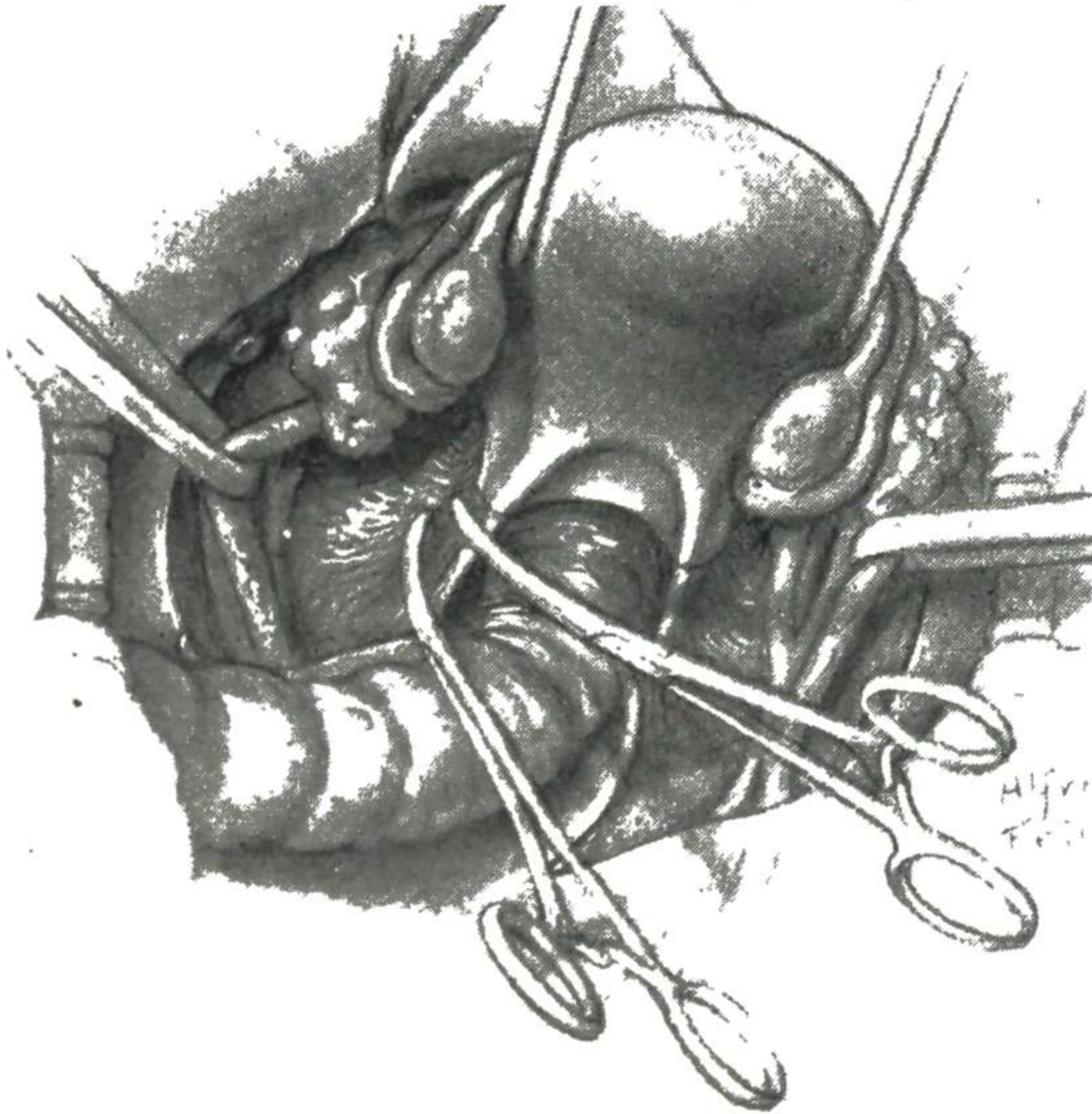
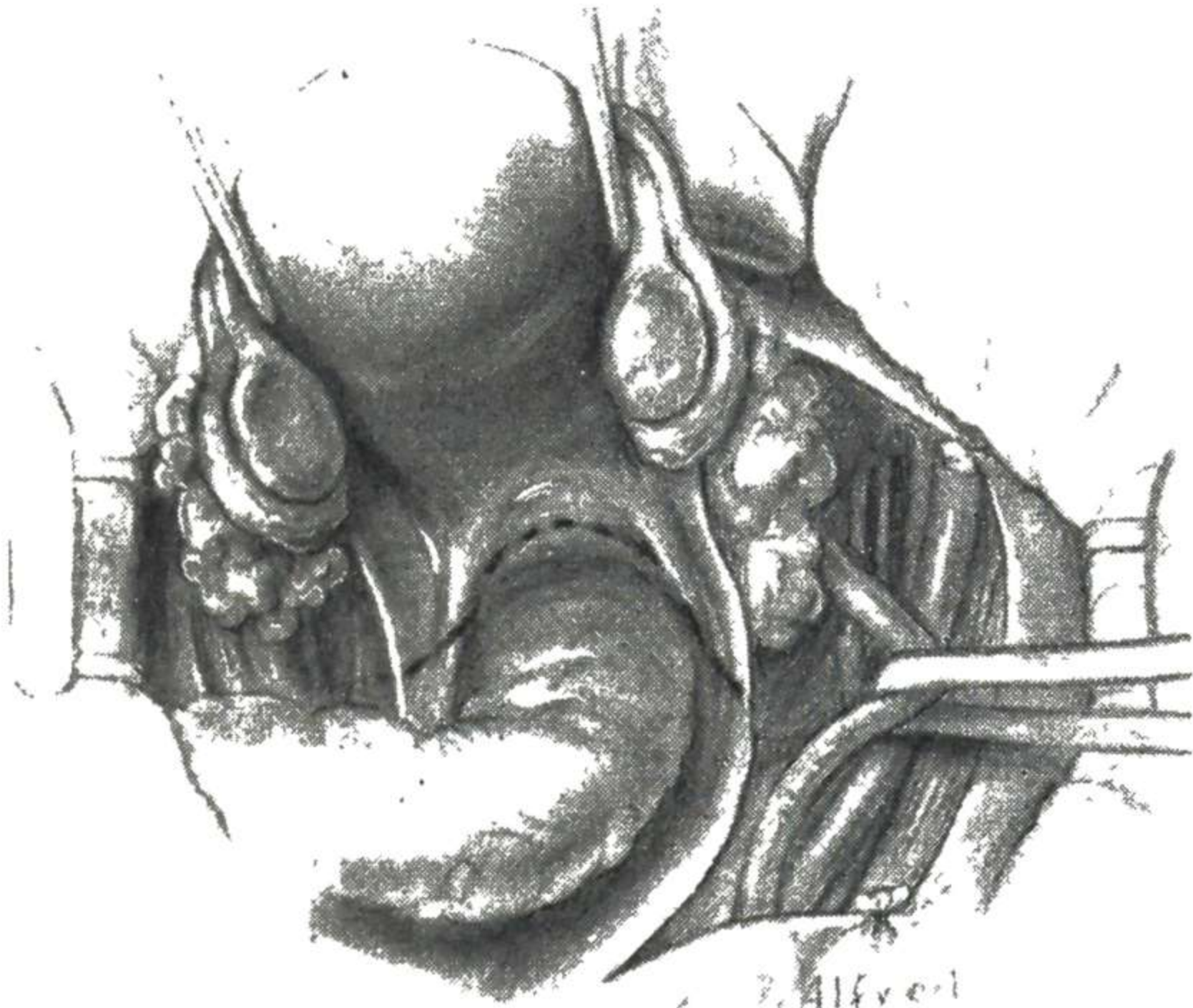


Fig. 124 (top).—Uterus is pulled strongly forward and upward to put medial leaves of peritoneum on tension and expose bottom of posterior culdesac. Dotted line shows proposed peritoneal incision

Fig. 125 (bottom).—Clamping of uterosacral ligaments, using a Moynihan gall-duct clamp (posterior) and large curved Pean hysterectomy clamp. Difference in curve of clamps allows easy scissors dissection. Tissues held in posterior clamp are then secured with suture ligatures.

(Courtesy of Twombly, G. H : Cancer 3:975-991, November, 1950.)

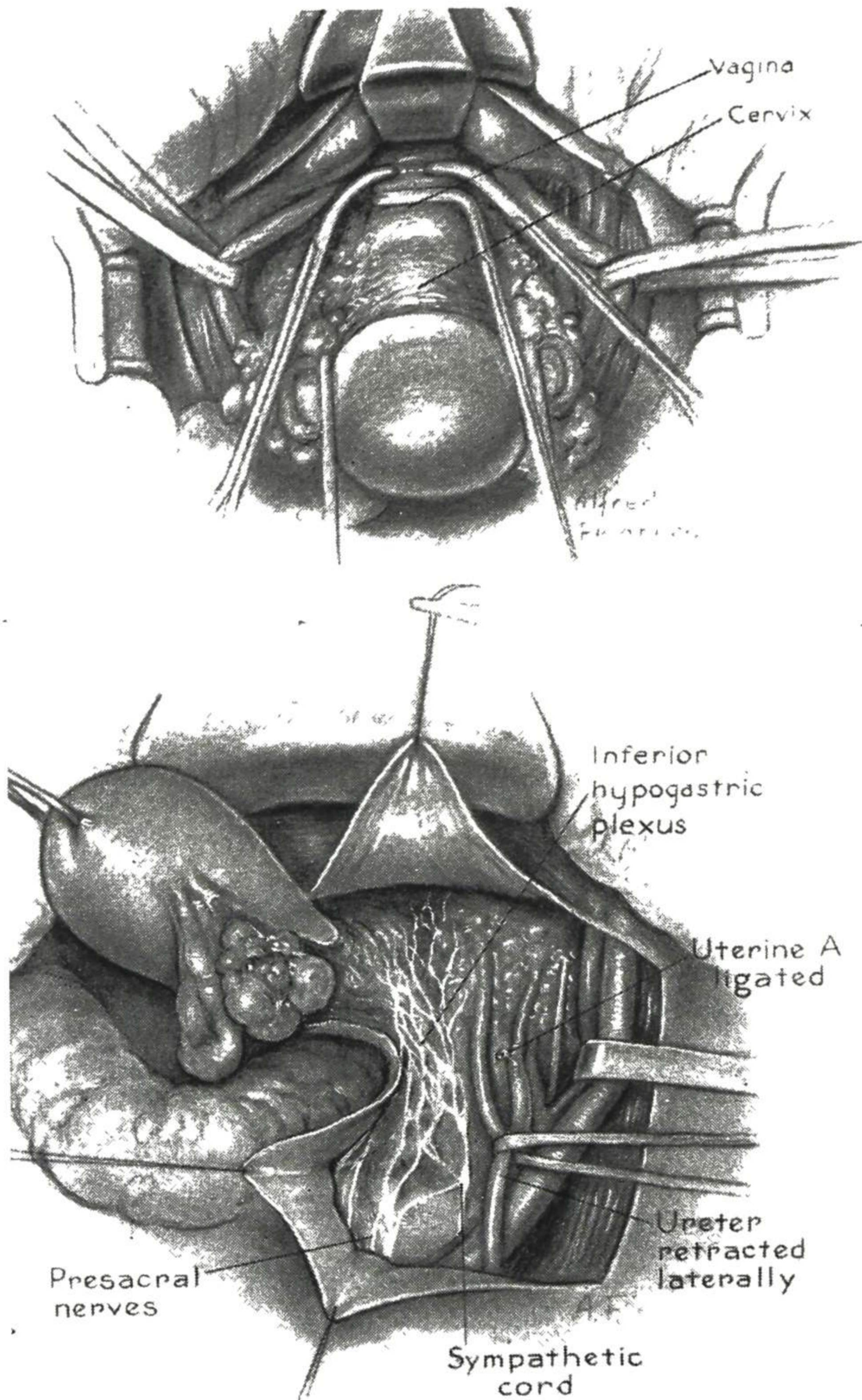


Fig. 126 (top).—Uterus, tubes, ovaries, parametrium and pelvic nodes attached only by skeletonized vagina 3-4 cm. below cervix. Right-angle clamp closes off upper part of vagina, preventing gross contamination of pelvis by cancer. Lower part of vagina is supported by Moynihan clamps; the vagina will be cut across between the clamps.

Fig. 127 (bottom).—Sympathetic nerves supplying pelvic viscera. (Courtesy of Twombly, G. H.: *Cancer* 3:975-991, November, 1950.)

ligaments which contain branches of the hypogastric arteries and veins running to the vagina. These ligaments are clamped and cut as far laterally as possible toward the pelvic walls. Dissection is carried toward the vagina until uterus, tubes, ovaries, parametrium and nodes are held in the body by the vaginal tube alone. This is skeletonized at a point 4 cm. below the posterior fornix and about 3 cm. below the anterior fornix (Fig. 126); the vagina is cut between clamps and the specimen removed in one piece. The vagina is then closed with figure-of-eight stitches of 0 chromic catgut, placed to invaginate the mucosa (Fig. 128). The space below the peritoneal floor may be filled with sulfamylon.<sup>®</sup> No drains are used.

The commonest postoperative complication is paresis of

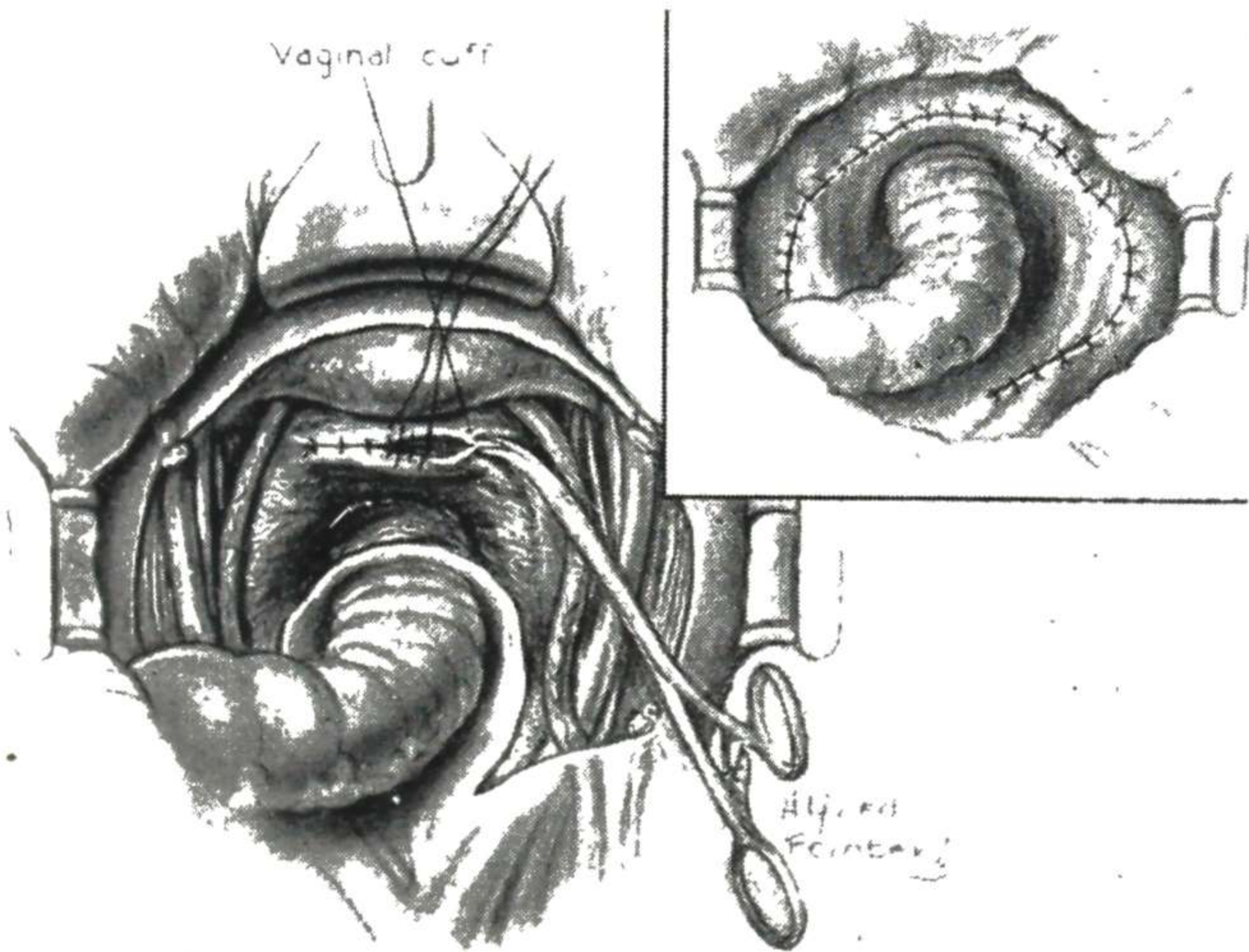


Fig. 128.—Vaginal cuff is closed without drains. Inset, raw areas are covered by sewing peritoneal edges together. (Courtesy of Twombly, G. H.: *Cancer* 3:975-991, November, 1950.)

the bladder. Sympathetic fibers supplying the pelvic viscera come from two sources, the presacral nerves that pass over the bifurcation of the aorta and into the pelvis over the sacral promontory and the sympathetic cord that lies beside the promontory. Presacral nerves divide into two main bundles sweeping to right and left around the rectum, unite with branches from sympathetic cords and come to lie in deeper parts of the uterosacral ligaments as the inferior hypogastric plexuses (Fig. 127). These nerves are necessarily cut in

radical hysterectomy. However, normal bladder function has returned in all cases observed although after a prolonged interval in some.

Postoperatively, constant bladder drainage with an indwelling catheter is carried out for one week. The patient can usually void spontaneously when the catheter is removed but may have large residual urine. She is catheterized at first twice and later once daily after voiding until residual urine is less than 100 cc. Penicillin, 400,000 units, is given twice daily and 0.5 Gm. streptomycin every six hours for one week. Patient is made to get out of bed briefly the first day and then for longer intervals; emphasis is placed on walking and standing rather than sitting. Patients who remain free from recurrence have general good health.

[This description of the technic of radical hysterectomy is excellent and deserves study by anyone who undertakes the radical operation. Most surgeons should be warned, however, that the operation cannot always be performed as easily as the illustrations would lead them to believe.—Ed.]

**Operative Treatment of Carcinoma of Cervix: Radical Panhysterectomy with Pelvic Lymph Node Excision** is described by Alexander Brunschwig<sup>4</sup> (Memorial Hosp., New York City). Such radical procedures are now possible because of the progress in pre- and postoperative care and in anesthesiology.

Preoperative studies of erythrocyte count, hemoglobin level, hematocrit and blood sugar, urea nitrogen, chloride and plasma protein levels are made and abnormalities corrected. Attention is given to weight loss and vitamin deficiencies, vitamins B, C and K being administered. Intravenous pyelograms are made; these may be supplemented by cystoscopy. The bowels are emptied the third and second nights and the second and first mornings before operation. On the day before surgery, 1,500 cc. of 5 per cent glucose in saline is given to compensate for fluids lost by catharsis. Blood is given as the operation begins.

**TECHNIC.**—With the patient in Trendelenburg position, a low midline incision is made, curving around and extending 4-6 cm. above the umbilicus. The right ovarian ligament is divided, the right lateral extraperitoneal pelvic space explored and the ureter located. Cephalad, the common iliac artery and vena cava are exposed; caudad, the opening is enlarged by transection of the round ligament. The lymph nodes and areolar tissues are swept down and off

(4) Am. J. Obst. & Gynec. 61:1193-1206, June, 1951.

of the vessels with a dissector and thumb forceps. With a dissector an opening is made in the areolar tissues mesial to and below the external iliac vein. The index finger is introduced, directed laterally to the lateral pelvic wall and swept anteriorly and posteriorly to free areolar tissues and nodes. Thus the contents of the obturator fossa are mobilized. The obturator nerve is isolated and allowed to fall away. The index finger is then hooked under the peritoneal reflection from the anterior lateral pelvic wall onto the anterior lateral bladder surface and this bridge of peritoneum incised. The hypogastric artery is ligated and divided, with care to avoid injury to the underlying large, thin-walled hypogastric veins, which may also be divided. Lymph nodes and areolar tissues are excised or swept downward and mesially against the detached broad ligament areolar tissues. This mobilization is carried to the musculofascial pelvic floor, which is denuded. The tissues overlying the sciatic nerve roots are similarly stripped. The tissues over the lateral aspects of the ureter are swept downward. The ureter is never stripped of areolar tissue, but a modicum of tissue is left about it to avoid sloughing with fistula formation. This point in the procedure is perhaps the weakest, since near the cancerous cervix the periureteral areolar tissue is likely to be invaded and yet must be left in situ. The index finger tip is inserted into the ureteral "tunnel" in the broad ligament to enlarge it and the upper outer portions are incised to expose the ureter to the bladder. Large uterine vessels must be ligated.

The peritoneal reflection from bladder to uterus is incised transversely and the bladder peeled forward. The dissection is carried to the left side in a similar manner after the sigmoid is freed and retracted upward. The uterus and adnexa are now held upward and forward, putting the uterosacral ligaments under tension. The peritoneum over the posterior upper portion of the vagina is transected and peeled downward, separating the rectum from the vaginal wall. The uterosacral ligaments are divided, and dissection is carried out about the cervix and vagina. The vaginal tube is transected between clamps so that at least half of the vaginal canal is removed.

Reperitonization is not carried out. A 4-5 in. wide gauze pack is placed in the pelvis, the end being inserted through the open vaginal cuff. Two soft rubber drains are inserted, one near each ureter, and brought out at the inferior angle of the midline incision.

When the lesion is large and fungating or there is appreciable spread onto the vagina, a vaginal phase is indicated to secure a large vaginal cuff and seal off the lesion to prevent spillage of tumor or spread by maceration during operation. An attempt is therefore made to obtain a cuff comprising the upper half to two thirds of the vagina.

**TECHNIC.**—The patient is placed in lithotomy position and bladder drainage assured by catheterization. Gauze sponges soaked in antiseptic are pressed against the lesion. A left lateral incision

(Schuchardt) is made, extending from the lower left portion of the introitus downward and out for 6-8 cm. and deeply to the left levator, which is partially divided to secure wide exposure. The incision is carried upward in the vagina to a point one-third or one-half way to the cervix. A Kocher hemostat is applied to the vaginal mucosa above the urethral orifice about halfway to the cervix, as a marker. A circular incision is begun from the inner end of the Schuchardt incision through the entire thickness of the vaginal wall. The bladder and rectum are pushed off this cuff while dissection about it is carried upward. Entrance into the peritoneal cavity is not envisaged. Once mobilized, the cuff is closed with the gauze sponges sewed in. Two to four gauze sponges are then inserted against the closed cuff and pressed laterally on each side. The patient is then placed in Trendelenburg position and laparotomy done as previously described. In the lower pelvic phases the procedure is altered. The palpating index finger seeks out the sponges, and, when found, they are removed and dissection proceeds to the liberation of the closed cuff. An alternative procedure to facilitate entrance from above into the space created by transection of the vagina is to separate the rectum from the posterior vaginal wall during the perineal phase and perforate the peritoneum of the pouch of Douglas to allow entrance of the index finger into the peritoneal cavity. The index finger then hooks under the ureterosacral ligaments, which are divided, and the space is thus entered.

Postoperatively, a catheter is placed in the bladder and left at least five days. The patient is catheterized every six hours after voiding until the residual urine is less than 100 cc. The gauze pack is removed in 24 hours with the patient in bed under pentothal<sup>®</sup> sodium anesthesia. If oozing of blood has been excessive, the pack may be left in another one or two days. Ambulation is started on the second or third day. Nothing is given by mouth for two or three days, infusions supplying all needs.

Hemorrhage or incision into the bladder, colon or ureters are the prime complications. There has been only one operative death in over 225 unselected patients (0.5 per cent).

**Results of Surgical Treatment of Cancer of Cervix Uteri.** Joe V. Meigs<sup>5</sup> (Boston) reports five year results in 75 patients undergoing radical hysterectomy and bilateral pelvic lymph node dissections for stages I and II. The abdominal approach was used and an attempt made to bare the pelvic walls and remove paracervical and paravaginal fat, lymph nodes and channels from the common iliac artery along the whole arterial and venous tree into the pelvis, beneath the bladder, around

(5) Am. J. Roentgenol. 65:698-708, May, 1951.

the rectum and into the obturator fossa. Meigs avoids irradiation in the surgical patient, except for research, since he feels that a firm, hard, fixed pelvis results.

Lymph nodes were cancerous in 18.7 per cent of patients, of whom 28.6 per cent survived five years. Lymph nodes palpable along the aorta contraindicate radical surgery. Irradiation does not destroy positive nodes in cervical cancer. Of 27 patients irradiated, 70.4 per cent survived; of those not irradiated, 83.3 per cent survived. Of 51 patients with stage I cancer, 44 (86.3 per cent) were living after five years, and of these, 3 had involved lymph nodes. Of 24 patients with stage II cancer, 15 (62.5 per cent) survived five years and one had involved lymph nodes. The chief cause of death was extensive involvement with disease, with resulting uremia, intestinal obstruction, pulmonary lesions, carcinomatosis or cachexia. Ureterovaginal fistulas developed in 10 (13.3 per cent), but radiation therapy offers nearly the same possibility of injury to ureter, bladder and kidney.

Taussig's transperitoneal lymph node dissection after irradiation of cervical cancer was done in 11 patients. Of the eight alive after five years, two of three with positive lymph nodes had lived five plus years. Retroperitoneal lymph node dissection (Nathanson) was done in 69 patients, and 8.7 per cent of 46 survivors had involved lymph nodes. This surgical procedure will probably prove satisfactory when the local lesion can be definitely destroyed. Results of radical operation fully justify surgery, but cases are so few that the whole plan should still be considered experimental.

[This is an excellent and conservative statement of the present status of radical panhysterectomy with lymph node resection for carcinoma of the cervix. It is well to emphasize that only men who have had considerable experience with pelvic surgery and who have available trained doctor and nurse assistants, proper instruments, ample blood for transfusion and good anesthetists should attempt to do these radical operations. Howkins (*Lancet* 2:872, Apr. 21, 1951) advocates a synchronous combined abdominovaginal hysterectomy whereby the abdominal operation is performed by one surgical team and the vaginal portion of the operation is done by another team, both operating at the same time. The purpose is to remove as much as possible of the vagina, which is of course a frequent site of recurrences. This is a more radical and thorough procedure than the classic Wertheim procedure and should improve the estimated surgical cure rate. It is particularly suitable when the growth has spread into the vagina. The author maintains that the operation is not technically difficult and should be performed as quickly as the classic Wertheim. The bladder and ureters are less likely to be damaged than in the classic Wertheim



operation since in the difficult part of the operation the two surgeons can assist one another. It is not suggested that this operation should supersede the classic procedure, but in some cases it will render difficult growths more easily operable. The vaginal operator who helped Howkins was Wilfred Shaw.—Ed.]

**Surgical Treatment of Carcinoma of Cervix.** Joseph W. Kelso<sup>6</sup> (Oklahoma City) performed 62 radical Wertheim hysterectomies with bilateral lymphoidectomy as an adjunct. In addition, presacral neurectomy was done in 47 cases on the basis that the patients might have recurrence and, if they did, would die with less pain. It was abandoned later in favor of extensive dissection. There was one operative death and five patients died later, three of distant metastasis and two of local recurrence.

Except for the earliest patients, all received radium four weeks before operation. All were adequately prepared. Indwelling catheters were placed before operation, thereby facilitating the procedure and preventing ureteral accidents. An attempt was made to remove all gland-bearing tissue in the pelvis, together with wide removal of the uterus and a variable, but large, amount of the upper vagina. All glands were dissected out completely, the ureters and blood vessels running across the pelvis being left free of any attachments and supporting tissue. Skilled anesthetists and use of spinal anesthesia and supplementation as needed reduced the hazards of prolonged surgery. Adequate blood replacement during operation to eliminate shock and postoperative maintenance of physiologic balance by intravenous administration of fluids fortified with glucose, minerals, proteins and vitamins were essential. Postoperative use of liberal amounts of antibiotics unquestionably allowed such extensive procedures to be done with a minimal mortality rate.

The 62 patients had varying degrees of malignancy: metastatic nodes were found in 9 (14 per cent) after extensive dissection of gland-bearing tissue. That this figure is below the 18.5 per cent originally reported by Meigs may be due to the fact that the tissues could not be examined as minutely as they should have been. When the extent of the operation is considered, the patients made unusually smooth recoveries. Two patients became ill, possibly with a radium reaction; in another, phlebitis developed, and one died of extraperitoneal abscess. Most patients had a urinary residual, but they were self-cor-

(6) J. Missouri M. A. 47:817-819, November, 1950.

recting. Five had ureteral fistulas, an incidence of 8 per cent.

[Brunschwig writes that the recent renewed interest in surgical treatment of carcinoma of the cervix must not be construed to indicate that surgery is preferable to treatment by irradiation. This is certainly not the case. As emphasized repeatedly by those interested in the problem, surgical treatment is being re-examined in certain institutions. It cannot be stated now that operation is a treatment of choice. Irradiation remains the standard treatment of carcinoma of the cervix, and this point cannot be overemphasized.

Simple total hysterectomy is wholly inadequate surgical therapy for carcinoma of the cervix. The so-called classic Wertheim operation does not represent the maximal surgical effort possible for an attack on cancer of the cervix. Any attempt to cope with cancer of the cervix by these operations will give results that might well discredit a surgical attack on disease. Radical panhysterectomy with pelvic node excision is a difficult procedure and should not be attempted by the occasional operator, nor should it be attempted by one who is not well qualified in pelvic surgery and surgery of the rectum, colon and the lower urinary tract.—Ed.]

**Cancer of Cervix Uteri: Australian Results, 1930-50.** Herbert H. Schlink<sup>7</sup> (Univ. of Sydney) has for 20 years combined radiotherapy and a Wertheim hysterectomy in all cases of cancer of the cervix, applying 30 mg. radium with 1 mm. Pt screenage in a rubber tube reaching from the fundus to the external os and 20 mg. radium with 2 mm. Pt screenage in the lateral fornices. They are left for 100 hours, after which the hysterectomy is performed. He and his colleagues, reviewing specimens from 1,000 cervical cancer patients, 500 of whom had been treated more than five years previously, found that radiotherapy does not eliminate cancer cells entirely and that lymph nodes invaded by cancer are not affected.

Only eight patients have been lost to follow-up. Immediate postoperative mortality (4.3 per cent) after radical Wertheim hysterectomy was due to shock in four, embolism in three, peritonitis or ileus in seven, urinary infection in three and lobar pneumonia in one. Survival rate after five years was 33.5 per cent and after 10 years 29.3 per cent. Among the stage IV cases (League of Nations' classification) only 4 of 95 patients survived between 1930 and 1944 and only 2 of 62 between 1930 and 1939. The five year survival rate after radium and surgery was 54 per cent if stage IV is excluded and 18 per cent after radium alone.

Since the use of blood transfusions, antibiotics and anticoagulants there have been no postoperative deaths. Since radium has been used preoperatively, the percentage of operable cases has increased to 50 per cent of all cases. Ureteral

(7) J. Obst. & Gynaec. Brit. Emp. 57:714-720, October, 1950.

postoperative complications are rare and most vesico- or recto-vaginal fistulas heal spontaneously.

Improved results can be obtained only by education of the profession, consultation with pathologists and radiotherapists in all doubtful cases and by establishment of preventive cancer clinics. The general practitioner should keep informed by reading the literature, use the speculum to discover a growth or to note excessive bleeding and submit a biopsy specimen to a competent pathologist. The Papanicolaou test is of value when other diagnostic aids are not available.

**Possibilities of Radical Surgery in Cancer of Cervix Uteri Recurrent after Radiation Therapy.** Alexander Brunschwig<sup>8</sup> (New York City) observed recurrent or persistent carcinoma limited to the cervix with or without vaginal, parametrial and pelvic lymph node invasion in 17 patients who then had radical hysterectomy with pelvic node excision. There were good results in 9 patients operated on 7-23 months after irradiation. These patients were well 8-29 months after surgery. Of the others, operated on 6 months to 7 years after irradiation, one had vaginal recurrence 23 months postoperatively and the other seven patients died 1-15 months after surgery. Thus appreciable palliation was achieved in 30 per cent of this limited, selected series. Best results were achieved in patients operated on about 13 months after irradiation. For 29 patients in whom carcinoma had invaded the bladder, partial pelvic exenteration was done, consisting of removal of the vagina, uterus, adnexae, pelvic lymph nodes and bladder with implantation of the ureters into the colon. Of these, six were well from several months to 29 months after surgery. For 53 patients with invasion of both bladder and rectum, complete pelvic exenteration including the colon was done; of these, 9 were well 13-32 months postoperatively. The patient well after 32 months had only extensive radiation necroses of the vagina, uterus, bladder and rectum with vesicovaginal and rectovaginal fistulas.

Extensive radiation necrosis is a valid indication for surgery, even though viable carcinoma may not be present. In both partial and complete pelvic exenterations approximately 23 per cent of patients died within 30 days. There were no operating room deaths. Previously less than 5 per cent of

(8) Am. J. Roentgenol. 65:720-725, May, 1951.

these patients survived the second year without surgery, and it now appears that radical dissection has something to offer these radiation failure patients.

**Ureteral Obstruction in Carcinoma of Cervix.** C. W. Aldridge and J. T. Mason<sup>9</sup> (Univ. of Michigan) studied 458 cases of cervical carcinoma seen over five years. Pyelographic studies on 333 of the patients revealed normal pyelograms in 219; in 114, either hydronephrosis or nonvisualization was demonstrated. Gross survival rate in the abnormal pyelogram group was 16 per cent compared to 62 per cent in the normal group. Though the percentage survival showed a decrease in the more advanced clinical stages of carcinoma, the rate was decidedly lower for all stages in the abnormal pyelogram group. This indicates the importance of ureteral obstruction in determining prognosis for any patient. Repeated pyelograms in 30 patients showed progression of obstruction in 25, all but 1 of whom died, and improvement in 5, of whom 4 are living. There was no patient with progression who did not also have advanced and progressing neoplastic involvement of the pelvis. Results of dilating the ureter in patients with unilateral hydronephrosis suggested that the trauma of dilatation might actually increase edema and stenosis and hasten development of autonephrectomy. Nephrostomy done in patients with advanced neoplasm and uremia did not materially improve prognosis.

There was close correlation between incidence of ureteral obstruction determined by pyelograms (34 per cent) and reported incidence of uremia as a cause of death as found at autopsy (40 per cent). Although the ureters received a significant amount of irradiation when cervical carcinoma was treated with radium, the authors were unable to demonstrate that irradiation commonly caused stricture of the ureter. Obstruction was usually due to extension of the neoplasm. Early diversion of the urinary tract, either by ureterosigmoid transplants or cutaneous ureterostomy, is preferable to late nephrostomy drainage or ureteral dilatation. Nephrostomy is indicated in patients with pyelohydronephrosis.

**Correlation of Histologic Grade, Clinical Stage and Radiation Response in Carcinoma of Uterine Cervix** with each other and with survival time was attempted in 100 selected cases.

<sup>9</sup> (9) *Am. J. Obst. & Gynec.* 60:1272-1280, December, 1950.

Pretreatment estimates of tissue response and use of histologic grading to gauge survival time have previously been unreliable as separate considerations. Robert W. Kistner and Arthur T. Hertig<sup>1</sup> (Harvard Univ.) restudied the diagnostic biopsy specimens and the follow-up biopsy specimens taken 10-21 days after x-ray therapy at the time of the first radium insertion, 10-14 days later at the time of the second radium insertion and either at the termination of radium therapy or 2-3 weeks later. The usual program consisted of an average total dose of 6,000 r given in an average of five treatments through three portals over 3 weeks and of two doses of 2,000-3,600 mg.-hr. radium within 10-21 days of each other for a total of 4,800-6,000 mg.-hr. Lesions were graded according to Warren's classification. Radiation responses were considered marked, moderate or minimal. Clinical staging was based on the League of Nations' classification.

Average age of the patients was 49.8 (25-77). Age could not be correlated with radiation response or survival. Thirty-four patients were placed in clinical stage I, 53 in II, 9 in III and 4 in IV. Four lesions were classified histologically as being in grade I, 77 in II, 9 in III, 9 as adenocarcinoma and 1 as adenosquamous. Over-all five year survival rate was 50 per cent. Salvage was about the same in each histologic grade but definitely correlated with clinical stage, ranging from 74 per cent in patients in clinical stage I down to 0 in those in stage IV. Radiation response of marked degree was somewhat greater in grade II and III lesions but could not be related to clinical stages. However, increased survival was evident in patients who had a marked response to irradiation; but when these cases were analyzed according to stage, the major factor affecting survival was found to be clinical stage rather than degree of response, as indicated by 100 per cent mortalities in stage III and IV patients even with marked response to radiation. Surgery is suggested as adjunctive therapy when radiation response is minimal.

**End Results of Radiation Treatment of Cancer of Cervix Uteri.** Since radium or x-rays alone are inadequate except in a lesion confined to the cervix, Herbert E. Schmitz<sup>2</sup> (Mercy Hosp., Chicago) combined them in therapy of 188 previously

(1) *Am. J. Obst. & Gynec.* 61:1293-1300, June, 1951.

(2) *Am. J. Roentgenol.* 65:715-719, May, 1951.

untreated patients. When microscopic proof of cancer was obtained, the patient was given 1,500 mg.-hr. radium weekly for a total dose of 4,500 mg.-hr. On the days radium was not in place, roentgen therapy was given through numerous ports for a total tumor dose of 3,500-4,000 r. Hospitalization for the entire time is preferred. Results show five year survival rates to be: group I (Henry Schmitz), 92.8 per cent; group II, 70.4 per cent; group III, 40.5 per cent, and group IV, 11.5 per cent, with over-all survival rate 43.6 per cent. If groups I and II were included under stage I (League of Nations), survival rate would be 75 per cent for this stage. The cell types were known in 75 per cent of cases but in no way aided prognosis, but response of the tumor to therapy and extension of the disease definitely influenced prognosis. Erythema, epilation, desquamation, enteritis, proctitis and cystitis are results of radiation experienced by all patients, but complete recovery usually follows within six weeks. Persistent complications reported are cystitis (22), diarrhea (11), colitis (6), dermatitis (4), vesicovaginal fistula (3), bowel obstruction (1), proctitis (3) and hemorrhage (1). Early detection is stressed.

**Growth and Spread of Cancer of Cervix Uteri.** Gray H. Twombly and Salvatore di Palma<sup>3</sup> (Columbia Univ.) believe cancer of the cervix begins as carcinoma in situ, for (1) serial section of the cervical epithelium discloses beginning infiltration in a fairly high percentage of cases of carcinoma in situ, and (2) sections of infiltrative cancer taken through the entire cervix or one entire cervical lip reveal carcinoma in situ in the mucosa beyond the margin of the infiltrative growth. In 60 cases of intraepithelial carcinoma average age was 41.9, and in 94 primary cases of infiltrative cancer, 49.6, suggesting that cancer in situ grows slowly before it becomes invasive. At the New York Cancer Institute, of 171 cancer patients who had received no surgical or radiation therapy, 58 per cent died in one year and only 4.6 per cent lived five years.

Cervical cancer tends to kill its host by local pelvic changes, particularly ureteral obstruction and pelvic sepsis, rather than by widespread metastasis. Partial or complete control of cancer in the cervix tends to give time for distant fatal metastases to appear. Unlike metastatic breast cancer, these usually involve periaortic nodes, parenchymatous or-

(3) Am. J. Roentgenol. 65:691-697, May, 1951.

gans, liver, lungs, spleen, brain, etc., sometimes the spine but rarely the bony pelvis. The commonest cause of death is ureteral obstruction or associated infection of the urinary tract. Operative relief from such obstruction has doubtful value unless there is some promising method of curing the primary tumor.

**Use of Radioactive Cobalt in Treatment of Carcinoma of Cervix.** After activation in the nuclear reactor, cobalt forms a relatively stable isotope with a soft beta ray which requires minimal shielding and has homogenous radiation. It can be machined to any desired shape before activation and constitutes an easily handled radioactive material. Allan C. Barnes, Joseph L. Morton and George W. Callendine, Jr.<sup>4</sup> (Ohio State Univ.) attempt to distribute tissue roentgen doses to the pelvis so that uninvolved viscera are protected while the malignancy receives adequate irradiation. Fine caliber needles of desired length and strength, template guides to provide precision of needle placement, and cobalt are used. After activation the cobalt cylinders are placed in the needles, with inert aluminum cylinders between to distribute linear intensity as desired (Figs. 129 and 130). This method permits individual grouping within each needle as well as varied needle arrangements within the pelvis.

**PROCEDURE.**—After careful clinical evaluation of the neoplasm, patients receive external x-radiation (2,000 r to 20 × 20 cm. anterior and posterior ports). Measurements to determine size of templates and arrangement of needles are made, and the individually designed applicators are inserted under pentothal® anesthesia. The first plate can have a small rod projecting from its surface and designed to fit into the cervical canal, or it may be held in place while the individual needles are inserted through appropriate holes. Each subsequent plate then fits on the preceding one. Generally the first plate carries the cervical needles, the second the paracervical and the third the parametrial. After insertion the applicator is packed in place and usually remains for six to seven days to provide approximately 6,000-7,000 tissue roentgens to the neoplasm.

Of 40 patients, 5 who had had previous ineffective treatment were incurable when cobalt therapy was instituted; 5 others had had inadequate precobalt treatment and 30 adequate treatment. Eight patients died within 11 months. The patients were no more febrile and toxic than those receiving a corresponding tissue roentgen dose of radium. At first, with

(4) Am. J. Obst. & Gynec. 60:1112-1120, November, 1950.

use of 16 needles and five day insertion, bowel reactions appeared; but use of more needles, reduction of dose/needle, use of the seven day period and angling of needles further forward in the pelvis have lessened severity and incidence of

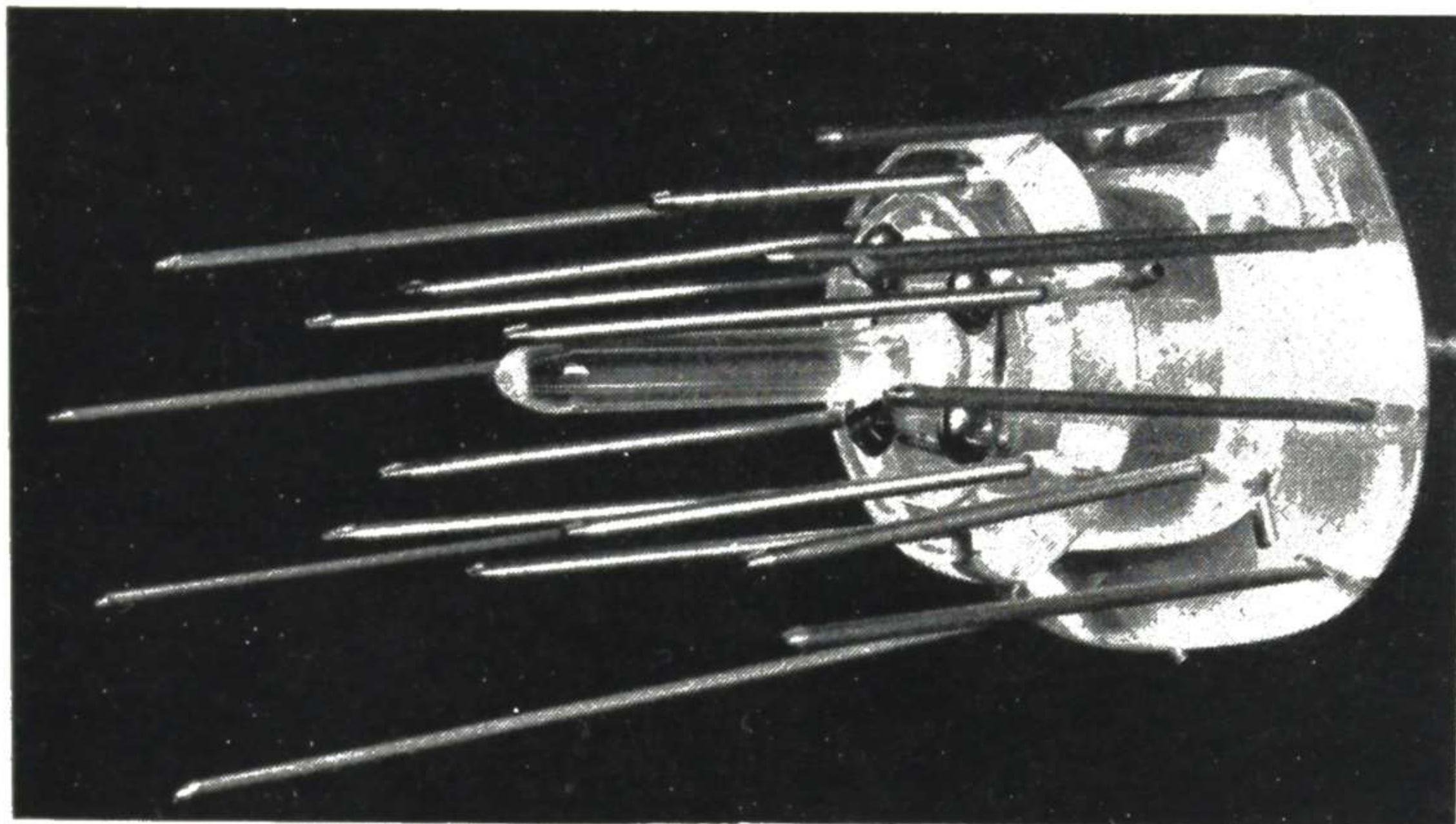


Fig. 129 (above). — Cervical needles placed through holes in first template; paracervical and wide parametrial needles through large plate at base.

Fig. 130 (left). — Anteroposterior film of patient with needles in place; needles and slugs between cobalt cylinders are aluminum; only cobalt shows on film.

(Courtesy of Barnes, A. C., *et al.*: *Am. J. Obst. & Gynec.* 60:1112-1120, November, 1950.)

bowel reactions. Nothing inherent in the patients' reaction to  $\text{Co}^{60}$  was found. An indwelling catheter was left in place during treatment, and bladder morbidity was rare. Geiger counts indicate that the field of radiation is satisfactory and the technic achieves the desired distribution effect with precision.



**Endometrial Carcinoma** in 330 patients is reviewed by J. H. Randall, D. F. Mirick and E. E. Wieben<sup>5</sup> (State Univ. of Iowa). Eighty-six per cent of patients were over age 50; 80 patients (24.2 per cent) were nulliparous. In 92.7 per cent the first and usually the only symptom was abnormal vaginal bleeding. Patients who had menstruated after age 50 constituted 56.7 per cent of the series. Cases were classified according to clinical stage and histologic group. X-rays, radium and surgery were used in treatment. Poor operative risks or patients with stage III or IV carcinoma had irradiation alone.

Present therapy consists of intracavitary radium in multiple foci followed in four to six weeks by hysterectomy. Radium is inserted at the time of diagnostic curettage and removed at once if the curettings are negative. Average total dose is 4,900-6,400 mg.-hr. Immediately before hysterectomy the uterine cavity is packed and the cervix closed with sutures. After exposure of the pelvic organs, the abdominal end of each tube is ligated. The entire uterus and adnexia are removed. Traction is applied only to the round ligaments and at no time is the uterus grasped with sharp instruments. All patients receive intrauterine radium regardless of extent of disease.

All deaths were considered due to cancer and no correction was made for natural attrition. Of 320 patients treated, 180 survived five years (56.3 per cent). Of 98 patients treated with intracavitary radium followed in four to six weeks by surgery, 80 survived five years (81.6 per cent). Advanced lesions accounted in part for the poor salvage of patients treated with x-ray and radium alone. Of 51 patients receiving x-radiation and surgery 28 survived five years (54.9 per cent). Intracavitary radium before surgery is superior to preoperative or postoperative x-ray therapy; this treatment has almost eliminated recurrence of carcinoma in the vaginal apex.

Patients with stage III and IV carcinoma and with more anaplastic tumors did poorly. Prognosis was more favorable in younger than in older patients. In 225 cases in which information was available, 36 per cent had fibromyomas and 13.3 per cent endocervical polyps. Cardiovascular disease was the disorder most often associated with endometrial carcinoma. Of the 10 deaths associated with treatment (3.03 per

(5) Am. J. Obst. & Gynec. 61:596-602, March, 1951.

cent), 8 followed hysterectomy, 1 curettage and 1 radium insertion.

**Time, Site and Treatment of Recurrences of Endometrial Carcinoma** in 266 women treated at New York Hospital (1933-49) are described by William F. Finn.<sup>6</sup> Incidence of recurrence is high during the first three years after treatment, but thereafter approximates 1 per cent annually. There was recurrence in 49 cases (18.4 per cent) within one year after treatment, in 34 (69 per cent) within two years, in 42 (85 per cent) within three years, in 7 (15 per cent) after three years and in 5 (10 per cent) after five years. Recurrence rate was 9 per cent when treatment consisted in hysterectomy alone and 25-29 per cent after all other forms of treatment. It was directly proportional to the anatomic extent of the carcinoma at time of treatment, being six times as frequent when the carcinoma had extended beyond the pelvic cavity (stage V) as when it was confined to the endometrium (stage I). It was also directly proportional to the histologic grade of the carcinoma and was five times as common after undifferentiated cancers (grade C) as after well differentiated cancers (grade A). Commonest sites of recurrence were the remaining pelvic organs, vagina, bladder, ureters, pelvic lymph nodes and pelvic peritoneum. Abdominal, pulmonary, bone, abdominal wall and breast recurrences were progressively rarer.

Treatment of recurrences was palliative in 27 patients because of their local extent or extrapelvic manifestations; survival averaged five months. X-ray and radium irradiation were used for vaginal and intrapelvic recurrences in nine patients, all of whom died after average survival of 1½ years. Surgery was palliative in six; it was definitive in seven patients with localized and solitary recurrences, six of whom were alive and apparently free from recurrence after an average of 1½ years.

More extensive use of hysterectomy with wider parametrial excision and of vaginal extirpation, occasionally with pelvic node dissection, would lower the recurrence rate. Low voltage x-ray irradiation by intravaginal cone may decrease the number of vaginal recurrences.

[Several gynecologists are questioning the advisability of performing a radical hysterectomy with removal of the lymph nodes in carcinoma of

(6) *Am. J. Obst. & Gynec.* 60:773-782, October, 1950.

the endometrium as well as in carcinoma of the cervix. Undoubtedly more women would remain free from cancer; on the other hand, there would certainly be an increase of primary mortality and of morbidity, particularly involving the urinary tract.—Ed.]

**Carcinoma of Corpus Uteri in Young Women** is discussed by Malcolm B. Dockerty, Sim B. Lovelady and Glenn T. Foust, Jr.<sup>7</sup> It is conceded that although cervical carcinoma occurs in women under 40 in only about 25 per cent of cases, carcinoma of the corpus uteri occurs on the average 10 years later. In 1904-44, 1,694 patients with carcinoma of the uterine corpus were treated at Mayo Clinic. Thirty-six were under 40 (2.1 per cent). This figure is considerably lower than the 5 per cent incidence cited by Speert.

The 36 patients presented symptoms that were primarily menstrual, especially prolonged menometrorrhagia, which was often interrupted by months or years of amenorrhea and associated with leukorrhea. All were more or less intractable to ordinary therapy such as use of hormones, curettage or implantation of radium. There was also a high incidence of sterility in the 28 married patients, the total number of children born to them being 20 and most recorded deliveries having occurred 10-15 years before admission. The shortest known interval between pregnancies was five years.

Thirteen patients were obese, with weight in excess of 150 lb., and 3 of these also exhibited hirsutism. Blood pressure was recorded for 26 patients; 10 were hypertensive. Despite the excessive bleeding, less than 20 per cent had clinical evidence of anemia. Pelvic examination showed numerous cervical abnormalities, with bloody discharge from the external os being noted in nine patients and other findings including cervical enlargement or deformity, fixation of the cervix, erosions, polyps and cystic cervixes being noted in a variable number.

Total abdominal hysterectomy was performed on 24 patients, hysterectomy alone was performed on 3 and radiation therapy alone was given to 3. Twenty-three replied to follow-up letters; 18 were alive five or more years postoperatively, 4 had died of carcinoma and 1 was alive with inoperable recurrence.

On gross examination of 33 uteri, 20 exhibited myohypertrophy and 8 contained fibromyomas which contributed con-

(7) Am. J. Obst. & Gynec. 61:9 6-981, May, 1951.

siderable bulk. Only five specimens weighed less than the normal 100 Gm. Microscopically, 26 were adenocarcinoma and 10 adenocanthoma.

Almost 20 per cent of the patients presented four or more of the cardinal features of the Stein-Leventhal syndrome. This may indicate that they had chronic hyperestrinism which eventually proved carcinogenic. Therefore, more attention should be paid to the possibility of carcinoma of the corpus complicating the Stein-Leventhal syndrome.

The presence of secretory endometrium in seven patients and of old or recent corpora lutea in the ovaries of nine indicated that endometrial carcinoma can occur with ovulation and premenstrual endometrium. Accordingly the authors advocate early and repeated curettage with vaginal smear studies in young patients with the symptoms described.

**Myometrium and Leiomyomas in Endometrial Carcinoma: Failure of Involution and Reactivation of Smooth Muscle Tissue.** Grossly and histologically, Siegfried Tannhauser<sup>8</sup> (Univ. of Buffalo) studied 58 uteri containing endometrial carcinoma. This study was initiated by the observation that uteri removed for endometrial carcinoma were larger than normal for the age group of the patients; e.g., in the late menopausal phase a small atrophic organ is expected but the ones removed looked like premenopausal uteri. Often they were two to three times normal weight and size, and the myometrium, instead of being thin, flabby, rubbery and a dead grayish pink, was thick, meaty, turgid, firm and deep pink or rosy. Degree of enlargement was unrelated to mass of the tumor, and quantitative studies led to the conclusion that the enlargement was due to endometrial hypertrophy. The term rejuvenation was considered most adequate to describe the macroscopic and microscopic changes.

The most characteristic myometrial rejuvenation was observed in nonirradiated uteri. At present the most commonly used treatment of endometrial carcinoma is intrauterine application of radium, followed in six to eight weeks by total hysterectomy. Radium treatment is accompanied by shrinkage of the uterus to half or less of its original size, which may be due to regression of the tumor or of the previously reactivated myometrium toward the involutional stage.

(8) *Am. J. Obst. & Gynec.* 61:265-275, February, 1951.

Leiomyomas present in carcinomatous uteri often participate in the process of rejuvenation; most of them are larger than those found in nonmalignant uteri. Grossly, they have the whorly, uneven cut surface of premenopausal tumors and are of elastic, resilient, turgid or succulent consistency.

Statistically, 1,095 nonmalignant and 58 malignant uteri were studied to determine the percentage of endometrial carcinomatous uteri in which myometrial rejuvenation was present, and weights and measurements of the two groups were compared. In all uteri removed for endometrial carcinoma, myometrium of the premenopausal type was present, whereas in the nonmalignant uteri of patients aged 50-60, only 23 per cent showed premenopausal type myometrium. Of 14 carcinomatous uteri from women over 60, 93 per cent showed various degrees of rejuvenation. The older the patient, the greater was the percentual weight increase of the malignant over the nonmalignant uterus. Not only was the average weight of the malignant uteri more than that of the nonmalignant ones, but in all age groups the weight of the smallest malignant uterus was greater than that of the corresponding nonmalignant one and the same was true of the largest specimens in each group. In patients over 60, if uteri with leiomyomas, adenomyosis and prolapse were discounted, all uteri weighing more than 60-70 Gm. showed malignancy.

The myometrium of uteri containing leiomyosarcoma showed the same changes as that of uteri containing carcinoma.

The findings appeared to support the hormonal causation theory of endometrial carcinoma. The role of estrogenic hormones in proliferative processes of the postmenopausal endometrium has been established by reports of endometrial hyperplasia and carcinoma following estrogen therapy or accompanying theca cell tumors. However, review of the literature revealed only one reference to this association of myometrial changes with endometrial carcinoma.

The authors concluded that a nonprolapsed uterus in a patient in the late postmenopausal age group which is distinctly larger than normal should arouse suspicion of malignancy or of hormone-producing ovarian tumor. The same is true of myomas which show signs of reactivation such as growth, pain or soft, meaty consistency on palpation. In

creased clinical consciousness of these signs may lead to diagnosis of malignancy in earlier and more favorable stages.

**Sarcoma of Uterus: Review of 33 Cases.** Sarcoma of the uterus comprised 0.15 per cent of all admissions to Women's Clinic of New York Hospital, 1933-49, 3.3 per cent of all genital tract neoplasms and 0.3 per cent of myomas. In the 33 cases reviewed by William F. Finn<sup>9</sup> there were 13 endometrial, 18 myogenic and 2 unclassified sarcomas. Thirty-one patients (93 per cent) were over 40. Chief symptoms were postmenopausal bleeding, abdominal pain and an abdominal mass. Enlarged uterus in 32 patients resulted from sarcoma in half and from associated myoma in the others. Cytologic smears were obtained in nine patients; results in seven were correct (five endometrial and two myogenic sarcomas); the two false negative reports occurred in leiomyosarcoma. There were six false negative diagnoses in this series, important because they delayed effective treatment.

Complete extirpative surgery was the treatment of choice, if feasible. Immediate postoperative mortality was 10 per cent; causes were hemorrhagic shock, peritonitis and heart failure. X-ray therapy was not effective in five patients with advanced sarcoma. Regardless of the histologic grade of the sarcoma, it is believed that the anatomic extent is the most important factor in prognosis. Only 1 patient is alive in whom sarcoma extended outside the uterus; 13 patients with sarcoma confined to the uterus are living. In all, 19 patients died; 6 had endometrial, 11 myometrial and 2 unclassified sarcoma. Autopsies on seven patients showed that metastases were the leading cause of death. Of the 14 survivors, 7 (2 with endometrial and 5 with myometrial sarcoma) have lived for less than five years; 7 (21 per cent) have survived 5-17 years (5 with endometrial and 2 with leiomyosarcoma).

**Sarcomatous Changes in Myomas of Uterus: Clinical Study of 21 Cases.** The commonest form of uterine sarcoma develops in a pre-existing myoma. Undifferentiated cells of mesodermal origin are present in the myoma from the outset, and some stimulus sets off their growth. H. W. C. T. Hansen<sup>1</sup> (Univ. of Basel) reports that uterine tumors were diagnosed in 2,093 patients in 14 years and the extirpated myoma or

(9) *Am. J. Obst. & Gynec.* 60:1254-1262, December, 1950.

(1) *South African M. J.* 24:644-648, Aug. 5, 1950.

uterus from 1,463 was examined histologically. Sarcomas developing in myomas were found in 18, an incidence of 0.9 per cent for all clinically diagnosed uterine tumors in hospitalized patients and 1.2 per cent for all histologically examined myomas. The low incidence of sarcomatous changes in myomas in hospitalized patients means that incidence in all myomas is still lower. Thus, removal of a myoma only because of danger of malignancy seems unjustified.

Of the 18 patients in this series and 3 others seen recently, only 3 had malignancy in the family history. Average age was 49. Important signs and symptoms of malignant changes were rapid increase in size of myoma in one patient, irregular vaginal bleeding in seven, sudden onset of pain in myoma in two, loss of weight and general debility in five and increase in size of myoma in menopause in one. The two most frequent complaints on hospitalization were lower abdominal pain and menorrhagia. In nine earlier cases, supravaginal or total hysterectomy alone was carried out; five of the patients ultimately died of sarcoma, although prognosis had been considered good after operation. This treatment is regarded as inadequate and almost all patients now receive roentgen and radium therapy postoperatively. Of four patients so treated, two were well and free from recurrences 1½ years later and another, 5 years later. Three patients were added to this group in the past year. In five cases in which the tumor was large and adherent with probable sarcomatous spread to neighboring organs, roentgen radiation only was done, with 100 per cent ultimate mortality. Excluding the 3 recent patients, 12 (60 per cent) eventually died of sarcoma.

[Galan, Duran and Valenzuela (*Bol. Soc. chilena obst. y ginec.* 15:139, August, 1950) report uterine sarcoma in 11 of 9,123 patients (1 per cent). However, since there were only 824 fibromyomas, incidence of the sarcoma in these neoplasms was 1.3 per cent. Among the 6,981 fibromyomas studied by Novak and Anderson (*Am. J. Obst. & Gynec.* 34:740, November, 1937), sarcoma was found in 0.56 per cent. Because of the low frequency of sarcomatous change in fibromyomas, there is no justification for removal of a myoma or of the uterus simply because of the possible danger of malignancy. This is contrary to the principles of treatment of ovarian tumors; all large ovarian growths should be removed as soon as they are discovered because there is a definite danger of malignancy, especially in solid ovarian neoplasms.—Ed.]

**Radical Groin Dissection for Carcinoma: Simplified Operative Procedure.** S. N. Mendelsohn and R. D. Mansfield<sup>2</sup>

(2) *Surg., Gynec. & Obst.* 92:432-436, April, 1951.

(Cincinnati) recommend bilateral dissection for carcinoma of the vulva, clitoris, anus and perineum and for metastatic cancers primary in the umbilical and infraumbilical areas of the abdomen, epidermoid carcinoma, melanoma and highly malignant connective tissue growths of the lower extremities.

**TECHNIC.**—A long incision, made from a point in the flank anterior to the tip of the twelfth rib, is carried in a slightly curved manner across the midpoint of the inguinal ligament into the thigh and over the femoral triangle. The saphenous vein is incised between ligatures and the lymph nodes lying along each side of it and those along and below the inguinal ligament together with one or two nodes found above the inguinal ligament in the hypogastric area and the fat in which these nodes are embedded are excised in mass. This is removed, exposing the deep fascia of the abdomen and thigh which is incised in the line of the skin incision. The inguinal ligament may be incised, if desired; if this is done, an anomalous obturator artery must be sought. The peritoneum is dissected medially, showing the entire course of the iliac and femoral vessels. The lymph nodes, tissue, vessels and areolar connective tissue are now dissected from the iliac nerves from the bifurcation of the aorta down and continued to the apex of the femoral triangle, either pushing the mass below the inguinal ligament, or incised at this level and the dissection continued below. The wound is closed in layers when dry, and one or two Penrose drains are inserted.

**Cancer of Vulva.** Narciso Díaz Bazan<sup>3</sup> reviews 73 cases from the Instituto del Radium, 1925-49, and 68 from the Hospital Curie, 1929-49, and adds 8 seen in private practice. The 141 cases of cancer of the vulva represented 0.25 per cent of the 55,480 case histories at the two hospitals. Incidence of cancer of the vulva with relation to cancer of the uterus was 3.6 per cent. Analysis of the 149 cases showed that cancer of the vulva appeared most often between age 51 and 60 (28.2 per cent); 24.2 per cent of patients were 41-50 and 20.8 per cent, 61-70. This age incidence is not in accord with statistics of other authors in which the most common age is 70. The youngest patient in this study was 2, the oldest 87.

More than three fourths of the patients were white, the rest either Negro or mestizo. Almost 64 per cent were multiparas and 16.9 per cent were nulliparas. One patient was concurrently pregnant. Metastases in inguinal lymph nodes were found in 62.3 per cent. The labia majora was the site of the initial lesion in 50.2 per cent, with more than half of these lesions on the right side. The next most common sites were

(3) Arch. Col. Med. El Salvador 3:1-21, March, 1950.



the urethral meatus, clitoris and labia minora. Histopathologic studies, done in 87 cases, revealed 80 cases of epithelioma (91.9 per cent), 4 of adenocarcinoma, 2 of sarcoma and 1 of melanoma. Of the epitheliomas, only one was a basal cell type.

Of the 141 hospital patients 25.5 per cent refused treatment. Of the 105 patients treated either completely or incompletely, 62 received roentgen or radium therapy, alone or in combination. Vulvectomy was done in 16. Evaluation of final results was impossible, because 58.2 per cent of the patients were not followed for five years. However, 4.2 per cent were known to have survived five years, and 34.7 per cent were known to be dead.

[This is a large series of cases of carcinoma of the vulva. It is unfortunate that 82 patients could not be traced and that only 16 vulvectomies were done. Most likely the condition was so advanced in most cases that more operations could not be performed. Still more unfortunate is the fact that 36 women refused treatment and many had incomplete therapy. In this series the distribution according to age differed from that generally observed, the largest proportion occurring in women 51-60, the second largest in the 41-50 group and the third largest in the 61 and 70 group.]

Fricke, Bowing and Decker (Am. J. Roentgenol. 64:86, July, 1950) reported 50 cases of primary vaginal cancers observed at the Mayo Clinic, 1933-48. In all cases primary treatment was with radium or roentgen rays or both. There has been a gradual improvement of the survival rate of the patients with primary malignant lesions of the vagina. It has coincided with improvement in radium technic and increased experience with this type of lesion. However, this is a highly malignant lesion and most difficult to treat. Perhaps the most important factor is that many patients with far advanced lesions receive very adequate palliation with radium and roentgen treatment and so can live without too much discomfort, although cure is impossible. The value of periodic pelvic examinations during and after the menopause must be stressed. Early recognition of these lesions would undoubtedly lead to a much higher salvage. Even innocent-appearing vaginal lesions should be subjected to microscopic examination to avoid missing the apparently benign but truly malignant lesion, primary in the vagina.—Ed.]

#### **Smear Preparations in Diagnosis of Vulvar Carcinoma.**

The genital smear method of studying malignant cells is valuable not only in identifying carcinoma but in quick differentiation between cancer and vulvar lesions of venereal etiology. Scrapings made with a thin metal spatula, after film has been removed from the lesion, result in the best smears. In three years, Bayard Carter, Louise A. Kaufmann and W. Kenneth Cuyler<sup>4</sup> (Duke Univ.) made 33,655 genital smears

(4) Surg., Gynec. & Obst. 91:600-604, November, 1950.

on 10,029 women. Squamous cell carcinoma of the vulva was found in 18 patients, or 4.1 per cent of the malignant lesions studied. Eleven patients were over 60 and 14 postmenopausal. Of 14 white and 4 Negro patients, 83.3 per cent were or had been married; 6 were nulliparas and 11 multiparas. Lesions involved the right labia in 11 patients, the left labia in 3, the entire external genitalia in 3 and the anterior fourchette in 1.

Of five cell types commonly found in smears from vulvar carcinomas, three have been described and illustrated by Papanicolaou and Traut. The authors describe the other two. One is a small basal cell with acidophilic cytoplasm and a large vesicular nucleus in which the perinuclear membrane is prominent. Chromatin forms a distinct open reticulum. There are usually multiple large nucleoli, and chromatin may be a faint orange. Cell outlines are generally indistinct and nuclei uniform in size and shape, which is round, sometimes ovoid. The second cell type is large and flat, resembling a highly cornified vaginal cell. Cytoplasm stains a bright orange-red. Nuclei are usually densely opaque, may be enlarged, vary in size, are irregular in outline and generally have jagged edges. This cell probably represents a degenerating form in a well differentiated carcinoma.

Some lesions reported in this series had existed only a short time in the knowledge of the patients. Metastasis had already occurred in at least two cases. Therefore, it should be obligatory for the examiner to make smears, especially in older age groups, of any vulvar lesion, however insignificant in appearance, and when biopsy may not seem indicated.

**Extended Radical Vulvectomy of Stanley Way.** Primary carcinoma of the vulva has been until recently a forbidding lesion, because of discouraging results of both surgery and irradiation. Stanley Way reported, for his extended radical procedure, an absolute three year survival rate of 88 per cent and a five year cure rate (in a series of 12 cases) of 83 per cent; Taussig's figures with a larger series are comparable. In the light of Way's results, carcinoma of the vulva now ranks next to uterine body cancer as the least malignant of female genital growths. This improvement in surgical results is welcome in view of the practically uniform failure of x-ray

and radium to produce even temporary alleviation of symptoms, any permanent diminution in size of tumor or an arrest of growth in lymph nodes.

According to Malcolm Stening<sup>5</sup> (Royal Prince Alfred Hosp., Sydney), the essential features of the extended radical operation are to: (1) overcome vagaries of lymph node involvement and remove all affected nodes; (2) prevent local recurrence by deep, wide and bilateral excision of the primary growth; (3) remove the potentially affected intervening lymphatics from the growth to the superficial nodes by removal of tissue in continuity and in one stage. Occasionally the operation must be modified if the urethra or anus is encroached on or frankly involved. Surgery is extraperitoneal, therefore degree of shock is lessened and the approach is not attended by undue bleeding. Eight patients, aged 53-81, were treated by the extended technic since December, 1949, with no primary operative mortality. One patient, aged 81, died three months after hospital discharge with a terminal pulmonary condition with hemoptysis. Average time for safe discharge with almost full healing was six weeks; average time of postoperative ambulation was five days.

[It is generally believed that carcinoma of the vulva has a very poor prognosis but, as pointed out by Stening, carcinoma of the vulva can be viewed in its true perspective as being, next to cancer of the uterus, the least malignant type of growth in the female genitals because approximately 50 per cent of cases can be prevented by simple excision of precancerous leukoplakia of the vulva and over 60 per cent of patients can be permanently cured. The operation, however, is extensive, and since many patients are very old, great skill, patience, ample blood transfusions and good team work are required.—Ed.]

**Consideration of Ovarian Tumors with Special Reference to Their Malignant Potentialities.** Andrew A. Marchetti<sup>6</sup> (Georgetown Univ.) prefers Taylor's classification of ovarian tumors.

- I. Dysfunctional cysts of follicle and corpus luteum
- II. Endometrial cysts and endometriosis
- III. Primary ovarian neoplasms
  - A. Epithelial tumors
    - 1) Serous cystadenoma and cystadenocarcinoma  
Special type: adenocystic fibroma (Frankl)
    - 2) Pseudomucinous cystadenoma and cystadenocarcinoma  
Special type: mucous fibroepithelioma (Brenner)

(5) M. J. Australia 2:823-827, Dec. 2, 1950.

(6) S. Clin. North America 30:1767-1775, December, 1950.

- B. Connective tissue tumors
    - 1) Fibroma and fibrosarcoma
    - 2) Rare connective tissue tumors (myoma, lymphangioma, etc.)
  - C. Teratomas
    - 1) Dermoid (cystic) teratoma
    - 2) Complex (solid) teratoma
      - Special type: struma ovarii
  - D. Tumors arising from specific cells
    - 1) Granulosa cell tumor
      - Special types: folliculome lipidique (Lecene); theca cell tumor
    - 2) Arrhenoblastoma
      - Special type: testicular adenoma (Pick)
    - 3) Dysgerminoma
  - E. Doubtful tumors
    - 1) Endothelioma
    - 2) Hypernephroma
    - 3) Mesonephroma (Schiller)
- IV. Metastatic tumors of ovary

It is estimated that ovarian cancer occurs in less than 1 per cent of patients admitted to a gynecologic service, comprises about 15 per cent of all primary ovarian tumors and about 15 per cent of reproductive tract malignancies. Among tumors of small dimensions, the risk of encountering an ovarian cancer is small.

Endometrial cysts and endometriosis may undergo definite malignant changes in very few instances.

Of primary ovarian neoplasms, epithelial tumors predominate. The serous and pseudomucinous cystadenomas have highest incidence among benign tumors, and serous cystadenocarcinoma among the malignancies. Connective tissue tumors are essentially benign, especially their prototype, the fibroma. Of the teratomas, the cystic type is essentially benign, the solid type essentially malignant. Among tumors rising from specific cells of the gonad, granulosa cell tumor is commonest. Malignant potentialities of granulosa cell tumor and dysgerminoma are great; the arrhenoblastoma is primarily benign. Metastatic tumors of the ovary are pre-eminently malignant.

Management of ovarian tumors is surgical, the extent depending on the findings. Prognosis depends on the patient's age, whether the tumor is cystic, semicystic or solid, unilateral or bilateral, whether the process is still limited or has extended or disseminated and whether it belongs to a group or type with low grade or highly malignant characteristics.

## MENSTRUAL DISORDERS

**Injection Study of Blood Vessels of Bleeding Uterus.**  
Robert L. Faulkner<sup>7</sup> (Western Reserve Univ.) injected a synthetic liquid latex into the vessels of uteri which had been removed because of functional bleeding. The spiral arteries of the endometrium could not be filled. Although there have been many studies and much has been learned about menstrua-

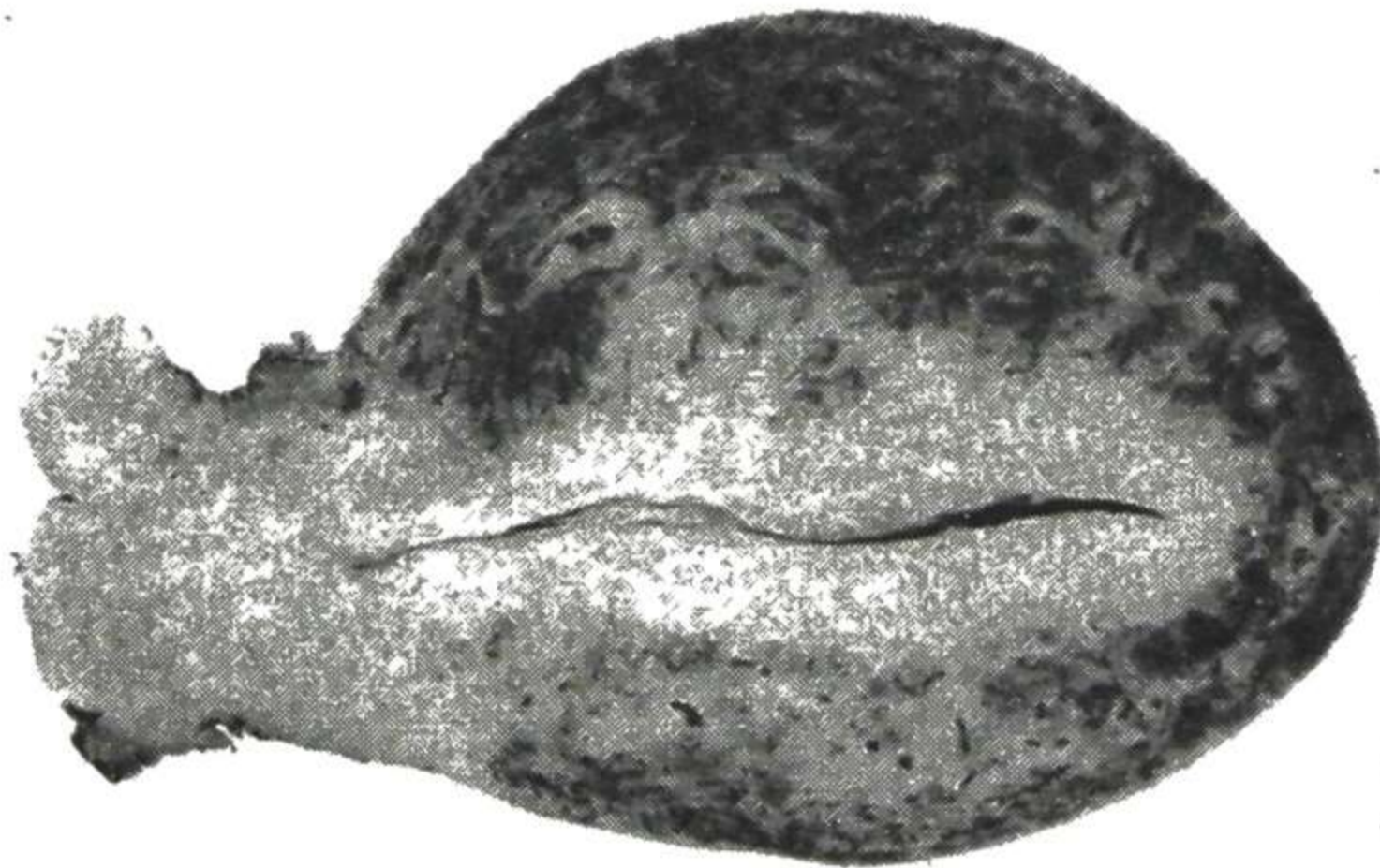
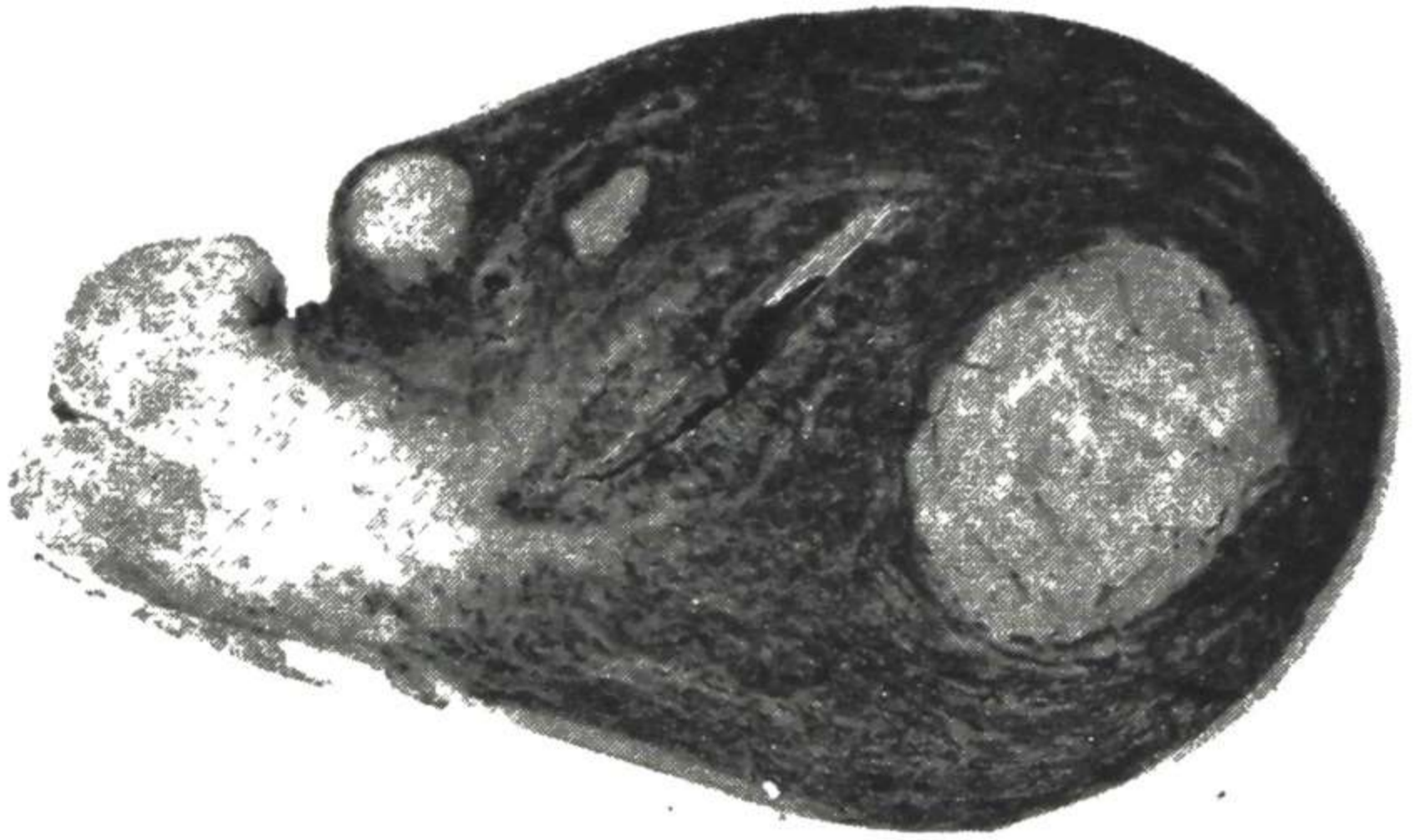


Fig. 131 (top).—During menstruation, venous mass appears in uterine cavity.  
Fig. 132 (bottom).—Little or no injection material in the inner myometrium and endometrium of a normal uterus after menstruation.  
(Courtesy of Faulkner, R. L.: *Am. J. Obst. & Gynec.* 61:766-773, April, 1951.)

(7) *Am. J. Obst. & Gynec.* 61:766-773, April, 1951.

tion, it is still a phenomenon and little knowledge concerning excessive uterine bleeding has been gained in the past 100 years.

Blood vessels of uteri which had bled irregularly or constantly from nonhyperplastic endometrium showed no definite vascular pattern, but had the ability to force venous injection mass into the uterine cavity at almost any time of the cycle (Fig. 131). Many uteri with hypermenorrhea without intermenstrual bleeding showed chronic passive congestion with dilatation or hypertrophy of the peripheral and endometrial veins.

In the uterus with good vascular control, little or no latex passed into the inner myometrium and endometrium immediately after menstruation (Fig. 132). In uteri bleeding from endometrial hyperplasia, patches of latex were apparent in the endometrial arteries and veins at almost any time. This supports the view that in hyperplasia there is hypertrophy or dilatation of the endometrial arteries.

**Diagnosis and Evaluation of Thrombocytopenic Purpura in Gynecologic Bleeding.** Walter J. Reich, Mitchell J. Nechtow, Alvin M. Kurzon and Thomas Mercer<sup>8</sup> (Chicago) report 15 cases in which the initial or predominating symptom was increased uterine bleeding. Patients were aged 15-58, with an average age of 30; two were under 20. Thrombocytopenic purpura is seen more often in females, and the genitourinary tract is a frequent site of bleeding. Uterine bleeding may commence at the expected menstruation time but differs from normal catamenia in profuseness and duration. The absence of other significant physical findings emphasizes the importance of incorporating a platelet count with the "routine" red blood cell count as a screening test in patients with hemorrhagic tendencies. Finding of pelvic lesions does not rule out presence of this disorder.

**Gonococci and Menstrual Cycle.** Tauno Putkonen and Kaarle Ebeling<sup>9</sup> (Kumpula State Hosp. for Venereal Diseases) studied the effect of different phases of the menstrual cycle on demonstration of gonococci in the cervix. Analysis was made of 807 smears and cultures obtained before treatment from 343 patients with cervical gonorrhoea. Positive re-

(8) *Am. J. Obst. & Gynec.* 61:589-595, March, 1951.

(9) *J. Ven. Dis. Inform.* 31:263-267, October, 1950.

sults for smears totaled 394 (48.8 per cent), for cultures 560 (69.4 per cent). Onset of menstruation was known in relation to 608 bacteriologic examinations during different phases of the menstrual cycle; onset of subsequent menstruation was known in 511. Results showed that the phase of the menstrual cycle is not important in demonstration of gonococci from the cervix by culture, since the incidence of positive results was about the same (70 per cent) during all phases. On the other hand, incidence of positive smears' was highest (59.6 per cent) during menstruation and slightly lower during the rest of the estrogenic phase. Significant decreases in the number of positive smears were obtained during the luteal and premenstrual phases. The lowest incidence of positive smears (36.4 per cent) was noted during the three days preceding menstruation.

**Effect of Menstruation on Skin Diseases.** The skin is influenced by the menstrual cycle through changes in the vasomotor system, increased reactivity to various stimuli, susceptibility to seborrhea and variations in perspiration. Skin diseases are often provoked or exacerbated and susceptibility to allergy increased. Acne, never observed before puberty, is particularly influenced. It may be due to too little ovarian activity, although seborrhea may be due to too much. Henri Vignes<sup>1</sup> (Paris) concludes that regulation of the patient's habits and use of sulfur are still more valuable than organotherapy in treating acne.

Erysipelas of the face often recurs during menstruation, sometimes at each period. Such episodes may indicate a streptococcic focus of infection, frequently rhinitis, and if repeated often may lead to chronic indurated edema. Erythema nodosum often appears premenstrually and toxic erythemas at onset of menses. Less often, eczema appears, either catamenial or recurrent, heralded a few days before the beginning of menstruation by pruritus, reddening and vesiculation in the zones previously affected. Anal fissures tend to become worse during menstruation, but injections of progesterone have given good results. Herpes appears before or during menstruation particularly in women complaining of dysmenorrhea; generally the same site, which may be the lips or genitalia, is affected. Hyperhidrosis is fairly common, and certain pig-

(1) *Gynéc. prat.* 1:219-229, 1950.

mentations increase at menstruation. Menstrual pruritus vulvae is not unusual, but the effect of menstruation on psoriasis seems slight. Scleroderma has been reported on cessation of menses, disappearing when menstruation recommenced. Seborrhoea often appears immediately before or after the beginning of menstruation, and urticaria is seen during the period in predisposed women.

Therapeutic results are contradictory, antagonistic hormones seeming to be as successful as those which should be most useful. It appears that the disorders in organic equilibrium producing these phenomena are not yet clearly understood.

**Further Observations on Age of Menarche** in relation to height and weight were made by Dagmar C. Wilson and Ian Sutherland<sup>2</sup> (Oxford) on 1,707 girls attending one boarding and five day schools in Dorset and one day school in Essex. Average age of menarche was determined by probit analysis which requires from each girl only her present age and whether or not periods have started. This is more accurate than direct questioning for age of onset.

In an earlier study in Oxford average age of day school girls at onset of menarche was 13.6. In the present day school group the average was 13.4, and in the boarding school, 13.9. The differences between the groups are significant, suggesting a relation between sexual maturity and social background, since the boarding school girls generally are more well-to-do. Over-all figures indicated that the age of menarche follows a normal frequency distribution, in which 1 in 100 will menstruate for the first time before 10 years 9 months and 1 in 100 after 16 years 3 months.

In each group, height and weight in any one age group were substantially greater among those who had attained the menarche. Both before and after menarche, there were interesting differences in mean height and weight. The greatest values throughout occurred at the boarding school and the lowest in the Dorset day schools. However, when a comparison was made of the height and weight of Oxford and Dorset girls who were at the same stage of sexual development and the same age at the time of study, the Oxford girls were superior in both. The conclusion, therefore, was that

(2) Brit. M. J. 2:862-866, Oct. 14, 1950.



absolute height and weight did not influence the age of menarche.

In a second study serial records of height and weight of 202 Sussex and 87 Yorkshire boarding school girls were taken, with particular interest in the four years following menarche. Mean ages of attainment of the menarche, with their standard errors, were  $13.11 \pm 0.09$  (Sussex) and  $13.82 \pm 0.14$  (Yorkshire). At each age, the Sussex girls were taller and heavier. Because the age of menarche was lower in Sussex girls than in girls of either day or other boarding schools, the conclusion that age of menarche tends to be greater in the more favored social and economic groups is doubtful. Comparison of girls at the same stage of sexual maturity but of different ages and girls of the same age but of different sexual maturity indicated that weight in adolescence depends not only on age but also on stage of sexual maturity. Similar comparisons with height instead of weight indicated that between 13 and 17 height varied only with age, being independent of sexual maturity. Body build (height in inches divided by cube root of weight in pounds) at the menarche was independent of age. For the following two years at least, girls become heavier for their height, to an extent which is also independent of age.

It is concluded that growth in the adolescent girl is of two types. On one, normal physical growth with age, is superimposed the changes specifically related to sexual maturation.

**Irregular Shedding of Endometrium** is a condition in which there is a prolongation of the normal process of shrinking, shedding, involution and finally epithelization of what had been secretion phase endometrium. According to John L. McKelvey<sup>3</sup> (Univ. of Minnesota), there may be sufficient blood loss to cause severe secondary anemia even though characteristically there is no interference with the general mechanism of hemostasis and clotting. The cycles may come at slightly prolonged intervals but usually are sufficiently regular to make it obvious that menorrhagia is present. The bleeding seldom lasts beyond 12 days although one patient bled for 21 days of a 32 day cycle. Shedding and involution are slow, incomplete (by reason of retention of a grossly abnormal amount of secretion phase, changed endometrium)

(3) Am. J. Obst. & Gynec. 60:523-527, September, 1950.

and irregular (all stages of involution may be seen histologically, scattered through a single endometrium). Typically the 30-40 age group is affected, the condition developing gradually or appearing suddenly with re-establishment of menses post partum or post abortum.

With one exception, every patient with the histologic picture of irregular shedding also had persistence of pregnane-diol excretion after onset of bleeding. Moreover, E. G. Holmstrom was able to reproduce the histologic lesion in human endometrium by administering progesterone during the last portion of the cycle and early menstruation. It would appear that, in irregular shedding, progesterone is present in sub-threshold quantity, insufficient to prolong the cycle significantly and preserve the endometrium but sufficient to interfere with normal shrinkage, shedding, involution and healing.

Curettage (on the fifth to eighth day of bleeding) is essential for diagnosis and is curative in almost half the cases. Many patients with minor degrees of duration and quantity of blood loss prefer to put up with the complaint when assured that it is devoid of danger. Near menopause, x-ray sterilization may be used. Occasionally in young patients with severe bleeding, hysterectomy may be necessary.

**Relation of Endometrium to Chorioplacental Development and Its Gonadotrophin Output.** This is a comparative study of the endometrium of 324 patients who had a history of sterility and/or abortion. Edward C. Hughes, Albert W. Van Ness and Charles W. Lloyd<sup>4</sup> (Syracuse Univ.) noted the histologic appearance of the endometrium and determined its content of glycogen, alkaline phosphatase and vitamin C. These values were further correlated with chorionic gonadotrophin output and in some instances with progesterone levels.

Samples of endometrium were reviewed on the 26th day of the cycle. Fifty-eight per cent of patients did not have normal endometrial glycogenesis. In 15 per cent of this group, there were ample amounts of alkaline phosphatase with this glycogen deficiency and this condition was accompanied by sterility. Other patients showed deficiency of alkaline phosphatase and/or vitamin C. In many instances the typical histologic picture of a secretory endometrium was found even in presence of chemical deficiencies.

(4) Am. J. Obst. & Gynec. 60:575-585, September, 1950.

In 126 abortions the following changes were noted: (1) thrombosis, necrosis and hemorrhage in 30.9 per cent; (2) immature development of chorionic villi in 59.9 per cent, characterized by avascularity and edema, even when the embryo was expelled alive; (3) premature separation of the circumvallate placental formation in 5.3 per cent; and (4) degeneration of the products in 3.9 per cent. The endometrium was of poor quality in 71 per cent of these cases.

Output of chorionic gonadotrophin was measured in 40 patients before abortion, and the levels remained much below normal when the cytotrophoblast failed to develop. When chorionic gonadotrophin output was low but secretion of progesterone was normal, the pregnancy continued for a longer time, but complications developed in later pregnancy and changes found in the placenta included immaturity, avascularity and edema of the villi.

Development of the trophoblast (and the chorion) depends on normal germ plasm, adequate endometrial secretion and enough chorionic gonadotrophin to stimulate the decidua to put forth adequate amounts of food for growth of the embryo. Alteration of these relations produces abortion in many instances. Endocrine abnormalities are usually found when there is a faulty endometrium. Satisfactory treatment of these patients should be directed to improvement of the endometrium before conception, in part at least through endocrine therapy.

**Premenstrual Tension** is a symptom complex which begins about 10-14 days premenstrually, reaches its peak shortly before menstruation and disappears dramatically after onset of menstrual flow. It is characterized by a feeling of mild depression or anxiety and is associated with symptoms such as headache, insomnia, emotional instability, fatigue, painful swelling of the breasts, increased appetite, low abdominal pain (not associated with ovulation), abdominal bloating, nausea with occasional vomiting, and rarely increased libido.

Joseph H. Morton<sup>5</sup> (New York Med. College) studied 29 patients with premenstrual tension by means of: endometrial biopsy before and after onset of menstruation (within 18 hours); vaginal smear taken during the premenstrual phase; premenstrual hormone assay on 24 hour urinary output; daily

(5) Am. J. Obst. & Gynec. 60:343-352, August, 1950.

record of basal temperature and body weight; basal metabolic determination; capillary permeability determination (fluorescein method); serum and urine sodium, potassium and chloride determinations made before and after menstruation, and oral sugar tolerance curves plotted in the premenstruum and occasionally postmenstrually.

Daily basal temperatures, endometrial biopsy, vaginal smear and urinary hormones indicated decreased or absent secretion of progesterone which permitted uninhibited increase in estrogen in the premenstrual phase. Basal temperatures failed to show the abrupt rise at midcycle attributed to progesterone secretion and often presented irregularities associated with diminished luteal activity. The endometrium displayed a proliferative (or hyperplastic) or mixed proliferative and luteal picture on biopsy, indicating diminished luteal activity. Vaginal smears showed persistence of cornified cells throughout the cycle. Urinary hormonal assays revealed subnormal or absent pregnanediol excretion in 10 of 14 patients tested. On the other hand, two women who had been castrated surgically and one postmenopausal woman were given large doses of estrogen, with subsequent development of symptoms of premenstrual tension.

The fluorescein test showed a trend toward increased capillary permeability in the premenstruum, especially in the breast. A tendency toward decreased sodium and slightly increased potassium in blood serum was noted in the premenstrual phase, whereas the opposite was found postmenstrually. Urinary output premenstrually was less than in the postmenstrual phase. Weight gain also occurred premenstrually. Basal metabolic rate ranged from  $-2\frac{1}{2}$  to  $-15$  per cent in most cases. Glucose tolerance tests showed increased premenstrual sugar tolerance in many cases, which accounts for increased appetite, craving for sweets, weakness, chronic fatigue and development of trembling of the hands described by patients as the "shakes." Some patients had hypoglycemic attacks which responded to ingestion of orange juice or milk.

On the basis of the results, Morton's approach to therapy was based primarily on the luteotrophic effect of chorionic gonadotrophin to increase progesterone secretion and thus correct the estrogen-progesterone imbalance. This preparation was given in doses of 500-1,000 units twice weekly for

the last two weeks of the menstrual cycle, but no injection was given within three or four days of the expected menstrual period. Edema and weight gain were combated with salt restriction and diuretic and antispasmodic drugs; for hypoglycemia, a high protein, low carbohydrate diet with frequent feedings was prescribed. Thyroid extract and vitamin B were given as indicated. With treatment, striking improvement ensued. Some patients who had not responded to psychiatric care improved mentally and physically. In one patient who uniformly lost sugar tolerance with menstrual onset to regain it at midcycle, large doses of estrogenic hormone decreased the amount of insulin required.

[Freed and I postulated a single mechanism for the development of the variety of symptoms of premenstrual tension. According to this hypothesis, premenstrual tension is due to sodium ion retention by the different tissues of the body under the influence of the ovarian steroids. This retention is associated with an increase in extracellular fluid in the tissues which may be microscopic or may develop into gross edema. The neurologic symptoms result from edema of the nervous system, probably the brain; the nausea and distention of the abdomen result from edema of the intestines, and the other symptoms arise from edema of the specific organs affected. On the basis of this hypothesis we instituted therapy designed to withdraw the excess sodium and associated fluid, administering ammonium chloride by mouth, although not in the usual diuretic doses. Apparently the ammonium ion is changed to urea, resulting in an excess of chloride ion. Patients are advised to omit table salt during the last two weeks of the menstrual cycle, at which time they take 0.6 Gm. ammonium chloride three times daily.

Argonz and Abinzano (*Endocrinology* 10:1579, December, 1950) treated premenstrual tension with vitamin A in two daily doses of 100,000 I.U. taken immediately after lunch and dinner, beginning the fifteenth day of the cycle and continuing to the first day of menstruation. Considerable improvement was obtained by most patients.

According to DeWit (*Acta endocrinol.* 5:173, 1950), of migraine related to menstruation, observed in 60 per cent of cases, pure premenstrual migraine is found in 30 per cent, and 13 per cent show premenstrual as well as intermenstrual migraine. Allergic reactions were noted in 39 women (56 per cent) and 11 had an attack of migraine as well. All 38 patients with premenstrual and menstrual migraine were allergic (38 cases), 11 having severe allergic reactions. If all cases of migraine were considered in which the attacks were related to the menses, positive allergic cases amount to 93 per cent. It might therefore be important to apply desensitization therapy in cases of premenstrual migraine.—Ed.]

**Metrorrhagia during Premenstrual Period Produced by Progesterone in Women with Normal Menstrual Cycles.** In a study of female sterility, I. Halbrecht<sup>6</sup> (Israel) found indications that in some women the secretion of corpus luteum was inadequate. The temperature curve, recorded regularly

(6) *Presse méd.* 58:845-846, July 22, 1950.

during several menstrual periods, showed a rapid fall several days before advent of the period or during the luteinic stage, which was shortened from the normal 12 or 13 days to 6 or 7.

Histologic examination of endometrial biopsies before onset of the period showed a poorly developed secretion. It seemed most probable that the sterility was caused by an endometrium poorly prepared for innidiation of the ovum.

Halbrecht gave 5 mg. progesterone daily, starting 15 days after onset of menstruation, to 113 women whose menstrual cycles were 27-29 days. In 76 patients, periodicity was not affected; in 8, menstruation was delayed two to five days. In 29 women, metrorrhagia, resembling in every respect normal menstruation, appeared after the 2d to 4th injection of progesterone, that is, on the 18th or 22d day of the menstrual cycle which it shortened by 4-11 days. The basal temperature curve, recorded over several menstrual periods, disclosed that metrorrhagia was not dependent on the condition of the endometrium and recurred every time the drug was given. In 51 cases, diethylstilbestrol was added to the progesterone without influencing results. Nine women treated with progesterone in the premenstrual stage became pregnant two to six months after treatment, but it is doubtful whether this was related in any way to administration of progesterone.

Halbrecht considers the use of progesterone injections in imminent abortion—a popular therapy—not only deceptive much of the time but in certain cases productive of increased hemorrhage during pregnancy.

[The author raises a pertinent question: Is it not possible that administration of progesterone during pregnancy may aggravate bleeding? In other words, could not the use of progesterone in cases of threatened abortion do just the reverse of what it is intended to do? Several years ago I had two patients with threatened abortion, in both of whom injection of progesterone was soon followed by severe uterine cramps and increased bleeding.

Lindemann (*Zentralbl. Gynäk.* 72:480, 1950) administered neostigmine to 73 women who were beginning to have an abortion. The ovum was expelled spontaneously in 56 cases and in 14 others after a second series of injections. However, the drug had no effect on intact pregnancies.—Ed.]

**Histology of Endometrium in "Organic Uterine Hemorrhage."** Arthur M. Sutherland<sup>7</sup> (Glasgow) compared histologic findings in the endometrium in 1,000 cases of abnormal uterine bleeding in the presence of gross pelvic disease with those of a previous series of 1,000 cases without gross pelvic

(7) *Lancet* 2:742-745, Dec. 9, 1950.

disease. Postmenopausal bleeding and all types of abortion were excluded.

In 90 patients in the present series organic pathologic lesions of the endometrium were found. Forty had chronic endometritis, compared with 110 in the previous "functional" series. Since chronic salpingitis or salpingo-oophoritis was present in 141 with organic disease and chronic parametritis in 27, high incidence of endometritis might reasonably be expected. Uterine polyps were found in 18 patients, tuberculosis in 9 and malignant disease in 23. All patients with malignancies were over 30; carcinoma of the uterine body occurred in 19 and sarcoma in 4.

Of the 910 patients without organic pathologic conditions, endometrial hyperplasia was found in 195, endometrial atrophy in 49 and irregular ripening of the endometrium in 18; 648 specimens appeared normal. These histologic findings are essentially similar to those in the functional series, except for the incidence of chronic endometritis. It is impossible to say how often the associated gross pelvic disease is responsible for abnormal bleeding in such cases. Though bleeding often stops after removal of the presumed causal condition, many patients with fibroids, salpingo-oophoritis or other gross pelvic lesions have normal menstrual cycles. Perhaps too much emphasis may previously have been laid on endometrial histologic appearance in functional uterine hemorrhage. The necessity for routine histologic examination of the endometrium in all cases of abnormal bleeding, whatever the patient's age, is apparent.

**Management of Functional Uterine Bleeding.** It is not sufficient to arrest bleeding in 50-60 per cent of patients as is the case when a single hormone is used. With combined hormone therapy, Robert B. Greenblatt<sup>8</sup> (Univ. of Georgia) states that excellent results may be expected in 95 per cent or more.

A combination of 10,000 R.U. estradiol benzoate, 25 mg. progesterone and 25 mg. testosterone propionate is given daily for three to five days. If bleeding stops promptly after the first injection, dosage may be cut in half on the second day and reduced to one-fourth on the third, fourth and fifth days. Bleeding usually stops in 6-24 hours, although spot-

(8) M. Clin. North America 34:1551-1565, September, 1950.

ting may continue for a few days. Withdrawal bleeding takes place one or two days after cessation of therapy; this will simulate a normal menses and will last four to six days. Withdrawal bleeding may seem excessive the first day or two but usually subsides gradually. The patient should be warned to expect withdrawal bleeding or she will believe hemorrhage has recurred. About 20 days later a course of 150 mg. anhydrohydroxy progesterone (10 mg. three times a day for 5 days) is given to induce withdrawal bleeding. Such a course is given each month for three to five months or longer until normal cyclic bleeding resumes. This can be determined by basal temperature records or suction curettage at onset of menses to learn if ovulation has occurred. Often, if there is spotting after arrest of bleeding, small doses of estradiol, estrone sulfate or a similar preparation may be given orally for 15-20 days followed by anhydrohydroxy progesterone.

After therapy, correction of the original cause of the bleeding should be undertaken. Thyroid therapy, if indicated, vitamins and iron medication should be administered. In women over 36, curettage should be performed to rule out malignancy; it may also be expedient in patients whose hemoglobin value is below 45-50 per cent. In some patients bleeding is due to a physical or psychic maladjustment, and results often may be influenced by suggestion. Endocrine therapy is most successful in correcting the underlying disorder when the patient is made receptive. It is particularly of value in adolescent girls or young women of childbearing age. Surgery and radiation therapy should be reserved for patients nearing or past the menopause.

[I have used the group of hormones recommended by Greenblatt, namely, 25 mg. progesterone, 25 mg. testosterone propionate and 1 mg. estradiol dipropionate, for four consecutive days in many cases of bleeding and have had fairly good results. It cannot be emphasized too often that the causes of bleeding must be eliminated; especially must carcinoma be ruled out before any endocrine therapy is given.

Kantor and Klawans (*S. Clin. North America* 30:287, February, 1950) maintain that since 75 per cent of all organically produced postmenopausal bleeding is due to malignancy, early diagnosis and treatment are the only real hope we have for reducing the death rate of female genital tract malignancies. The authors present a useful tabulation of differential diagnosis of all bleeding which may occur during the menopause. Their incidence of 75 per cent for cancer as the cause of postmenopausal bleeding is higher than that reported by several other investigators. In a study by the authors in 1932, the incidence of malignancy was 68.58 per cent.—Ed.]



**Estrogen Therapy in Relation to Functional Uterine Bleeding.** All patients with presumed functional bleeding should have a preliminary diagnostic curettage to eliminate unsuspected organic conditions of the endometrium. In 1,000 patients with abnormal uterine bleeding in absence of gross pelvic pathology, Arthur M. Sutherland<sup>9</sup> found 139 organic endometrial lesions (chronic endometritis in 110, uterine polyps in 11, tuberculosis in 10 and malignant disease in 8). In patients with a reasonably regular menstrual cycle, curettage should be performed in the premenstrual phase. If it reveals no endometrial abnormality, repeat curettage may be necessary on or after the fifth day of a subsequent bleeding period to determine whether the cause is irregular shedding of the endometrium.

In 861 cases there was no histologic evidence of organic disease. Such patients should be followed; many will be cured by curettage, but others require further treatment. With rare exceptions, either hysterectomy or radiotherapy is preferable to endocrine treatment for persistent bleeding in patients over 40. Patients 20-40 can usually be treated successfully with estrogens or, when endometrial hyperplasia is pronounced, with androgens. The patient not improved by such treatment should be hospitalized again for further study, including detailed blood examination, estimation of prothrombin time and urinary vitamin C, basal metabolic rate, Wassermann reaction and, in circumstances previously indicated, repeat curettage. Patients with a possible psychologic basis for the bleeding should be seen by a psychiatrist.

[I agree with Sutherland that in many cases of bleeding in the reproductive period, i.e., between 15 and 45, the menorrhagia can often be treated successfully by estrogens. Of course, the male hormone can be successfully used in the same type of cases. As pointed out by Elghammer and his associates (1950 YEAR BOOK, p. 526), physicians should study the systemic blood clotting mechanism in women who have profuse uterine bleeding and not focus their entire attention on the local changes in the pelvis. In some cases of abnormal uterine bleeding antiheparin factors such as toluidine blue are distinctly helpful.—Ed.]

**Evaluation of Irradiation Therapy for Nonmalignant Uterine Bleeding at University of Virginia Hospital:** William N. Thornton, Jr., John M. Nokes and Dwight J. Brown, Jr.<sup>1</sup> reviewed 348 cases of benign uterine bleeding treated by

(9) Proc. Roy. Soc. Med. 43:731-734, October, 1950.

(1) Am. J. Obst. & Gynec. 61:75-79, January, 1951.

intracavity irradiation or roentgen ray therapy from 1925 to December 1948. Average age of patients was 47.5 years. Abnormal bleeding was associated with fibromyomas in 79 cases. A total of 259 patients (74.1 per cent) received 1,500-3,000 mg.-hr. of irradiation. Tendency to increasing dosage in the past decade is probably due to recurrent bleeding associated with use of small dosages.

In 178 (51.2 per cent) cases, all but 2 followed from 6 months to 21 years after initial treatment, 26 nonmalignant and 8 malignant complications developed. In three patients adenocarcinoma of the endometrium developed 14, 4½ and 3 years after initial treatment; papillary adenocarcinoma involving the cervix, uterus and ovary developed in one 3 years after treatment; sarcoma eventually developed in three, one of whom also had adenocarcinoma; cervix carcinoma appeared in one 5¾ years after original therapy and adenocarcinoma of the ovary in one, 4½ years after treatment. Recurrence of bleeding was the chief nonmalignant complication, treated by curettage, hysterectomy or additional irradiation. Despite careful selection of patients, it is not always possible to exclude cases in which pelvic irradiation is contraindicated. One patient died after intracavity irradiation in an unrecognized pelvic tuberculosis. Surgery with preservation of ovarian function is preferred to pelvic irradiation in women age 40 or younger. At present, pelvic irradiation should be reserved for patients with benign endometrial bleeding requiring treatment in whom major surgery is contraindicated.

[I fully agree that prolonged follow-up is necessary to evaluate the end results of pelvic irradiation for benign uterine bleeding. I have encountered carcinoma of the endometrium many years after irradiation for nonmalignant uterine bleeding. During the last few years, except in extremely poor operative risks, I have given up irradiation for benign uterine bleeding, preferring to remove the uterus either vaginally or abdominally.—Ed.]

**Ill Effects of Radium Menopause**, discussed by Hugh C. McLaren<sup>2</sup> (Univ. of Birmingham), include flushing and sweating, loss of libido and premature senile changes in the genital tract. A total of 118 patients were examined an average of two years after receiving intrauterine radium (2,400 mg.-hr.). Flushing, the outstanding symptom, was severe in 4 per cent of patients, moderately severe in 45 per cent, mild in 44 per cent and absent in 7 per cent. Incidence of serious

(2) Brit. M. J. 2:76-80, July 8, 1950.

and persistent flushing after irradiation was three times normal. Spontaneous cure resulted in only 13 patients; 4 grew worse with time and the remaining 54 (76 per cent) continued to have flushing of unabated severity.

Reliable evidence as to the effect of radium on sex urge was available in 143 cases. Sex urge, which was already depressed or lost in about 50 per cent, suffered further as a result of radium castration. Of 77 patients estimated to have normal libido, 55 (71 per cent) had striking diminution or became entirely without libido after treatment. Orgasm, already infrequent or absent in 61 (48.4 per cent) before treatment, was further affected by radium; 34 patients (52 per cent) who normally achieved orgasm found this no longer possible. Dyspareunia was evident in about 10 per cent. Vulvitis secondary to vaginitis was observed in 2 of 82 patients and the introitus appeared abnormal in 7 of 72. Bleeding mucosal spots, termed senile vaginitis, were noted in 11 of 68 patients examined. In addition, atrophic changes were noted in the cervix, and 70 per cent of vaginal smears examined showed varying numbers of intermediate or senile cells.

Patients should be followed by the gynecologist who induced the menopause rather than by the family physician. If patients are seen at three to four month intervals for three years, severe flushing and minor genital lesions may be diagnosed and adequate dosage of diethylstilbestrol established to improve ill effects after radium. By these simple measures most of the criticism leveled at radium therapy could be overcome and further support given to it as a safe and effective means of dealing with intractable menopausal bleeding.

[I long ago gave up use of radium for benign conditions, except in rare instances and in poor risk patients. I am not concerned about the induction of menopausal symptoms, because these would occur anyway, even with the natural menopause. I am somewhat concerned about the development of carcinoma years after the use of radium, because of my personal experience and because of the report by Corscaden, Fertig and Gusberg (1946 YEAR BOOK, p. 556). These authors followed up 958 women who had been irradiated for benign climacteric bleeding and found the incidence of cancer to be 3.4 times the incidence in the normal population. Speert and Peightal (Am. J. Obst. & Gynec. 57:261, 1949) found that 21 of 270 patients (9 per cent) with endometrial cancer had had irradiation for benign conditions, but in 3 of the 21 the carcinoma was diagnosed within 18 months after radiotherapy, so, the cancers may have been present at the time of irradiation.—Ed.]

**Causes and Treatment of Menopausal Bleeding** are discussed by John I. Brewer<sup>3</sup> (Northwestern Univ.). Age 45 was

(3) Postgrad. Med. 9:419-422, May, 1951.

selected arbitrarily as the relative time of beginning of the climacteric and one year after the last menstrual period as the end. Any bleeding one or more years after cessation of the last menstrual period is abnormal and should be investigated, however minimal. From 5 to 17 per cent of women with abnormal bleeding during the climacteric have malignancy of the genitalia. Investigation of patients must go far beyond clinical examination, since it is absolutely impossible, visually or by palpation, to diagnose early cervical carcinoma. Biopsy may be used instead of Papanicolaou smears, but use of both will increase correct diagnoses. Patients with abnormal bleeding are often not investigated because of previous curettage, although re-examination should take place at definite intervals. There may be no investigation because the patient is receiving estrogens. Estrogens should be discontinued; if bleeding continues over three weeks it must be assumed to be due to a specific lesion and not to endocrine therapy.

Patients should be hospitalized if it seems improbable that bleeding is from a polyp; if bleeding is continuous or continues after polypectomy; if smear, biopsy or polyp suggests malignancy; if dilatation is necessary for cervical stricture; if the pedicle or polyp is large, or if polyps recur. Patients with fibroids and bleeding are usually treated by hysterectomy. Cervical carcinoma is treated by radium (4,000-5,000 mg.·hr.) followed by roentgen therapy (7,000-9,000 r measured in air). Preliminary radium therapy is preferred for endometrial cancer, followed in about four weeks by complete abdominal hysterectomy and bilateral salpingo-oophorectomy. Usually, roentgen therapy is also given. Functional bleeding is best managed by curettage; if this is unsuccessful, vaginal hysterectomy is performed. In general, curettage relieves about a third of patients. The remaining two-thirds are preferably treated by vaginal hysterectomy. Indications for hysterectomy are: abnormal bleeding after dilatation and curettage, profuse or persistent bleeding or presence of persistent atypical cells in the vaginal smear. In almost all patients with relaxation plus bleeding, prolapse of the uterus plus bleeding, uncontrollable anemia or a large uterus which may contain adenomyosis plus bleeding, vaginal hysterectomy is performed. Other indications are severe dysmenorrhea plus bleeding, coexisting pelvic pain of unknown origin and concern of the patient over malignancy.

Since incidence of cancer is about 60 per cent in women with postmenopausal bleeding, these patients must be investigated without exception. In postmenopausal and climacteric patients, irradiation is not used for benign lesions; hysterectomy or more minor surgery is preferred. Irradiation is used when there are definite contraindications to hysterectomy or malignancy is present.

**Rational Therapy for Secondary Amenorrhea.** Ideally, endocrine therapy should re-establish normal cyclic ovulatory menstruation without necessitating continuous therapy. Metabolic and physical defects must be corrected in an effort to reinstitute ovulation, and estrogen and progesterone administered as substitution therapy to induce bleeding. Such substitution therapy may have a stimulative effect on the pituitary gland or ovary or both. However, simple substitution therapy in treatment of menstrual disorders is not adequate therapy. Every effort must be made to stimulate the ovary or eradicate the factors that depress it.

William P. Given, Ralph W. Gause and R. Gordon Douglas<sup>4</sup> (Cornell Univ.) treated 50 patients with estrogen in the form of ethinyl estradiol (eticylol<sup>®</sup>) and anhydrohydroxy progesterone (lutocylol<sup>®</sup>), a form of oral progesterone that can be administered sublingually or buccally. Initial therapy in most cases included weight reduction and administration of thyroid. Attempts were made to bring the basal metabolic rate to —8 per cent or above. The patient was given 50 mg. progesterone (lutocylol<sup>®</sup>) parabuccally daily for four days, if after three months no menses occurred on weight reduction and adequate replacement of thyroid. The same medication was repeated on the 23d to 26th day of the subsequent cycle, if adequate withdrawal bleeding followed completion of the initial four day course. If bleeding did not occur after two courses at monthly intervals, ethinyl estradiol (eticylol<sup>®</sup>) was given in doses of 0.02-0.05 mg. daily for 21 days, followed by 50 mg. progesterone linguets<sup>®</sup> daily for 4 days. Patients were seen regularly during the third week of the cycle, and all therapy with progesterone or estrogen and progesterone was discontinued if the basal body temperature chart showed evidence of ovulation at this time.

Every patient bled as a result of therapy. One patient bled

(4) New England J. Med. 243:357-362, Sept. 7, 1950.

after weight reduction of 18 lb. Twenty per cent of the patients menstruated three to five months after thyroid therapy was initiated, and 39 (78 per cent) failed to menstruate after weight reduction and thyroid replacement; of these, 25 responded to a course of progesterone linguets.<sup>®</sup> Fourteen (28 per cent) did not respond to either thyroid or thyroid and repeated courses of progesterone. All 14 eventually menstruated after completion of the estrogen-progesterone therapy. Of the 50 patients, 20 showed evidence of ovulation at least once during follow-up study. Five pregnancies occurred in this group.

[The fact that all 50 treated patients with secondary amenorrhea were made to bleed shows that this is possible in nearly all instances. However, this does not mean that these 50 patients were capable of having babies. In 20 of the 50 patients, ovulation was noted one or more times, but one does not know in how many cases ovulation would have occurred without treatment. There were only five pregnancies among the 50 patients (10 per cent). As a rule there is no harm in permitting young girls to go to age 17 without menstruating, provided a rectal examination reveals nothing abnormal. However, after 17, efforts should be made to induce menstruation. Unfortunately there is no successful specific therapy. The girls who require thyroid therapy, should of course, have it; in fact, they should have had it before age of 17. Estrogens and progesterone given singly or in combination will produce bleeding but rarely ovulation. Pituitary preparations are the logical agents for inducing ovulation, but available preparations give results far from satisfactory. When the usual methods fail, x-ray treatment of the pituitary gland may be tried. Only experienced roentgenologists should carry out this type of treatment.

Kurland (*Fertil. & Steril.* 2:61, January, 1951) reports on 12 patients treated with pregnant mare's serum in six years. Four became pregnant and delivered babies at term. All had anovulatory cycles, proved by endometrial biopsies and basal temperature readings. Total dose was 150 Cartland-Nelson units in the form of gonadogen<sup>®</sup> given intramuscularly in three equally divided doses on days 1, 3 and 5 following the end of menstruation. This is a surprising result when we consider that Rydberg and his associates use enormous doses of pregnant mare's serum, noted in several previous YEAR BOOKS.—Ed.]

**Experiences in Use of Extended Method of Hypogastric Sympathectomy (Sympathycectomia Hypogastrica Subtotalis) in Treatment of Primary Algomenorrhea.** Paavo Vara<sup>5</sup> (Univ. of Helsinki) recommends that the term algomenorrhea be used instead of dysmenorrhea to define all painful conditions synchronous with menstrual bleeding, the latter term being limited to dysfunction of the menstrual mechanism, with or without pain. For algomenorrhea Vara resects the hypogastric sympathetic nerve.

(5) *Acta obst. et gynec. scandinav.* (suppl. 5) 30:1-47, 1950.

TECHNIC.—A vertical abdominal incision is made and appendectomy performed. Then the posterior parietal peritoneum is incised and stripped from the subperitoneal tissue, after which the fibers of the presacral nerve can be seen. A segment of about 5 cm. is resected; the middle sacral artery and vein are ligated and cut to expose the promontory. The sympathetic trunk is identified 1-2 cm. from the promontory. The first sacral ganglion is stripped from its bed and the sympathetic trunk divided caudal to it. The fifth lumbar ganglion is freed and the trunk divided above it. The resection includes 4-6 cm. of sympathetic trunk. Nerve ends are ligated, parietal peritoneum is sutured and the wound is closed with catgut. The operation is always bilateral.

This procedure was performed on 65 patients aged 19-40. In most cases preliminary tests were made before operation. Forty-nine women were single and 16 married, 4 of whom had children. Sympathectomy was successful in 49 patients and partially successful in 4. Menstrual flow became normal and there were no urinary or intestinal complications. Postoperatively, nine women gave birth to infants; all had painless and rapid deliveries. The dilatation stage was short and pain absent, except when pressure was applied on the rectum in the final stage.

In all cases studied histologically the cranial hypogastric plexus and sympathetic ganglions showed degenerative changes. This suggests that painless movements of the uterus may become painful because of hypersensitivity of the sensory nerves.

Patients with algomenorrhea are those whose vegetative nervous system reacts to the slightest irritation, which produces a reciprocal chain reaction between primary cause and secondary effect, each component intensifying the action of the other.

[Alleviation of pain in 98 per cent of cases is a better result than anyone has obtained except Cotte, who devised the operation of pelvic sympathectomy. From my experience I should say that when patients are properly selected for sympathectomy, 85-90 per cent should be improved. Cotte, one of the foremost gynecologists in France, died Jan. 3, 1951.

Dumont (*Gynec. et obst.* 50:35, 1951) analyzed the labors of 38 primigravidas who gave birth to children after pelvic sympathectomy successfully done to relieve dysmenorrhea. Seventy-six per cent had much less pain than usual during labor, but this diminution in pain occurred only in the first stage, which appeared to be shortened.—Ed.]

**Anovulatory Menstruation in Women.** Ada S. H. Wong, Earl T. Engle and C. L. Buxton<sup>6</sup> (New York City) obtained 47 endometrial biopsy specimens from 36 sterility patients

(6) *Am. J. Obst. & Gynec.* 60:790-797, October, 1950.

with proved anovulatory cycles. None had had previous hormone therapy. Biopsies were done within 48 hours before the onset of menstrual flow to exclude cases of doubtful ovulation or short secretory phase.

The basal body temperature chart, the most popular method for determination of ovulation, is not as reliable as endometrial biopsy since there may be a variability of as much as four or five days between ovulatory temperature rise and actual ovulation.

Anovular cycles in the 36 patients varied from one to five; 19 patients were anovular continuously while under investigation for several months to a year and the others periodically so. Thirteen patients had normal menstrual history and one menorrhagia; the rest had had oligomenorrhea or secondary amenorrhea. The first group were mostly sporadically anovular. In sterility patients a clinical history of obesity, hirsutism or menstrual irregularities suggests anovulation since these findings are manifestations of hormonal imbalance.

The endometrial picture of anovular cycles can be classified as (1) active and (2) inactive proliferative. In the former, aberrant mitoses, many of which are apical in position, seem to be in various stages of extrusion; in the latter, mitoses are absent but the so-called peg cells are apparently in a similar process of being extruded. This suggests low estrogenic activity. The coiled endometrial arterioles form few loops and are seen only in the deeper layer of the endometrium so that many specimens do not contain arteriolar fields at all. These arterioles are thin walled and differ strikingly from their counterparts in the secretory endometrium.

**Hormonal Changes Following Low Dosage Irradiation of Pituitary and Ovaries in Anovulatory Women.** A. E. Rakoff<sup>7</sup> (Jefferson Med. College) studied 12 patients: 7 had gonadotrophic deficiency, 4 primary ovarian deficiency and 1 an adrenogenital syndrome. All were observed for at least two years before radiation therapy and had failed to respond to usual methods of treatment, including administration of various vitamins and hormones. Urinary assays for gonadotrophins, estrogens and, in one case, 17-ketosteroids were done weekly for one month before irradiation. Basal temperature charts were made and vaginal smears studied cytologically;

---

(7) *Fertil. & Steril.* 1:504-516, Nov.-Dec., 1950.



in most cases endometrial biopsies were also done. These studies were continued during the treatment period (Kaplan's technic was used) and for six months after irradiation.

Seven patients were clinically improved, two becoming pregnant and five having improved menstrual function. Improvement in hormonal status, noted in a month or two, appeared in some patients with each type of endocrine disorder but most consistently in those with gonadotrophic deficiency. Hormonal excretion patterns suggested that the primary beneficial effect was usually on the ovaries, but there was a possibility of a primary effect on the pituitary in some patients with gonadotrophic deficiency. No untoward effects were noted.

Studies on animals have not been of much help in determining the mechanism by which irradiation is effective. One group of investigators failed to note any change in normal physiologic function in rabbits given varying dosages to the pituitary gland. In another study small or moderate dosage to the pituitary of rabbits produced no change in the gland or ovaries. When dosage was increased to 1,000 r, given in five divided doses over two weeks, corpora hemorrhagica and corpora lutea appeared in the ovaries of some of the animals. Inhibition of ovarian function and other unfavorable changes were reported when similar large doses were given to mice. No significant beneficial or harmful effects followed low dosage irradiation of the pituitary of anovulatory monkeys.

The ovaries of animals and man are quite sensitive to x-rays. Irradiation may cause not only functional inhibition but also a variety of histologic changes, including production of tumors in certain strains of mice. The corpus luteum is apparently much more resistant to irradiation than are the follicles. Few studies have been made on animals with low dosage irradiation of the ovaries. In one, some congestion was noted after 1/10 of an erythema dose to rats; release of estrogen may have resulted.

**Dysmenorrhea and Pelvic Autonomic System.** The smooth muscle syncytium of the uterus requires a highly co-ordinated pattern of contractility to carry out the physiologic functions of expelling desquamated endometrium with each recurrent menstrual cycle, of accommodating the growing fetus and, at

term, of assuming a rhythmic pattern of hyperirritability in the fundus while its lower segment becomes passive. Knowledge of other smooth muscle behavior suggests that control over its functions resides within the autonomic nervous system supplying the organ. However, the autonomic nerves to the uterus do not extend beyond the subserosa. Furthermore, it is known that presacral sympathectomy and procaine block of the parasympathetics of the broad ligament do not interfere with labor. William Bickers<sup>8</sup> (Bishop DeGoesbriand Hosp., Burlington, Vt.) studied the effect of electric excitation of sympathetic and parasympathetic nerves during presacral neurectomy. Stimulation of the sympathetics resulted only in vascular dilatation, whereas stimulation of the parasympathetics resulted in striking increase in the muscular activity of the myometrium.

It was concluded that uterine contractions of labor are modified by hormone influence but depend in large part on the intrinsic capacity of the myometrium to expel the fetus entirely apart from any stimulation received by way of nerve pathways.

The myometrium of a sexually mature person is constantly undergoing spontaneous rhythmic contractions under hormonal influences. Estrogen is essential to this motility. During the preovulatory phase, the contractions are of low amplitude, high frequency (two to three minutes) and hypertonic. In the postovulatory or progestational phase, contractions are more regular, high in amplitude, hypotonic and less frequent. Presacral neurectomy does not alter this pattern.

However; presacral neurectomy relieves the pain of dysmenorrhea, in part, by blocking the afferent pathways from the uterus. The vasomotor mechanism controlling the blood flow through the myometrium is also modified by the operation and may be a factor in pain relief.

**Preovulatory Administration of Methyltestosterone in Refractory Functional Dysmenorrhea.** William Filler<sup>9</sup> (New York Univ.) treated 22 patients, all under age 30; 13 were married and 4 had at least one child. Physical condition was essentially normal in most cases. One 10 mg. tablet was given three times a day for six days before the estimated ovulation

(8) South. M. J. 43:889-893, October, 1950.

(9) J. A. M. A. 143:1235-1238, Aug. 5, 1950.

time. Although Filler had previously obtained some good responses to premenstrual administration of progesterone or methyltestosterone, in the 10 patients of this group who had received progesterone and in the 11 who had taken androgens premenstrually, none had even partial relief. However, treatment failed in none of the 22 cases in which methyltestosterone was given before ovulation. Complete freedom from pain was obtained by 16 and partial relief by 6. Follow-up period ranged from three months to more than one year. Results of treatment of 11 patients with conditions other than functional dysmenorrhea were almost universally poor.

Basal temperature records and premenstrual endometrial biopsies indicated that ovulation was not suppressed by preovulatory administration of methyltestosterone in this dosage. Nevertheless, Filler believes that if accurate quantitative tests were available to determine hormonal titer in the postovulatory phase, it could be demonstrated that the drug given in the preovulatory phase, even in these dosages, effects a change in such concentrations. This in turn produces diminution of pain in true functional dysmenorrhea.

[The fact that methyltestosterone does not prevent ovulation makes it far more advantageous for treatment of dysmenorrhea than estrogens in women who want children. In those who are not anxious for pregnancy, it does not matter much whether one uses estrogens or androgens. In contrast with Filler's results, McGregor observed success with estrogens in only 55 per cent of his patients, although in most series the percentage of success with estrogens to overcome dysmenorrhea is considerably higher.

Unlike other gynecologists who use moderate doses of diethylstilbestrol to inhibit ovulation but not menstruation, Karnaky (Arizona Med. 7:25, May, 1950) advocates large doses to keep the patient amenorrheic. He does this to "recondition" or "mature" the myometrium. He continues this therapy from six weeks to nine months and says that the results are most gratifying because 80 per cent of his patients improved. Of course, if one stops menstruation completely, one will also stop dysmenorrhea, but Karnaky maintains that the good results persist even after the patient begins to menstruate again.—Ed.]

• **Anti-Pitressin® Factor in Treatment of Dysmenorrhea** was investigated by William Bickers<sup>1</sup> (Burlington, Vt.). Primary dysmenorrhea is characterized by symptoms arising from uterine muscle dysfunction (hypertonicity, dysrhythmia and inverted pressure gradients interfering with expulsion of endometrial debris) and symptoms related to altered electro-

(1) New England J. Med. 243:645-648, Oct. 26, 1950.

lyte metabolism and water retention. Ovulation is an essential precursor of dysmenorrhea.

Evidence is accumulating that the vascular bed is the source of dysmenorrhea. Hypogastric nerve resection relieves the pain, at least in part, through its vasodilating effect. Pregnancy may give relief through the same mechanism. In a simple experiment, stimulation of the hypogastric plexus by a low voltage current after insertion of an intrauterine balloon produced vasoconstriction, as shown by uterine pallor and altered patterns of uterine contractions of dysmenorrheic type. On division of the plexus and stimulation of the distal end, uterine flushing occurred, with drop in tonus and slow rhythmic pattern of contractility.

In animals, vascular response to pitressin<sup>®</sup> can be reduced by repeated injections. It seemed reasonable to assume that if vascular response could be reduced by repeated administration, such desensitization to pitressin<sup>®</sup> might make the vascular bed of the myometrium nonresponsive to the physiologically induced vasoconstrictor of menstruation. Therefore an attempt was made on 19 patients with severe primary dysmenorrhea to desensitize the vascular system to pitressin.<sup>®</sup> The last 16 received pitressin,<sup>®</sup> 10 units in oil, the fifteenth day of the cycle, then every other day until menstruation started. There were no unpleasant reactions. Of the five not completely relieved for 6 to over 12 months, two were proved later to have pelvic endometriosis. Prodromal menstrual symptoms were significantly improved in all 16.

[Bickers states it has long been known that, in the laboratory, repeated injections of pitressin<sup>®</sup> to animals over a period of days is followed by progressive loss of vascular response to the hormone. He uses this and other laboratory observations because the information may be utilized clinically in management of patients with primary dysmenorrhea. I do not like to rub it in, but in the 1950 YEAR BOOK OF OBSTETRICS AND GYNECOLOGY (p. 292) will be found an article by Bickers entitled, "Uterine Muscle Physiology from Laboratory to Bedside: A Treacherous Crossing."

Greenblatt, Barfield and Hammond (Am. J. Obst. & Gynec. 61:565, March, 1951) reported that priscoline<sup>®</sup> overcomes dysmenorrhea. It seems to direct treatment to the area of the lesion, in contradiction to previously suggested technics of therapy. The high percentage of side effects with oral medication may in a large measure be circumvented by parenteral use of this drug.—Ed.]

**Estrogen Therapy in Primary Dysmenorrhea.** T. N. MacGregor<sup>2</sup> studied 38 women with incapacitating pain at the

(2) Proc. Roy. Soc. Med. 43:738-740, October, 1950.

menses which had begun at the menarche or during early years of womanhood. Most patients had been previously treated by various analgesics and antispasmodics and some had undergone minor surgery. Detailed personal and menstrual histories were obtained, and patients recorded daily rectal temperatures during the entire observation period. Premenstrual endometrial biopsies were performed when possible. Treatment was usually not instituted until the type of menstruation, whether ovulatory or anovulatory, was determined. Thereafter an attempt was made to suppress anterior pituitary activity and thus inhibit ovulation by administration of daily doses of estrogen for the first 20 days of the cycle. When temperature records or biopsy material indicated that ovulation had been suppressed, estrogen was given daily from the 14th-24th day of the cycle. Dosage was increased, if necessary, during subsequent cycles according to the effect produced. Generally, postovulatory or premenstrual estrogen was stopped after three months if symptoms were not greatly relieved.

The menstrual cycle was ovulatory in 33 (87 per cent) of 38 cases. In 20 of 30 ovulating patients preovulatory administration of estrogen, ethinyl estradiol 0.05-1 mg. or dienestrol 1-10 mg., suppressed ovulation and relieved dysmenorrhea. In only 1 of 10 in which ovulation was not inhibited was pain relieved. Relief was temporary, pain recurring with the next ovulatory cycle in all but four patients (13 per cent) who were apparently cured. In premenstrual or postovulatory estrogen therapy with ethinyl estradiol 0.05-0.15 mg. or dienestrol 3-15 mg., 55 per cent of patients were cured or relieved but 24 per cent relapsed; there was no benefit in 21 per cent. These findings support the contention that unopposed estrogen-induced bleeding is painless and further indicate that primary dysmenorrhea is always preceded by ovulation. Although estrogen therapy can be of only limited value until more is known about the concentration of ovarian hormones in painless ovulatory menstrual cycles, it helps numerous patients and should be considered before use of operative procedures.

**Ureteric Dysmenorrhea.** Grantley Dick Read<sup>3</sup> reports three cases with intractable pain at menstruation.

(3) Lancet 1:312-315, Feb. 10, 1951.

CASE 1.—Woman, 36, had an 8 week abortion at age 26 and no other pregnancy. She complained of lassitude, depression and back-ache before menses. At menses, suprapubic pain extended across the lower abdomen, then upward around the right loin, with severe exacerbation every few minutes. There were distention of abdomen, sensation of pressure and fulness in vagina and sometimes frequency of micturition. Examination revealed only slight low dorsal scoliosis and ptosis of right kidney. Intravenous pyelography showed right kidney ptosis with kinking of ureter directly below junction with renal pelvis. Both ureters were tortuous and irregular in outline. The right ureter was dilated with Braasch bulbs up to no. 22. Nephropexy was undertaken. The sympathetic nerve supply was interrupted by stripping the upper end of the ureter and the renal artery back to the aorta. Symptoms disappeared after surgery.

CASE 2.—Woman, 43, childless, had one miscarriage at 28. She had always had menstrual discomfort but for 10 years pain had been very severe at onset, being suprapubic at first and extending across the lower abdomen to the right iliac fossa with some stabbing pain in the left iliac fossa and groin; attacks came every few minutes with feeling of pressure in the vagina. Medicines had been ineffective. Examination was negative except for a tender point to the right of the fundus uteri, distinct from the ovaries and uterus. Cystoscopy revealed striking pseudomembranous trigonitis and basal cystitis. The ureters, tortuous and irregularly dilated, were gradually dilated to Braasch 24. Menstrual discomfort did not recur; mental and physical improvement has been dramatic.

CASE 3.—Woman, 25, married four years but childless, had had severe spasmodic pain for six years, with menses chiefly on the left side and in the left iliac fossa. Medication, dilatation and curettage gave no relief. Dyspareunia and two to three hours' pain always followed orgasm. Examination revealed slight ptosis of the right kidney and area of tenderness left of the body of the uterus. Cystoscopy revealed trigonitis involving both ureteric orifices. Retrograde pyelography revealed bilateral ureteritis, more pronounced on the left. The pelvic ureter was dilated to Braasch 24. Symptoms disappeared after dilatation; with outlook on life changed and fear of pregnancy gone, she became pregnant.

These cases, examples of a large category, indicate that though manifestations of disease in the female organs or reproductive function may be primary and local, they may also be secondary to disorganization of almost any physiologic body function. Psychologic factors are extremely important. These patients had no relief from drugs, hormones, dilatation and curettage. Cystoscopic and urinary tract examinations were not made. There were no tumors, neoplastic change or inflammation to account for symptoms which, previously considered uterine in origin, were relieved by treat-

ment of the ureter. Ureteric peristalsis recurs at intervals corresponding to attacks of colic described by these patients. The sense of fulness and dropping in the vagina common to all three disappeared after dilatation of the lower third of the ureter.

The fear-tension syndrome is applicable to the inflamed pelvic ureter which is supplied through the hypogastric plexus by the same nerves as, under emotional stress, give rise to abnormal tensions, and therefore pain, of labor. This syndrome can be arrested by eliminating either psychic or somatic causes. Pain can be relieved by drugs and analgesics. Psychic rectification can break down the syndrome, and fear-destroying mental processes can be implanted. Dilatation often relieves spasmodic pain temporarily but does not remove the cause; with care, tissue destruction is negligible. If through psychic stress, anxiety recurs, pain returns, necessitating repetition of dilatation and psychologic rectification until bases of fear have been eliminated.

**Presacral Neurectomy in Treatment of Dysmenorrhea: Report of 125 Cases.** Presacral neurectomy is the treatment of choice in properly selected cases of primary uterine and secondary dysmenorrhea, according to J. J. Fertitta, Sam Fertitta and K. T. Miller<sup>4</sup> (Beaumont, Tex.). Successful results depend on proper selection of patients and complete excision of the superior hypogastric plexus. Few, if any, failures should occur in true primary uterine dysmenorrhea. Analysis of failures in cases of secondary dysmenorrhea reveals that most patients fall into one of the following categories: (1) those with psychoneurotic backgrounds who responded poorly to psychotherapy; (2) those in whom consideration of age, childbearing, etc., temporized the surgeon's decision to perform radical surgery for endometriosis or chronic pelvic inflammatory disease and (3) those in whom subsequent surgery revealed incomplete resection of, or reconstitution of, the superior hypogastric plexus.

Of the 125 cases of intractable dysmenorrhea treated by presacral neurectomy, 80.4 per cent were of the primary type and the others of either a true secondary or mixed type. All patients had failed to respond to routine conservative measures such as correction of hygienic deficiencies, use of mild antispasmodic, analgesic and sedative drugs, and psychothe

(4) *Surgery* 28:729-734, October, 1950.

apy as indicated. Neither endocrine therapy nor cervical dilatation gave sustained satisfactory results. At operation all grossly pathologic ovaries except those containing only simple cysts were removed. Oophorectomy or salpingo-oophorectomy was performed in 71.4 per cent of patients with secondary dysmenorrhea. Uterine suspension of the Mayo-Barrett or Norris type was done in 48 per cent of primary and 58 per cent of secondary type cases. Appendectomy was performed routinely.

There were no significant postoperative complications. A sanguinous cervical discharge occurred during the immediate postoperative period in 18 per cent of patients. Complete relief from dysmenorrhea was experienced by 88.5 per cent of patients in the primary and 75 per cent in the secondary group. A decrease in both degree and duration of pain was noted by 8.62 per cent of the primary and 20 per cent of the secondary group. There was less than 50 per cent improvement, considered failure, in 3.88 per cent of patients with primary dysmenorrhea and 5 per cent with the acquired type. In view of the high incidence of failures after correction of pelvic pathology alone in severe secondary dysmenorrhea compared to the favorable results achieved when these procedures are combined with presacral neurectomy, and in view of the minimal morbidity and mortality after the latter procedure, the authors believe that presacral neurectomy should be done routinely in many of these cases.

[Even though complete relief from dysmenorrhea was obtained in 88.5 per cent of the patients, I do not see why 150 women were operated on for this condition. To the 125 cases reported in the paper are added 25 cases in a footnote. The population of Beaumont is about 65,000. I feel certain that there should not have been 150 women with dysmenorrhea subjected to abdominal operation in seven years by one group of surgeons. It is difficult to evaluate what presacral neurectomy did for the patients in this series because uterine suspension was performed in 48 per cent of those with primary dysmenorrhea and in 58 per cent of those with secondary dysmenorrhea, and appendectomy was performed routinely on the women who still had an appendix. Also, oophorectomy or salpingo-oophorectomy was performed in 71.4 per cent of those with secondary dysmenorrhea. This is a lot of meddlesome surgery for dysmenorrhea.—Ed.]

**Androgen-Estrogen Treatment in Menopause.** Long term estrogen therapy, excessive dosage or undue sensitivity may cause nausea, uterine bleeding, nervous tension, edema and accelerated tumor growth. S. J. Glass and M. R. Shapiro<sup>5</sup> (Beverly Hills, Calif.) found that a combination of 0.5-1 mg.

(5) GP 3:39-42, March, 1951.



estrogen and about 5 mg. testosterone gave desirable results without significant complications. To demonstrate the superiority of combined dosage of estrogen and androgen, four preparations in identical tablet form were given to 92 menopausal patients. Tablet 1 contained 0.25 mg. diethylstilbestrol; tablet 2 contained 5 mg. methyl testosterone and 0.25 mg. diethylstilbestrol; tablet 3 contained 5 mg. methyl testosterone; tablet 4 was a placebo. Subjective criteria to determine effectiveness of preparations were relief from flushes, sweats, nervousness, palpitation and arthralgias. Objective data sought were changes in vaginal cytology, skin (acne and hypertrichosis), hypertension and body weight.

More than 72 per cent of patients preferred tablet 2, clear evidence of superiority of combined androgen-estrogen therapy in achieving optimal symptomatic relief. Range of daily dosage giving best results in the first 14-21 days of treatment was 5-10 mg. testosterone and 0.5-1 mg. estrogen. For maintenance therapy, daily dosage was 2.5-5 mg. testosterone and 0.25-0.5 mg. estrogen. Comparison was made in 40 patients between the androgen-estrogen tablet and a buccal tablet containing 0.5 mg. crystalline alpha-estradiol and 2.5 mg. testosterone. No striking difference in therapeutic effectiveness was observed, an indication perhaps that buccal administration of steroids in lower dosage may have equally good results. Clinical responses to combined hormonal therapy were such that this treatment is recommended in management of the menopausal syndrome.

**Evaluation of Estrogen, Androgen, Estrogen-Androgen Combination and Placebo in Treatment of Menopause** was made by Robert B. Greenblatt, William E. Barfield, Joseph F. Garner, Guy L. Calk and John P. Harrod, Jr.<sup>6</sup> (Univ. of Georgia). Personal equations and suggestive factors were eliminated by labeling bottles AE-1, AE-2, AE-3 and AE-4, of which it was known that one contained an estrogen, one an androgen, one an estrogen and an androgen and one a placebo.

A total of 284 courses of therapy with the four different preparations were administered in varying sequence to 102 women with menopausal symptoms. Most patients were given a bottle containing 100 tablets and usual dosage was 3 tablet

(6) J. Clin. Endocrinol. 10:1547-1558, December, 1950.

daily for 30 days. AE-1, which was diethylstilbestrol (0.25 mg.), gave satisfactory relief from hot flashes and other symptoms in 96.9 per cent of 88 patients, but nausea accompanied therapy in 30.5 per cent and uterine bleeding in 34.2 per cent. AE-2, which was 0.25 mg. diethylstilbestrol and 5.0 mg. methyltestosterone, relieved menopausal symptoms in 89.6 per cent of 73 patients and the hypoestrogenic vaginal smear was improved in all. Increased libido was reported by 23.5 per cent and, in comparison with AE-1, increased well-being by 66 per cent. AE-2 had the additional beneficial effect of lowering incidence of breast turgidity, pelvic congestion and nausea. Transient mild acne, hoarseness and increase in facial hair were noted in 13.2 per cent. AE-3, which was 5.0 mg. methyltestosterone, was unsatisfactory in 23.6 per cent of 63 patients. Half reported lowered incidence and decreased severity of hot flashes; acne, hoarseness or hirsutism was noted in 12.8 per cent and increased libido in 42 per cent. AE-4, which was a placebo, abolished menopausal symptoms in only 7.1 per cent of 60 patients; 83.8 noted no improvement, nor was there change in vaginal smears.

In general the estrogen-androgen combination gave the best results. Androgens and estrogens apparently modify the specific action of each other but do not neutralize one another, for hirsutism, hoarseness and acne occurred concurrently with uterine bleeding and maturation of cells in the vaginal smear in patients given combined therapy.

[Glass and Shapiro agree with Greenblatt and his associates that combined hormone therapy gives better results than estrogens alone. For many years I have used a combination of estrogen and androgens in selected women for menopausal disturbances. I give it to all women who do not seem to benefit from estrogen therapy, to those with any tendency to bleed following use of estrogens, to those with a bad family history of carcinoma or who themselves have had a carcinoma, to women who need a tonic, to those who are mentally depressed and to those who complain of decrease of libido or who fear such a decrease. Results have been good. I have not encountered nausea from estrogen in 30 per cent of my patients. Nor have one third of my patients who had a uterus bled following estrogen therapy. Perhaps it is because the doses I use are very small. In fact, I rarely prescribe more than 0.25 mg. of an estrogen daily. As Greenblatt and his associates point out, even though the estrogens are combined with androgens, the androgens may produce disagreeable disturbances. Hence, one must be on guard for symptoms and signs of virilism.

Pollosson, Hadur and Blanc (*Bull. Assoc. gynéc. et obst.* 2:226, 1950) believe that 50 mg. testosterone given castrated or menopausal women with functional disturbances causes marked amelioration of symptoms very

soon after the injection. This effect is reinforced if one administers vitamin E at the same time. Vitamin E alone, even in daily doses of 500 mg., is not sufficient. In women who cannot for some reason take estrogens, 50 mg. testosterone should be given every week.

Karnaky (Surg., Gynec. & Obst. 91:617, November, 1950) lists 10 different agents to control side reactions of diethylstilbestrol, including sour milk, pentobarbital sodium, persistence in taking diethylstilbestrol, vitamin B<sub>6</sub>, antihistamines, vitamin B complex, testosterone propionate, progesterone and vitamin C. In my opinion it is better to switch to some other preparation than to give all this heroic and expensive medication to overcome the disagreeable reactions to diethylstilbestrol.—Ed.]

---

## ENDOCRINOLOGY

**Research on Adrenal Sexual Zone.** J. Botella Llusia and A. Cano Monasterio<sup>7</sup> (Madrid) attempted to determine whether or not the stimulating effect of gonadotrophin on castrated rats could be due to estrogenic impurities in the injection preparation. Testes were removed from 11 white rats, each 25 days old and weighing 30 Gm. Three rats were used as controls. In four, beginning 15 days after castration, 150 I.U. of physex (gonadotrophin) was injected daily for seven days. The rats were then killed and the seminal vesicles and adrenal glands examined. Fifteen days after castration the other four rats were given daily injections of 6 mg. testosterone acetate for six days followed by a three day rest. Then 200 I.U. of physex daily was given for five days; the rats were then killed.

The seminal vesicles of control animals were atrophied and the adrenal cortex showed reticular hypertrophy representing the initial stage of formation of the X zone of Deanesly and Howard. The rats given gonadotrophin had seminal vesicles 10 times the size of those in control animals. In the adrenal cortex, growth of the reticular zone was more advanced. In animals given testosterone and gonadotrophin seminal vesicles were even larger than in the gonadotrophin group. The adrenal cortex showed a characteristic reaction of displacement of fuchsinophilic material near the reticular zone.

These experiments showed a stimulatory action of gonadotrophin on the seminal vesicle of castrated rats. The slowing

---

(7) Acta ginec. 1:403-408, 1950.

up of involution of the masculine organs is due to action of the adrenal cortex. The gonadotrophin acts on the seminal vesicles by stimulating the sexual portion of the cortex. Under gonadotrophic stimulation the cortex protects the sexual organs, both masculine and feminine. Thus it may be affirmed that under gonadotrophic stimulation the adrenal cortex acquires a vicarious sexual action.

**New Contributions to Study of "Third Gonad."** José Bottella Llusia<sup>8</sup> (Madrid) suggests the possibility of a special zone in the cortex, which, being dependent on the reticular formation, is an endocrine, behaves as part of the gonadal mesenchyma and like that reacts to ponceau red and is sudanophobic, in contrast with the fascicular formation which is sudanophilic. This zone, especially before birth or during castration, seems related to sexual life in the role of a vicarious or reserve organ. Its function is that of a gonadotrophic, and not corticotrophic, hormone. Under its influence, estrogens are produced in the female and 17-ketosteroids in the male.

The substance, by its embryology, chemistry, physiology and endocrinal behavior, appears to be a part of the gonadal tissue, and like it responds to pituitary stimulation. All these properties justify its designation as the "third gonad," an endocrinosexual tissue destined to fulfill the function of a gonad at certain moments of life. Pathologically, it is the origin of the neoplasias or hyperplasias which produce the adrenogenital syndrome, and its lack of embryologic development produces a state characterized by sexual developmental anomalies. Its existence is independent of suprarenal metabolism, both physiologically and clinically. For these reasons it is justifiable to consider that the suprarenal cortex has two distinct functions: (1) that which we already know, and (2) that of the "third gonad."

**Clinical Use of Hormone Determinations in Urine.** H. de Watteville<sup>9</sup> (Geneva) illustrates the criteria essential before recommendation to the clinician of any new method of hormone determinations by the example of pregnanediol determinations by the chromatographic method. (1) Technical reliability, as determined by specificity, yield, precision and sensitivity, is established. (2) Correlation must exist between

(8) *Rev. mex. cir.* 18:377-386, December, 1950.

(9) *Edinburgh M. J.* 57:403-412, September, 1950.

activity of an endocrine gland, blood level of its hormone, response in the target organ and the excretory products estimated. Correlation between pregnanediol excretion and corpus luteum function in 64 cases was studied. In 47, pregnanediol values agreed with the histologic picture in endometrial biopsies. On the whole, pregnanediol determinations are a reliable test for corpus luteum function. The presence of pregnanediol in the urine indicates presence of progesterone in the body, whatever its origin—ovarian, placental or from administration. (3) Clinical changes must be associated with differences in hormone levels greater than normal variability and technical errors; this is well illustrated by pregnancy tests. In early pregnancy urinary estrogen and pregnanediol values rise slowly; hence pregnancy tests are based on determinations of urinary gonadotrophins which increase greatly. As pregnancy proceeds, gonadotrophin levels drop while estrogen and progesterone values rise. Hence, for diagnosis of late pregnancy disorders due to or associated with hormone deficiency, estrogen or pregnanediol determinations are preferable. A sudden or steady drop of pregnanediol values in a series of repeated determinations is more important than a single result. Low pregnanediol excretion in toxemia was associated with stillbirth or fetal underdevelopment and seem to indicate prophylactic cesarean section to save the fetus provided it is viable.

Investigation of menstrual endocrinology offers opportunities for clinical application of hormone assays. The Farris method, by following the rise in urinary gonadotrophin excretion, permits determination of ovulation time. Amenorrhea, whether due to persistence of follicles or to follicular atresia, is reflected by high or low urinary estrogen levels. Pregnanediol determinations have been used to confirm diagnosis of persistent corpus luteum and of luteal deficiency in cases of abnormal uterine bleeding. The pregnanediol chemical test should be combined with the biologic test for gonadotrophin in cases of doubtful pregnancy. In cases of sterility pregnanediol studies give more information regarding luteal activity than the vaginal smear and are complementary to endometrial premenstrual biopsy or may even replace it.

Thus, in diagnosis, hormone determinations indicate whether glandular functions are normal, increased or defi-

cient. In therapy they may serve as a guide and aid in evaluation. Hormone treatment is not indicated when excretion levels are normal, e.g., in threatened abortion with uterine contractions due to extragenital causes, when pregnanediol values remain normal. The effect of diethylstilbestrol on pregnanediol excretion in threatened or repeated abortion is controversial. However, it appears that pregnanediol values, if determined by a specific method, can be shown to decrease under diethylstilbestrol treatment.

Among 140 pregnanediol determinations made in 100 cycles, normal as far as menstrual histories were concerned but including a number of myoma cases, values in the myoma cases appeared to be generally lower than in most of the others. This agrees with histologic evidence of progesterational deficiency in the endometrium of many myoma patients.

[Most claims for relative therapeutic effectiveness of estrogens are based on their activity in laboratory animals, principally rats and mice. The assumption that data so obtained can be accepted for the human being has caused considerable confusion in the standardization of estrogen therapy. Results obtained from assays differ widely, and Freed (J. A. M. A. 117:1175, 1941) concluded that any statement regarding the relative therapeutic activity of estrogens on the basis of animal assays is liable to considerable error. For this reason, at present the only satisfactory test object for the therapeutic efficiency of estrogens seems to be the human being.

There are a number of ways of assaying the activity of estrogens in human beings. Some investigators use the changes in vaginal mucosa of menopausal women following estrogen administration as an index of estrogen activity, in a manner similar to that in a castrate rodent. This method requires considerable experience in reading and interpreting vaginal smears properly and the reading is subject to experimental error. Furthermore, since untreated menopausal women have varying degrees of proliferation of the vaginal mucosa, this cannot be an entirely satisfactory means of assay. Also, there is no evidence that the vaginal mucosa of a group of menopausal women will respond uniformly to a definite amount of estrogens.

An attempt has been made to use the endometrium for assaying estrogens administered during the menopause. The procedure is distinctly more cumbersome than use of vaginal smears and is open to even more criticism. Untreated menopausal women by no means uniformly present an atrophic endometrium. Many show not only endometrial proliferation but actual hyperplasia. Hence, endometrial changes cannot be used as criteria for estrogen activity. The end point in assay of estrogens in human beings should be the subjective response of menopausal patients. Even though evaluation of such a response may be obscured by numerous uncontrolled factors, this method should be selected for a number of reasons, not the least of which is the fact that the chief purpose of administering estrogens is to relieve menopausal patients of their subjective symptoms.

Newman (Am. J. Obst. & Gynec. 60:661, September, 1950) implanted crystalline estradiol preparations intramuscularly in 40 patients aged

38-63 with symptoms of ovarian deficiency with the menopause. Vaginal smears and clinical improvement were the criteria of estrogenic effect. All patients responded favorably, while 75 per cent showed good to excellent results with weekly injections of 0.5-2.0 mg. There were no local signs of irritation at the site of injection. Newman considers the aqueous suspension of estradiol the preparation of choice from the standpoints of estrogenic activity, convenience to patients and physician, prompt and prolonged action and economy.

Bishop and Kennedy (*J. Endocrinol.*, supp. 6, 1949) implanted 100 mg. estradiol pellets. In women who have an intact uterus, flooding begins 60-90 days after implantation. These authors attribute the flooding to induction of endometrial hyperplasia, so the patients were given injections of four doses of 10-20 mg. progesterone on alternate days. With periodic progesterone treatment during the effective period of an estrogenic implant, withdrawal bleedings will be produced to resemble the normal menstrual flow in length and amount. I see no reason to resort to implants of estradiol in view of the effective oral preparations we have today. The one possible exception is cases of metastases with carcinoma of the breasts. Of course not all patients who bleed excessively have endometrial hyperplasia, for profuse bleeding may occur from endometrium of any type, even an atrophic one.

Anderson (*Quart. J. Med.* 19:67, January, 1950) points out that the synthetic estrogen dienestrol has a metabolic effect like that of the natural estrogen, estradiol, in promoting calcium retention in women with postmenopausal osteoporosis. Dienestrol ameliorates the subjective symptoms. Suggested treatment includes administration of dienestrol, vitamin D and calcium glycerophosphate to secure a high calcium and phosphorus intake.

Bishop, Richards and Perry (*Lancet* 2:818, Apr. 14, 1951) compare the potency of estrogens in man by giving the estrogen daily by mouth in 14 day courses to amenorrheic women and recording whether estrogen withdrawal bleeding takes place. Their results indicate that diethylstilbestrol sulfate is  $\frac{1}{2}$  as potent as diethylstilbestrol, estrone is  $\frac{1}{20}$  as potent and equilin  $\frac{1}{3}$  as potent.

I should like to emphasize a fact often overlooked—that fully half of all women who go through the menopause do not require estrogen therapy. It is unfortunate that nearly every woman in the late forties who complains to her physician of vasomotor and nervous disturbances is given estrogen hypodermically or orally. Even many women in their early forties who still bleed regularly but complain of vague but distressing symptoms are given estrogens. It is a serious mistake to give estrogens to women who have not stopped menstruating and even to some who have had a true menopause, i.e., cessation of bleeding. In most cases, estrogens will have to be administered for years if their use is not restricted and limited to the minimum from the start. Many women can be carried through the trying days of the change of life by encouragement and phenobarbital. And if estrogens must be prescribed, there is little need to give them hypodermically.—Ed.]

**Pregnanediol Determinations in Clinic and in Research.** H. de Watteville<sup>1</sup> (Univ. of Geneva) states that the obstetric usefulness of these determinations has been obscured by failures in technic such as the use of morning rather than 24 hour specimens, lack of specific chemical methods and a tendency

(1) *J. Clin. Endocrinol.* 11:251-266, March, 1951.

to generalize unduly or to apply findings unselectively to all cases. In the normal menstruating woman, pregnanediol is excreted only during the corpus luteum phase, and even then daily variation is so great that a single determination has little meaning. Prolongation of the luteal phase by huge doses of gonadotrophin in four cases suppressed bleeding and gave good correlation between serial pregnanediol excretions and endometrial biopsies. Pregnanediol is thus a good indicator of luteal function and can be used for evaluation of abnormal vaginal bleeding. Pregnanediol levels are increased in normal pregnancy, in persistent corpus luteum and certain ovarian and adrenal tumors; pregnanediol is low or absent in abortion, anovulatory cycles and luteal deficiency.

Pregnanediol excretion during the first months of pregnancy is similar to that in the menstrual cycle, and diagnosis of pregnancy is preferably made by biologic assay of gonadotrophins. Excretion rises during the later months, and comparison of values obtained in disturbed pregnancies with the mean excretion curve throws valuable light on prognosis. In threatened abortion or premature labor with favorable outcome, values are below the mean curve but not lower than its limits of variability. In spontaneous abortion, the pregnanediol level is extremely low or even absent. In threatened abortion, sudden or steady drop in serial determinations is more informative than a single value and is frequently associated with placental damage. It may occur while the Aschheim-Zondek reaction is still positive. It is useless, of course, to give progesterone to patients in whom pregnanediol values are normal.

Pregnanediol excretion was compared in 123 cases of pregnancy and threatened abortion with biologic gonadotrophin assays. Tests were judged "correct" if low pregnanediol (less than 50 per cent of expected value) and negative gonadotrophin values were obtained in patients with abortion. Pregnanediol and biologic tests were correct in 50 cases and incorrect in 35; the biologic tests were incorrect 28 times and pregnanediol only 10 times in the remaining 38 cases. The chemical test, being quantitative, is thus more reliable, but in any case the test is only part of the total clinical evaluation.

In toxemia, pregnanediol excretion seems very erratic. But if one separates cases in which the baby is dead or under-



developed from those in which it is normal, pregnanediol excretion is low in the former and normal in the latter. Placental insufficiency and consequent deficient progesterone production may be responsible for low pregnanediol excretion as well as other complications in this mysterious condition.

**Endogenous Allergy to Steroid Hormones: Nature of Certain Disorders Related to Ovarian Function.** Similarity of symptoms in ovarian pain and congestion-fibrosis syndromes, premenstrual distress, painful breasts and the climacteric indicates a common etiology. George P. Heckel<sup>2</sup> (Univ. of Rochester) states that allergy to steroids is an important etiologic factor although it is not readily demonstrated. Skin tests on 256 patients, of whom 40 were controls, showed that positive results may appear in apparently normal men and women. Skin sensitivity to steroids was nonspecific and variable; patients whose reactions were negative one day might show several reactions later. Most patients who showed sensitivity to one steroid were also sensitive to others having unrelated biologic activity.

When sesame oil and peanut oil were compared as vehicles, sesame oil produced more reactions in sensitive subjects. About the same number of reactions occurred with a control injection of sesame oil alone as with peanut oil alone. The skin test appeared to be more sensitive when steroids were dissolved in sesame oil U.S.P.

Clinical conditions studied included ovarian pain and congestion-fibrosis syndrome, premenstrual distress, painful breasts (including chronic cystic mastitis), the climacteric, endometriosis, hypogonadism and headache related to menstrual cycle. The importance of allergy in etiology was illustrated by (1) greater frequency and degree of skin sensitivity than those in normal persons, (2) aggravation of symptoms by steroids to which sensitivity was demonstrated and (3) coincidence of increased skin sensitivity to steroids and exacerbation of symptoms.

Hyposensitization was attempted in a number of patients who had shown positive skin reactions. The steroid diluted in 0.05 cc. oil (or microcrystalline suspension of steroid in an aqueous vehicle) was given by shallow subcutaneous injection one to three times weekly. Usually patients themselves or

---

(2) Surg., Gynec. & Obst. 92:191-208, February, 1951.

family members gave injections every other day on outer surfaces of arms or thighs.

Hyposensitization with steroids, notably pregnanediol, was followed by relief from symptoms often enough to make it a useful form of therapy. It was the only satisfactory treatment in most of the patients. Hyposensitization may be attempted without previous skin testing, using steroids which are most likely to offend. Pregnanediol is most apt to elicit reactions; estrone is next and then estradiol and progesterone. Flare-up of old skin tests and recurrence of symptoms during emotional stress indicate the importance of psychogenic factors; probably part of the benefit of hyposensitization is due to suggestion.

**Some Observations on Relations of Estrogens and Progesterone to Contractions of Nonpregnant and Pregnant Human Uterus.** J. S. Henry, J. S. L. Browne and Eleanor H. Venning<sup>3</sup> (Montreal) used the Knaus method, employing an intrauterine bag and cannula, to make tracings of uterine contractions. Comparisons were made of tracings obtained at different times in the luteal phase of normal cycles, cycles with deficient luteal phases and artificial cycles.

Uterine contractility or sensitivity to pituitrin<sup>®</sup> was not inhibited in any of these cycles. Estrogen alone did not increase uterine activity or render the myometrium more sensitive to pituitrin.<sup>®</sup> There was some evidence that estrogen was not essential to uterine contractions. For production of maximally efficient and typical luteal contractions, as occur at the end of a normal cycle, both estrogen and progesterone must act on the myometrium together for an adequate time and in suitable quantities and proportions. If either or both is deficient in amount or the time of their action is too short, the contraction will be less well developed than normal. Estrogen and progesterone are synergistic in their action on the myometrium. They are not antagonistic in their effects on the uterus.

Contractions of the myometrium are probably myogenic in origin. This spontaneous contractility is influenced by estrogen and progesterone, which act in combination to produce maximal spontaneous activity. The activity is greatest during the years of sexual maturity and reaches a maximum of efficiency when the uterus is physiologically called on to

(3) *Am. J. Gynec. & Obst.* 60:471-482, September, 1950.

expel its contents, at the end of the normal cycle and at the end of normal pregnancy. The cause of onset of labor is not known, but it may be related to this hormonal mechanism.

Functional dysmenorrhea may be due to some disproportion between the estrogen and progesterone produced in the corpus luteum of the cycle just ended. In abortion, the inefficiency of the mechanism is seen in the low pregnanediol output, which may almost always be detected before the first symptom, and in the inadequate uterine musculature, which permits the dead products of conception to be carried for varying periods before it is able to expel them.

Since the corpus luteum and the placenta secrete both hormones, any therapy aimed at replacement of luteal function in the cycle or in pregnancy must combine estrogen and progesterone.

**Inactivation of Antidiuretic Hormone of Posterior Pituitary Gland by Blood from Pregnant Patients.** Wm. J. Dieckmann, G. F. Egenolf, B. Morley and R. E. Pottinger<sup>4</sup> (Univ. of Chicago) completed 22 experiments (15 with blood from pregnant patients and 7 control experiments, 4 with incubation and 3 without).

**METHOD.**—Twenty ml. blood from the subject was added to 5 ml. of 4 per cent weight/volume of sodium citrate. Pitressin<sup>®</sup> (Parke Davis), 0.5 ml., containing 20 pressor units/ml., was added to 19.5 ml. saline solution; 0.2 ml. of the resulting solution was added to 25 ml. citrated blood. After incubation at 38 C. for one hour, the blood was centrifuged 20 minutes; 10 ml. of plasma was drawn off for use. Thus the final dose was 0.04 units or 0.002 ml. pitressin.<sup>®</sup>

Test subjects were given 1,200 ml. water initially within 30 minutes and 300 ml. at 60 and 120 minute periods to a total of 1,800 ml. Urine specimens were taken every 30 minutes from an indwelling catheter. When the 60 minute urine specimen was obtained, diuresis was well established and 10 ml. plasma given intravenously. Effect of pitressin<sup>®</sup> on subsequent urine volumes and on chloride, sodium and potassium concentrations was noted.

Pitressin<sup>®</sup> 0.04 units, and pitressin<sup>®</sup> and blood, with or without incubation, from nonpregnant patients given at the 60 minute level of diuresis caused a drop in the 90 minute urinary output. Pitressin<sup>®</sup> and blood from pregnant patients that was not incubated caused a similar drop. Pitressin<sup>®</sup> incubated with blood from patients late in pregnancy resulted

(4) Am. J. Obst. & Gynec. 60:1043-1050, November, 1950.

in less reduction of urinary output or even increased urinary output.

In the controls the 90 minute concentration of chlorides was conspicuously increased; in the pregnant blood experiments, chloride values were only slightly increased or even lowered. Sodium and potassium levels parallel results obtained with chlorides.

The antidiuretic effect of pitressin<sup>®</sup> incubated with blood from patients in the last half of pregnancy is absent or noticeably diminished.

**Vasodilatation of Rat Testis in Response to Human Chorionic Gonadotrophin** was demonstrated by Carl G. Hartman, Nathan Millman and J. Stavorski<sup>5</sup> (Raritan, N. J.) by (1) more intense redness of exposed tissue, (2) depth of grayness of the tissue after perfusion with India ink, and (3) a photometric method. The last is thoroughly objective, probably too cumbersome to serve as a routine pregnancy test, but may have value in research. Male rats of any age in the reproductive period may be used. The hyperemia of the testis closely parallels that of the ovary in the Salmon-Farris test.

**METHOD.**—The specimen, consisting of a lump of tissue from the inner mass of the testis, is laid on a glass slide having a glass shim 0.3-0.35 mm. thick on each end. With a second slide the tissue is pressed down to make a film the exact thickness of the shims (the same shims are used for all preparations of a given experiment). Testes of adult rats will yield a specimen from each end; one specimen is procurable from an immature rat. The film should cover the hole in the diaphragm but not run out beyond the edges of the slide. The specimen holder is placed directly against the coverplate of the photocell and the top of the cell compartment closed. A 420  $\mu$  filter is used. The Photovolt Lumetron is adaptable to these technics. A preparation of testis from a control rat is used to adjust the instrument for maximal transmission and to establish a reference point.

Density change should be 20 per cent or higher to be considered significant. Ten cc. urine from a woman two to three months pregnant injected intraperitoneally into rats causes a 30-50 per cent increase in density. Readings are best made 17-24 hours after injection. Urines of women five to seven months pregnant failed to produce pronounced testicular changes. In rats primed with estrone, action of the

(5) *Fertil. & Steril.* 1:443-453, Sept.-Oct., 1950.

pregnancy urine was not potentiated. Neither estrogens nor androgens themselves had a dilating effect on testes.

**Ovulation after Unilateral Oophorectomy, as Determined by Endometrial Biopsy and Basal Body Temperature.** Women with only one ovary can lead normal sexual and reproductive lives. Presumably the ovary remaining after unilateral oophorectomy assumes all functions formerly exercised by both. Because normal ovarian function is thought to be clinically best recognized by basal body temperature curves and studies of endometrial pattern, M. James Whitelaw<sup>6</sup> (Phoenix, Ariz.) investigated this problem in 42 unilaterally oophorectomized women and a like number of controls by these two methods. Rectal temperatures were taken at the same time each morning on arising, by both groups. Abnormalities such as colds, late hours and sleeplessness were noted. Endometrial suction biopsies with a Novak curet were done no later than six hours after onset of menstruation. Biopsies were done for a minimum of four consecutive menstrual cycles: 168 on 41 unilaterally oophorectomized subjects and 182 on controls.

In the oophorectomized series, biopsy revealed typically normal progestational endometrium in 164, minimal secretory activity in 3 and no evidence of progesterone effect in 1. Monophasic basal body temperature curves occurred in two of the patients with minimal endometrial secretory activity. In one third of curves no drop was noted previous to the rise; in 18 there were striking variations from normal as evidenced by slow three to four day rise or abrupt variations during the luteal phase. In three patients monophasic curves occurred with a normal secretory endometrium. In the controls, 172 biopsies showed advanced secretory endometrium, 8 a mixed type and 2 an anovulatory pattern. Both patients with no evidence of secretory activity and three with endometriums of mixed type had monophasic temperature curves during these particular cycles. Almost one third of curves failed to show a drop just before the rise. In 10 cycles the rise was gradual; in 14 the preovulatory phase was characterized by one or two sharp peaks. In eight patients monthly curves varied widely and in six, although the curves were monophasic, the endometrium revealed typical secretory activity.

(6) Surg., Gynec. & Obst. 92:747-750, June, 1951.

Comparison of the endometrial patterns of the control and unilaterally oophorectomized groups showed no basic differences. A single ovary was capable of normal endocrine response as well as assumption of functions formerly shared by both. In large series of sterility cases, endometrial biopsies have indicated that anovulatory cycles occur in 5-15 per cent of patients. In 350 biopsies, Whitelaw noted anovulatory cycles in slightly less than 0.9 per cent. Although there was general agreement between endometrial and basal body temperature patterns, they did not correlate perfectly. Unusual body temperature curves occurred when the endometrial picture was normal.

**Endocrine Therapy in Gynecologic Practice** is discussed by Jacob Kotz and Morton S. Kaufman<sup>7</sup> (Washington, D. C.). Functional bleeding in the woman past the child-bearing age is best treated by preliminary curettage to rule out malignancy and then by radium. Hysterectomy is preferable to radium therapy when microscopic examination gives doubtful results or there is some other indication for laparotomy. In puberty and in maturity bleeding must be controlled when the patient is first seen and recurrences prevented. When bleeding is great, transfusions and curettage are in order, but if time permits, a thorough study is indicated. The vaginal smear is valuable not only in ruling out malignancy but in determining the most suitable type of hormone therapy. If the vaginal cornification count is high, 25 mg. testosterone with 25 mg. progesterone daily is given parenterally for three to seven doses; this is followed by 25 mg. testosterone propionate and 10 mg. progesterone daily for the first three to four days of the next three or four periods. When the count is low, 5-10 mg. estrone sulfate is given daily for 20 days followed by 50-100 mg. progesterone sublingually daily for 10 days. If bleeding occurs the drug is discontinued, but the estrone is resumed on the fourth or fifth day of bleeding; this treatment is continued for three to four cycles. An endometrial biopsy is done on the first day of the fourth cycle and if secretory endometrium is found treatment is discontinued. If the count is normal, 25-50 mg. progesterone in sesame oil is given every day until bleeding is controlled, and 50-100 mg. progesterone is given orally for three to five days

(7) *J. Internat. Coll. Surgeons* 15:569-575, May, 1951.

during three or four succeeding periods. Gonadotrophins have proved disappointing.

In treating dysmenorrhea, almost every endocrine product has been tried but none has been eminently successful in all cases; treatment must be individualized. Estrone sulfate, 5 mg., may be given, starting as soon as the period is over and continuing until about the 23d day of the cycle. In patients wishing to become pregnant, androgen in 10-20 mg. doses orally daily during the last phase of the cycle is sufficient. Thyroid extract is used when the basal metabolic rate is low. Insulin, 10 units daily, and thiamine, 100 mg. daily, seem to help by improving the general health.

Endocrine treatment of amenorrhea is far from satisfactory. In the past few years, radiation and endocrine therapy have been combined. Treatment should not begin before age 18. The Kaufman method consists of giving 2 mg. diethylstilbestrol or 2.5 mg. estrone sulfate daily for 15 days, followed by 60 mg. pranone<sup>®</sup> daily for 5 days. Treatment is repeated for three months, beginning with the cessation of each induced menstrual flow. By this method, the patient bleeds from a premenstrual type of endometrium.

For severe premenstrual tension, testosterone is given buccally or sublingually in 10-20 mg. daily doses, starting about one week before the period; in patients near the menopause roentgen or radium castration is best. For severe pain from mastodynia and adenosis, estrogens, progesterone, androgens and chorionic gonadotrophin have all given good results. Sterility in women with anovulatory cycles may be treated with progesterone in 50 mg. doses during the second half of the cycle.

Estrogenic therapy is the most effective for menopausal symptoms. Synthetic estrogens are not used because of side effects. When symptoms are severe, up to 5 mg. estrone sulfate daily is used; after symptoms are relieved, 1.25 mg. is given daily or every other day for two months. A second or third course may be needed. In patients in whom estrogens produce bleeding, testosterone, 10 mg. daily sublingually, for two to three months may be used.

**Cortisone in Gynecology** is discussed by M. A. Migliavacca<sup>8</sup> (Milan). Experimentally it produced rapid matura-

(8) *Gynéc. et obst.* 2:216-218, 1950.

tion of follicular ovarian substance with massive luteinization of the ovary; animal experimentation suggested gonadotrophic action, indicating an extraovarian source of hormones in the adrenal cortex. Cortisone in two women caused intense, rapid progestative action. Its biologic properties affect the sexual hormones. Cortisone seems to influence the nature of menstrual periods but not gonadotrophic activity of the pituitary or estrogenic activity. It affects the uterine mucosa without necessarily involving the anterior lobe of the pituitary.

[Since cortisone is now being used for many conditions, it is natural that it should be employed in gynecology and obstetrics. However, since we know so little about the dangers of this potent agent, I urge great caution in its use during pregnancy. We are not too sure about its effects on a pregnant woman and we know practically nothing about the effects on the child.

Courrier and Andrée (*J. A. M. A.* 146:493, June 2, 1951) studied the effects of cortisone on gestation in rabbits. Some rabbits aborted with separation of the placenta; in others a hemorrhage occurred. After injections given between the 10th and 14th days of pregnancy autopsy revealed, besides living fetuses, evidences of resorbed ones; fetuses were diminished in size, and placentas were pale. When injections were given between the 15th and 21st days, all fetuses were macerated, and ovarian yellow bodies were small and pale. The authors concluded that cortisone has a deleterious effect on the gestation of rabbits, especially if injected after the 15th day of pregnancy.—Ed.]

**Use of Ovarian Transplants for Hormonal Replacement Therapy** has a definite place in gynecologic surgical technic, according to C. L. Buxton and Ada S. H. Wong<sup>9</sup> (Columbia Univ.). Nineteen of 44 patients who underwent this type of therapy for chronic pelvic inflammatory disease, uterine fibromyoma, benign ovarian cyst, endometriosis and/or ectopic gestation were adequately followed for up to 20 years. In five, the uterus had been left in situ. In four, spontaneous menstruation developed postoperatively and continued for four months to over two years (one patient was still menstruating regularly). Menstruation returned 3-12 months after operation. Had intrapelvic ovarian tissue been left, menstruation would probably have resumed immediately after operation. Five patients complained of a periodically tender mass at the site of implantation, but none considered it severe enough to warrant either removal or radiation therapy. Vaginal smears and urinary estrogen excretion studies showed evidence of estrogenic activity in a large percentage. In one patient who menstruated regularly and had a minor swelling

(9) *Am. J. Obst. & Gynec.* 60:401-405, August, 1950.



in the area of the transplant during the midcycle, endometrial biopsy on three separate occasions disclosed a well developed secretory endometrium, which indicated progesterone secretion by the implant and therefore corpus luteum formation. It was the authors' practice to insert three or four strips of apparently normal ovarian tissue 2 cm. long and 4 or 5 mm. in diameter in several areas in the rectus muscle with no suturing except for closure of the fascial sheath and repair of the abdominal incision.

Reimplantation of ovarian tissue has a high percentage of success insofar as resumption of estrogenic secretion by the ovarian transplants is concerned and such a small percentage of uncomfortable or undesirable postoperative complications that the technic seems to be a more reasonable treatment method than substitution therapy for an indefinite period to prevent premature onset of a surgical menopause. If a cyst forms in the transplanted ovarian tissue, as it does occasionally, the transplant is so superficial that it may be either aspirated or removed if necessary under local anesthesia. Furthermore, if the uterus has been left and menstruation recurs in an undesirable manner (i.e., menorrhagia or metrorrhagia), a little radiation to the transplant is highly effective. The rectus muscle site for the ovarian transplantation has been used almost exclusively in recent years, probably because of the vascularity of muscular tissue which enables the transplant quickly to acquire its own blood supply.

[Several years ago I performed ovarian transplantation in young women both of whose ovaries were removed, usually for bilateral dermoid cysts. I transplanted the ovarian tissue into the rectus muscles just as the authors do. In France, some gynecologists transplant the ovarian tissue into the labia majora. I have not resorted to ovarian transplantation in recent years because we now possess potent oral ovarian preparations.

Whenever a piece of ovary can be left in situ, this is far preferable to ovarian transplantation. Perhaps all of us take out too much ovarian tissue, particularly in cases of pelvic inflammatory disease. Our rationale for removing some normal ovarian tissue with the diseased parts is that the tissue left behind often degenerates or becomes cystic and requires a second operation. Despite this it is amazing how often a small healthy piece of ovarian tissue left in situ will continue to function, as proved by absence of menopausal symptoms and by vaginal smears. When ovarian transplantation is resorted to, one must remember that nearly always about three or four months elapse before there is evidence that the ovarian transplant is active.

Béclère (*Actual. chir.* 3:321, 1949) studied the menstrual disorders after removal of one ovary. They consist of disturbances in rhythm of

the menses with occasional periods of amenorrhea or metrorrhagia. The remaining ovary frequently becomes hypertrophied and cystic. Often there is a premature menopause between 35 and 43. Investigation revealed irregular outbursts of excessive gonadotrophic excretion followed by irregular periods of hyperestrinism. This increase in gonadotrophin accounts for the hypertrophy and cystic degeneration of the remaining ovary and the phenomena produced by hyperestrinism. Bécère advises against the use of estrogens in women who have only one ovary. The amenorrhea should be treated only with progesterone.—Ed.]

**Value of Ovarian Autografts.** Michel Blanc<sup>1</sup> (Montmorcency) believes that except in tubular sterility, in which transplantation of part or all of the ovary is into the uterus, the site of choice for free grafts is into the labia majora where they can be explored and remain in the genital sphere. The field of application of ovarian autografts is extensive, for no hormonal therapy gives equally good results, but grafting should be reserved for cases in which the ovary cannot be left in situ.

Before transplantation the ovary must be rendered as normal as possible by destruction or enucleation of cysts. The largest possible amount of ovarian tissue must be used. After removal of the corpus luteum the ovary is cut in half longitudinally and one half implanted in each labium or into the sheath of the abdominal muscles. The latter procedure may cause some discomfort and even pain from pressure of constricting garments during menstruation.

After a latent period of one to three months the autografts usually take well, although a few are absorbed. Their functional action persists for three to six years, depending on dimensions and value of the graft and age of the patient. Menopausal disturbances cease or decrease in severity and if the uterus has not been removed, menstruation recurs more or less provisionally. If function of the graft lessens, it can be reactivated with injections of folliculin or gonadotrophic hormones.

The inconvenience of ovarian autografts is minimal when compared to the beneficial effect on general metabolism and on the genital tract of castrated women. In 13 castrated women, the degree of folliculin impregnation was controlled by vaginal curettage.

Autografts into the uterus of ovaries with intact vascular and nervous connections in women after double salpingectomy

---

(1) *Gynéc. et obst.* 49:360-378, 1950.

were made with good results. Menstrual periods became regular and, when fertilization was possible, false pregnancies sometimes occurred. This method is inconvenient in several respects. The graft may be isolated from its vascular pedicle by twisting during operation. The ovary may be surrounded by an inflammatory process, isolating its epithelium from the lumen of the uterus and precluding the possibility of fertilization. Expansion of the uterus during development of the ovum predisposes to abortion, and presence of a secreting body on the uterine wall favors rupture during pregnancy or delivery.

In free grafts into the labia majora the ovarian tissue has to acquire its blood supply, which takes about three months. Signs of castration are evident during this period, but thereafter normal follicular cycles are established and the graft enlarges and becomes painful on pressure. In 80 per cent of cases the signs of castration disappear and basal metabolic rate returns to normal. In 50 per cent of the cases reported average duration of activity of the graft was six years.

**Effect of Male Hormone Combined with Thyroid Hormone in Cancer of Breast and Genitalia in Women.** A. A. Loeser<sup>2</sup> (London), originator of male hormone cancer therapy in women, states that despite its beneficial effect this therapy does not permanently cure cancer. To overcome derangement of thyroid metabolism resulting from massive doses of testosterone propionate he has given thyroxin concomitantly in nine cases of cancer, feeling that the results of this combined therapy are superior to those with the male hormone alone. Masculinization, often encountered in earlier cases, was less pronounced, and weight gains and edema from fluid retention in the tissues were not noted.

A possible objection to use of thyroid hormone is that it stimulates cellular metabolism and may increase development of malignant cells by accelerating mitosis and therefore tend to favor formation of metastases.

In the nine cases reported, Loeser injected 1,000-3,000 mg. testosterone intramuscularly or directly into the tumor and combined this with thyroxin by mouth, which was continued indefinitely. Histologic sections of the cancerous mammary tissue from patients treated by injections directly into the

---

(2) *Gynéc. prat.* 1:179-190, 1950.

tumor showed much more striking degeneration of cancer cells, modification of cytoplasm and formation of larger quantities of fibrous tissue inside and around the tumor and some decrease in mitotic figures as compared with those in which the hormone was given intramuscularly. The peripheral portions of the tumor in the former were less affected than the central portion of the tumor which had received the injections.

Testosterone given in the dosage described raised the level of serum phosphatase, decreased the inorganic phosphatase ratio, displaced toward the left the coagulation of serum albumin and increased urinary excretion of 17-ketosteroids, whether or not thyroxin was given.

Of nine patients given the combined therapy, one had endometrial, one ovarian and seven mammary carcinoma. Four of six breast cancers became operable after treatment. Length of observation after treatment was too short for definite evaluation of the effects, but this study may encourage further application of the method.

[Loeser was the pioneer in the use of male hormone for postoperative recurrence of breast carcinoma. He performed his first experiments in 1937 and has continued his interest in the subject. Now he reports improved results from combined use of thyroid and testosterone.

The report of the Council on Pharmacy and Chemistry of the A. M. A. on "Current Status of Hormone Therapy of Advanced Mammary Cancer" (J. A. M. A. 146:471, June 2, 1951) emphasizes that three palliative measures are available to deal with metastatic mammary cancer: surgery for localized lesions, irradiation and hormone therapy. For most osseous or soft tissue lesions, irradiation is the treatment of choice; lung lesions and widespread osseous or soft tissue metastases may best be treated with hormones. Testosterone propionate is preferable for premenopausal women regardless of site of lesions. However, castration is usually more effective in premenopausal women and should be done if there are no contraindications. In women five years or more postmenopausal, estrogens are best for soft tissue and lung metastases. Although osseous lesions of postmenopausal women respond equally to testosterone propionate and to estrogens, superiority of testosterone in controlling subjective symptoms, particularly pain, makes it appear to be the drug of choice for these metastases. An effective dosage schedule of testosterone propionate seems to be 50 mg. three times weekly. Minimal total dose is about 3 Gm., and minimum length of therapy should be three months before one concludes that a patient will not respond. Minimal total dose of diethylstilbestrol, dienestrol, premarin® and the dimethyl ether of diethylstilbestrol appears to be about 4 Gm. and minimal duration of therapy, three to six months. For ethinyl estradiol and estradiol dipropionate, minimal total dose appears to be 200 mg. and minimal duration of therapy, three to six months. It is suggested that hormone treatment be continued until there is reactivation or steady progression of the disease. Cessation of therapy after reactivation may result in another

regression. Change of therapy to another hormone may also bring about a second favorable response. Both testosterone propionate and the estrogens, in the doses mentioned, produce unpleasant side effects in many patients. Two side effects, edema and hypercalcemia, are dangerous and require constant observation and early corrective measures. Estrogen therapy may cause severe uterine bleeding requiring curettage. With prolonged bleeding, the possibility of endometrial carcinoma or activation of myomas must be considered.—Ed.]

**Employment of Androgens in Gynecology** is discussed by Erling Østergaard.<sup>3</sup> Testosterone propionate is used in parenteral androgen therapy since it exerts a more pronounced and prolonged effect than free testosterone. Orally, methyltestosterone is utilized better than testosterone propionate. In monkeys, testosterone inhibits ovulation and menstruation and causes hypertrophy of the clitoris. At laparotomy on women with normal menstruation who had received 300 mg. or more of testosterone propionate in three to four weeks, the ovaries were devoid of mature follicles or recent corpora lutea. This inhibition of the ovarian function is transitory, since normal menstruation reappears 6-12 weeks after cessation of therapy. Many instances of conception and normal pregnancy have even occurred after discontinuance of treatment. Besides inhibiting ovarian function indirectly, testosterone also directly counteracts the action of estrogenic hormones. In postmenopausal patients given simultaneous injections of testosterone and estrogen, atrophic vaginal epithelium persisted. When only estrogen was given, the atrophic epithelium became normal cornified mucous membrane. Another example of the estrogen-inhibiting effect of androgen is its ability to check estrogen withdrawal bleeding. At laparotomy, 125 mg. testosterone intravenously caused pallor in the uterus in two minutes, probably owing to contraction of uterine muscle and constriction of endometrial vessels.

With 200 mg. testosterone/month, no changes in the endometrium were seen, whereas doses of 300 mg./month constantly produced endometrial changes consistent with abolition of ovarian function. Doses of 500 mg./month produced virilization in about 20 per cent of patients. Changes in voice sometimes proved to be irreversible, but other signs of virilism usually disappeared when therapy was discontinued.

The clinical study of androgen therapy includes its use in functional menorrhagia and metrorrhagia, menometrorrhagia

(3) Acta obst. et gynec. scandinav. 30:106-127, 1950.

in myofibroma, endometriosis, the menopause, dysmenorrhea, frigidity, premenstrual tension, mastopathy and chronic mastitis and cancer of the breast. Dosage was 25 mg. testosterone propionate every other day six times, then every three days to a total up to 250-300 mg. Treatment was continued with methyltestosterone orally, 10 mg. daily, and later 5 mg. daily for some months if necessary. Testosterone therapy has had definite value in functional forms of menometrorrhagia and estrogenic menopausal bleeding. Androgen effects are a little more dubious in menometrorrhagia due to myofibroma, endometriosis, dysmenorrhea, frigidity and premenstrual tension. In some cases of metastatic carcinoma of the breast, a palliative effect was noted.

The effects of androgen in the female may be divided into the following phases: (1) attenuation and inhibition of estrogens, (2) inhibition of gonadotrophic activity of the pituitary, and (3) direct effect on the uterine musculature and endometrial vessels. In larger doses, androgens may induce an arrhenomimetic phase which disappears with cessation of therapy.

**Transmucosal Administration of Methyltestosterone, Free Testosterone and Testosterone Propionate: Clinical Comparison** in dysmenorrhea, loss of libido, cyclic hypermenorrhea, premenstrual tension, endometriosis, dyspareunia, dysuria, cyclic headaches and mastodynia was made by William E. Barfield, J. P. Harrod, Jr., and Robert B. Greenblatt<sup>4</sup> (Med. College of Georgia). Sixty-three co-operative, reliable patients who had been on comparable dosage schedules and had received 107 courses of therapy were studied. In general, a course consisted of buccal administration of 15 mg. of a preparation or placebo daily for at least 30 days. Occasionally, 4-30 mg. was given daily.

Factors considered in evaluation of comparative effectiveness were, when applicable, changes in libido, frequency of orgasm, relief from dysmenorrhea or dyspareunia, improvement in cyclic hypermenorrhea, relief from pain in mastodynia, and incidence of acne, hoarseness and occasionally mild hirsutism. All three preparations proved effective in dosages of 5-30 mg. daily. Satisfactory response was obtained to 80, 67.3 and 64 per cent of the courses of methyltestosterone,

(4) *Am. J. Obst. & Gynec.* 61:1354-1359, June, 1951.

free testosterone and testosterone propionate respectively. In equivalent dosages the last two gave more or less equally good, but less dramatic, results than those obtained with methyltestosterone. Since, unlike the other two, methyltestosterone is effective when ingested, its greater effectiveness might be due to utilization of the dissolved portions of the linguets which are inevitably swallowed during administration.

These results do not refute the usefulness of free testosterone or testosterone propionate. Methyltestosterone is not always well tolerated. In some patients it causes nervousness or nausea. Furthermore, it induces creatinuria and in hyperthyroidism seems to enhance the metabolic rate also.

**Male Pseudohermaphroditism: Some Endocrinologic and Psychosexual Aspects.** In male pseudohermaphrodites congenital anomalies of the external genitalia result in confusion of sex. Since most are certified and reared as females, practical and psychologically correct care of these persons is a gynecologic responsibility. The consensus is that persons with testes but with gynecoid psychosexual desires and orientation should have these trends furthered by appropriate surgery and estrogenization. In most instances such treatment results in less trauma than acceptance of the sex certified on the birth certificate and demand that the person conform to it.

E. C. Hamblen, F. Bayard Carter, James T. Wortham and Juan Zanartu<sup>5</sup> (Duke Univ.) studied 11 male pseudohermaphrodites, aged 4 years, 9 months to 27 years, regarding histopathology of the testes, levels of urinary gonadotrophins and 17-ketosteroids and psychosexual orientation. Location of the testes may be abdominal, inguinal, labioscrotal or scrotal. Specific degeneration in these cases concerns the seminiferous tubules—cytologically the germinal epithelium and functionally the Sertoli cells. There is usually pronounced tubular fibrosis. In six patients in whom determinations were made, hypergonadotropuria was 2.25-8.75 times average normal. The degree is proportional to degeneration of the tubules, which presumably results in failure of release of pituitary-inhibiting hormone. Preoperative values of urinary 17-ketosteroids varied from one-third low range to slightly above normal.

(5) Am. J. Obst. & Gynec. 61:1-19, January, 1951.

Castration usually reduced urinary 17-ketosteroids 20-60 per cent. Estrogen therapy caused less striking reduction. The cause of gynecomastia in 6 of 11 patients before estrogen therapy was not known but was probably related to abnormal steroid metabolism, involving the adrenal cortex. Since 8 of 10 (omitting the youngest patient) were certified and oriented as females, sexual orientation and psychosexual behaviorism cannot be considered prime functions of the gonads.

Castration is an important phase in furthering gynecoid orientation because (1) participation of the testes in abnormal steroid metabolism is avoided, (2) estrogenization is facilitated, (3) neoplasia of cryptorchid testes is avoided and (4) the patient feels more secure, knowing that the undesired male gonads have been removed. Flushing commonly followed castration but was promptly relieved by estrogen therapy. Post-castrational hypergonadotropuria was reduced to normal by estrogen therapy and recurred when estrogens were discontinued. Estrogenization in male pseudohermaphrodites produced responses similar to those of apubescent or hypopubescent females, subject to the limitations imposed when female internal genital organs are absent. The lowered android pitch of the voice was not altered by treatment. Estrogen therapy may produce striking growth and development of hypoplastic uteri; when therapy is given cyclically, regular withdrawal bleeding may result.

From the standpoint of psychologic expediency and clinical practicality the correct sex is that which the person desires and to which there is orientation, usually that certified at birth. Neuropsychiatric assistance should be sought in determining sexual orientation. There should be full understanding by the patient and parents of what is planned and can be done. Complications may arise when it seems necessary to alter sex from that certified by birth registration. The frequent needs for copies of birth certificates may create a psychologic and social crisis. In these circumstances, the birth certificate should be altered to indicate the new sex. Such patients also pose a question as to the meaning and legality of homosexuality. One patient, following castration and without estrogen therapy, married as a female and reported normal coital activity and connubial adjustment. Among questions



yet to be solved is the legal status of such a marriage, if evidence was submitted that the patient was a castrated male, despite certification at birth as a female.

[Not everyone will agree with Hamblen and his associates that castration is an important phase in the furthering of gynecoid orientation and development of male pseudohermaphrodites with this sexual trend. In many cases the gonads have been left in situ without apparent harm. The gonads may even do some good because of their metabolic effects as well perhaps as through their endocrine effect. Everyone agrees, however, that the histologic structure, i.e., the type of gonads present, should be disregarded and that the individual should be maintained in the sex in which he or she grew up. Great tragedies have followed operations to make individuals conform with the histologic sex of the gonads when they had been reared in the opposite sex. In most gonadal males or male hermaphrodites reared as females, a functioning vagina can be made, but the reverse is not true. It is not possible to perform any operation which will permit a gonadal female or female hermaphrodite to have sexual intercourse.

Hinman's article also is full of useful advice concerning the treatment of this unfortunate group.—Ed.]

**Laurence-Moon-Biedl Syndrome: A Confused Symptom Complex.** Because of diagnostic laxity, manifested by failure to include the extraendocrine characteristics originally described and by presumption, rather than actual proof, of hypogonadism, this syndrome has become a confused symptom complex. The original description includes a pentad of congenital characteristics: congenital or heredofamilial hypogonadism, mental retardation, atypical retinitis pigmentosa, obesity and skeletal deformities, specifically dwarfism and polydactylism. Walter S. Keifer, James T. Wortham, Juan Zanartu and E. C. Hamblen<sup>6</sup> (Duke Univ.) reviewed the literature and the gonadal status of nine female patients presumed to have the Laurence-Moon-Biedl syndrome and concluded that females with the characteristics of the syndrome as originally described are very rare. In none was the hypogonadism qualified as that of congenital ovarian aplasia or hypoplasia with hypergonadotropuria or as that due to deficient pituitary stimulation, as manifested by hypogonadotropuria. Also in observations of male patients presumed to have hypogonadism there was no actual proof of its existence.

The Laurence-Moon-Biedl syndrome should be diagnosed only when the original classic pentad of characteristics is present. Hypogonadism should be real, not presumed or prognosticated. It should be qualified by studies of urinary gonadotrophins, urinary 17-ketosteroids, testicular biopsies.

(6) Am. J. Obst. & Gynec. 50:721-730, October, 1950.

and other appropriate methods. The syndrome may be incorporated, on the findings of these studies, into subgroups of congenital ovarian aplasia or hypoplasia or congenital testicular aplasia, hypoplasia or degeneration.

**Syndrome of Large, Pale Ovaries and Its Differentiation from Adrenogenital Syndrome and Cushing's Disease.** Robert B. Greenblatt<sup>7</sup> (Med. College of Georgia) states that, in pure cases, differentiation is aided by the following signs: hirsutism with striking femininity in the Stein-Leventhal syndrome, increased strength and true virilism in androgenitalism and muscular weakness and pseudomasculinization in Cushing's disease.

The syndrome of large, pale ovaries is characterized by amenorrhea, sterility, hirsutism, pain (rare) and menometrorrhagia (occasional). On palpation or pneumoperitoneum, ovaries are found to be symmetrically enlarged; laparotomy shows them smooth, elongated and freely movable (Fig. 133). Sections usually disclose small cysts in the ovarian cortex (Fig. 134). Histologic examination shows a thick fibrous capsule, usually with increased fibrosis of the ovary and hyperplasia of theca cells. Scattered primordial follicles may be found in the cortex though sometimes there are too few to be seen. Many follicular cysts are usually evident, many lined with varying layers of granulosa cells surrounded by several layers of hypertrophic theca cells. Some follicles, however, have lost granulosa cell layers, and the follicle wall shows hyalinization.

Of 10 patients, aged 13-32, all had feminine aptitude and habitus, with well developed breasts. Hirsutism was present without other masculine features, such as enlarged clitoris or voice change, and amenorrhea or menorrhagia after periods of amenorrhea was noted. Vaginal smears were estrogenic, progestogenic or androgenic, and endometrial biopsies usually showed estrogenic endometrium or cystic glandular hyperplasia. Large, pale, abiotrophic ovaries were found at operation. Urinary 17-ketosteroid values were normal in seven, moderately high in three; urinary 11-oxycorticoid values were normal or low in the seven tested, and urinary gonadotrophins were high in four, normal in two. Two of three tested showed excess luteinizing hormone. Symptoms often began in early

(7) *Postgrad. Med.* 9:492-500, June, 1951.

adolescence, but the syndrome became well defined in the second or third decade. All married patients complained of sterility.

Wedge resection of the ovaries is the treatment of choice and is often followed by resumption of cyclic ovulatory menstruation.

The adrenogenital syndrome refers to true masculinization due to hyperactivity of corticosexual adrenal hormones. It is closely simulated by masculinizing ovarian tumors. With prenatal development of the lesion, pseudohermaphroditism

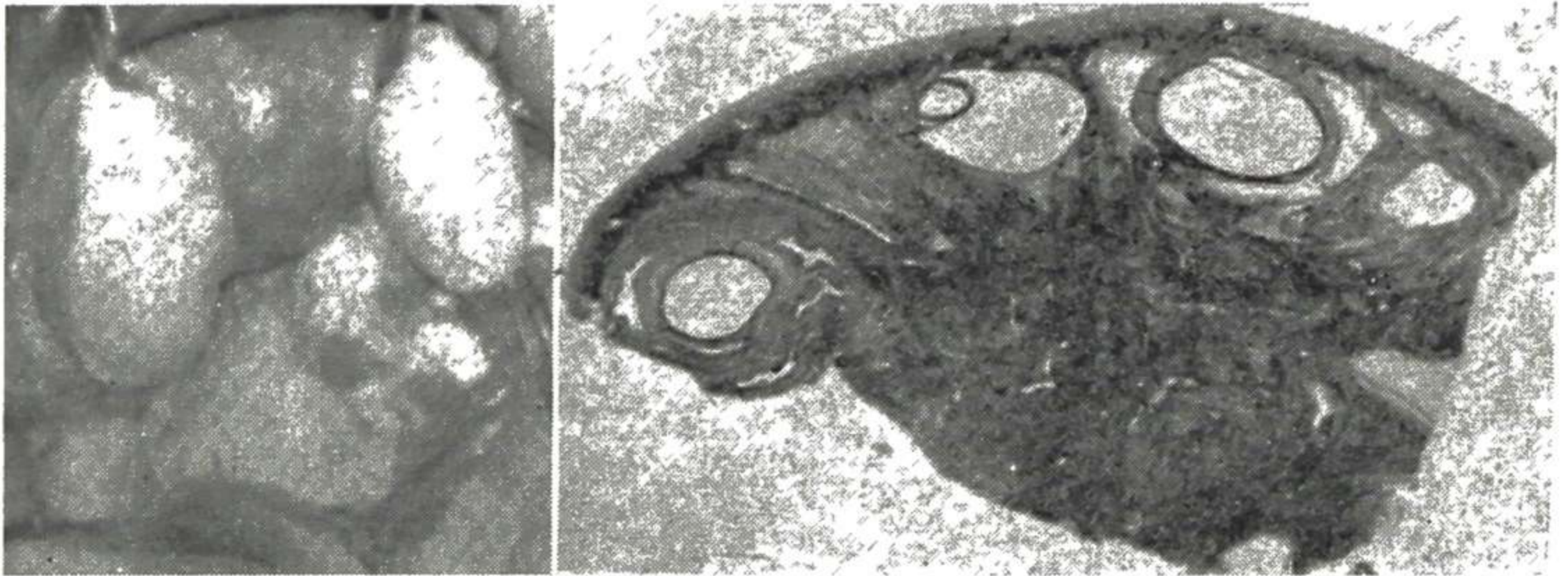


Fig. 133 (left).—Bilaterally elongated, enlarged pale ovaries in Stein-Leventhal syndrome.

Fig. 134 (right).—Photomicrograph of transected ovary, showing numerous small cystic areas occupying cortex.

(Courtesy of Greenblatt, R. B.: *Postgrad. Med.* 9:492-500, June, 1951.)

is usual, with enlarged clitoris, rudimentary or absent vagina, masculine habitus, hair distribution and psyche, and infantile uterus, tubes and ovaries. With onset in puberty, masculinization is usually less complete; there may be precocious puberty with enlargement of clitoris and labia majora, appearance of pubic hair and hirsutism. Sometimes breast growth and menstruation occur. Onset after puberty results in hirsutism, amenorrhea, lowering of the voice, enlargement of clitoris and, sometimes increased muscular strength. In this syndrome, excess corticoids conserve protein instead of converting it to sugar; sugar metabolism is usually undisturbed. Obesity and hypertension are unusual. Diagnosis is confirmed by normal values in glucose and insulin tolerance tests. Urinary excretion of 17-ketosteroids is 40-150 mg./24 hours (sometimes 1,000 mg. or more); 11-oxycorticoid values are usually normal. Urinary excretion of beta-ketosteroids is

usually high with adrenal cortical tumors, but not with adrenal hyperplasia. Pyelograms showing distorted calices and rotated and displaced kidneys suggest adrenal tumor. A palpable solid ovarian tumor suggests arrhenoblastoma or hypernephroma of the ovary. Surgical removal of unilateral adrenal tumors usually restores gynecic function.

Whereas adrenogenitalism is primarily a sexual disturbance, Cushing's disease is metabolic, a hypergluconeogenesis from intrinsic adrenal disorder. This disorder is secondary to pituitary overstimulation of the adrenal. Nitrogen balance is negative, stored fat and protein loss excessive. Symptoms include obesity, usually of the face and trunk, hypertension, skin atrophy, depression of gonadal function, lowered sugar tolerance, erythrocytosis, osteoporosis, fatigue and weakness. Chest and facial hypertrichosis are conspicuous. Common complications are cardiac decompensation, chronic nephritis and nephrolithiasis. The 17-ketosteroid excretion may be normal or slightly increased. When the adrenogenital and Cushing's syndromes overlap the signs of metabolic disorder appear together with virilism. An enlarged adrenal gland or adenoma indicates surgery. Roentgen therapy to the pituitary is also helpful, particularly when x-rays show an enlarged sella turcica.

Hirsutism without endocrine or metabolic disturbance is called idiopathic hirsutism and may be due to hair follicle sensitivity to intrinsic androgens. Therapy is experimental; electrolysis is advised for facial hirsutism, depilatories for growth on the body.

**Use of B-Complex and Vitamin C for Prevention and Elimination of Nausea and Vomiting from Diethylstilbestrol** is reported by Karl John Karnaky<sup>8</sup> (Baylor Univ.). Folic acid and possibly other B complex vitamins are essential in estrogen metabolism. Deficiency of these vitamins therefore may cause the side reactions which follow diethylstilbestrol therapy in 6-10 per cent of women. In 80 consecutive patients, 1-5 cc. soluble vitamin B complex intravenously prevented or eliminated reactions in 75. If given the day of the first 9:00 p.m. dose of diethylstilbestrol, it usually prevents reactions for four to seven days, at which time another injection may be given if necessary. If secondary reactions occur, soluble

(8) *Surg., Gynec. & Obst.* 91:617-620, November, 1950.

vitamin B complex given intravenously will control them in 5-30 minutes and prevent recurrence for 4-7 days. The injection may be repeated daily if indicated or whenever reactions recur, without untoward effects. Tablets containing vitamin B complex, taken three times daily and at bedtime, also inhibited or lessened reactions. Comparable results were obtained with micronized triple diethylstilbestrol, combined in a tablet with B complex vitamins, including folic acid, and vitamin C. Vitamin C has been shown to aid in reducing the reactions.

Routine administration of testosterone propionate intramuscularly and by mouth plus soluble B complex vitamins intravenously and incorporation of B complex and vitamin C in micronized diethylstilbestrol tablets made the side reactions negligible.

METHOD.—Testosterone propionate, 50-100 mg., is given intramuscularly and soluble B complex, 1 cc., intravenously the day before the 9:00 p.m. dose of diethylstilbestrol ( $\frac{1}{4}$  of a 25 mg. desplex tablet). If the patient has side reactions to diethylstilbestrol, injection of soluble B complex is repeated and diethylstilbestrol dosage reduced by  $\frac{1}{4}$  tablet and increased  $\frac{1}{4}$  tablet every seventh instead of every fourth day.

Side reactions were lessened in 40 consecutive nonpregnant patients; 38 had no vomiting and most had mild reactions. Of 40 nonpregnant controls given plain 6.25 micronized diethylstilbestrol tablets without B complex, 38 had nausea and vomiting.

