Chapter 28
Surgery for Benign Disease of the Ovary

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DEFINITIONS

Accessory ovary—An additional ovarian mass close to the normally placed ovary and connected to it by the utero-ovarian or infundibulopelvic ligament.

Fertility preservation prior to cancer therapy—Affording the patient prior to provision of chemoradiation therapy a host of options that provide for ovarian tissue, embryo, or oocyte cryopreservation as well as surgical procedures designed to protect the ovaries from radiation therapy.

Fimbria ovarica—The structure attaching the infundibulum of the fallopian tube to the distal pole of the ovary. It is vitally important to the fimbrial ovum capture mechanism.

Malpositioned ovary—An ovary located above the pelvic brim because of a lack of normal descent into the pelvis. It may be elongated, but it remains attached to the uterus by the utero-ovarian ligament and to the fallopian tube by the fimbria ovarica.

Ovarian cortex—The outer layer of the ovary consisting of an outer zone, which is mainly collagenous (tunica albuginea), and an inner zone, which is less fibrous and more cellular and contains the germ cells (primordial follicles).

Ovarian medulla—The inner region surrounding the hilum of the ovary. It contains no follicles, only blood vessels and the remnants of the tubular structures that are homologous to the male testis (rete testis).

Ovarian remnant—Persistent ovarian tissue unintentionally left behind following oophorectomy.

Prophylactic oophorectomy—In genetic mutation carriers, that is, BRCA1 or BRCA2, removal of both ovaries upon completion of childbearing in an effort to minimize chance of ovarian cancer.

Residual ovary—Symptomatic ovarian tissue following removal of the ovary.

Supernumerary ovary—An additional ovary that has no direct or ligamentous connection with a normally placed ovary. It is located at a distance from the normally placed ovaries.

Tumor markers—Substances identified in higher than normal amounts in blood, urine, or body tissues of patients with specific malignancies. They are produced directly by the tumor or as a response to the presence of cancer, that is, indirect marker.

Tunica albuginea—Condensed ovarian stroma that forms a fibrous capsule.

Evaluation and management of benign disease of the ovary continues to unfold with new and challenging clinical alternatives. Progress has occurred with regard to understanding the genetics of ovarian function, new surgical approaches to ovarian disease, and a host of knowledge that clinicians should be aware of. The population is living longer, and cancer survivors are increasing exponentially. All of this leads us to focus on enhancing our understanding of preservation of ovarian function; expanding the potential for conception, which includes determining treatment related to decreased postoperative adhesion formation; and addressing an array of other aspects related to ovarian activity.

It has been established that the ovaries and fallopian tubes are sensitive to ischemia from surgical trauma; adhesions may develop as a result; the normal anatomic relationship between fallopian tubes, ovaries, and uterus may be altered. Knowledge regarding anatomy and embryology of the ovaries and other reproductive organs complemented by mastery of the principles of microsurgery that can be applied to virtually any surgical procedure are the prerequisites for excellent results following ovarian reconstructive surgery. Embryology and anatomy are addressed in this chapter with emphasis on the importance of the anatomic relationship of the ovary to other pelvic organs in the section on the evaluation and management of an adnexal mass. State-of-the-art surgical procedures—both via minimally invasive, robotic-assisted and laparotomic approaches and techniques devised for the reconstruction of the ovary—for restoration of normal pelvic anatomy are presented in the context of specific pathology or other abnormal conditions that require surgical intervention. This chapter also focuses on pediatric and adolescent gynecologic surgical procedures that are performed when ovarian

pathology is identified.

EMBRYOLOGY

The reproductive system is derived from mesoderm. The primordium of the urogenital ridge is divided into two segments. One is the nephrogenic ridge, that is, metanephros derivatives, the renal system; the other is the gonadal ridge for development of the reproductive tract. Gonads are a reflection of three origins: mesothelium, mesenchyme, and primordial germ cells. The paramesonephros gives rise to the fallopian tubes and the uterus. Two gonadal ridges arise early in gestation (4 to 5 weeks) in the

developing embryo as thickening on the medial aspect of the coelomic cavity adjacent to the mesonephros. These gonadal outgrowths are composed of coelomic epithelium and underlying mesenchyme projecting into the future peritoneal cavity. The epithelial and mesenchymal cells of the gonadal primordia are of mesodermal origin (large, spherical ovoid germ cells that originate extragonadally in the wall of the yolk sac and migrate to the developing gonads). Until the 6th week of gestation, the gonads of the two sexes remain morphologically indistinguishable. The presumptive ovaries remain undifferentiated until the onset of meiosis at the end of the first trimester. The ovarian cortex is a single germinal epithelium. The tunica albuginea lies beneath the cortex and is composed of connective tissue. The stroma is composed of fibroblasts, smooth muscle, endothelium, and interstitial cells, including undifferentiated theca cells and corpora albicans.

Sexual differentiation requires initiation by various genes, along with a single gene determinant on the Y chromosome (testis-determining factor), which is necessary for testicular differentiation. In XX individuals (in the absence of a Y chromosome), the bipotential gonad develops into an ovary.

The mechanisms responsible for gonadal sex differentiation are largely unknown. Investigators have theorized the presence of a testis-determining factor (H-Y cell-surface antigen on the short arm of the Y chromosome) that is elaborated by a specific gene. Meiosis-inducing and meiosis-preventing substances, both of which are produced by cells derived from mesonephric structures adjacent to the gonad, are the agents of regulation of ovarian and testicular germ-cell differentiation. The balance between these two substances varies between the two sexes and at different stages of development. The meiosisinducing substance predominates in the fetal ovary. Maternal ovarian hormone production is not required for differentiation of the germ cells or, apparently, for later development of the fetal reproductive tract. Various ultrastructural studies have shown no specific changes in fetal granulosa cells that can be definitely associated with steroid hormone secretion such as is identified in the fetal Leydig cells. Thecal cells play an essential role in steroid synthesis in the adult ovary, but they do not appear until later in gestation and even then retain a relatively undifferentiated appearance. Fetal pituitary gonadotropin production begins as early as 10 weeks gestation and reaches peak levels at midgestation. Gonadotropins have a major influence on follicular development in the adult ovary, but evidence for a similar function in the fetus is lacking.

GENE EXPRESSION

Understanding of the genetics of the ovary continues to evolve. With the advent of polymerase chain reaction (PCR), real-time PCR, fluorescence in situ hybridization, single nucleotide polymorphism, and a host of other genetic advances, understanding of ovarian function has reached a new level (**Fig. 28.1**). **Table 28.1** provides information regarding genes and associated phenotype.

Genes often are associated with specific clinical problems, for example, Kallmann syndrome, a genetic condition that results in the failure of pubertal development. Hypogonadism associated with a total lack of sense of smell (anosmia) or a heavily reduced sense of smell (hyposmia) characterizes the syndrome. Premature ovarian insufficiency (POI) is characterized by hypergonadotropic hypogonadism, which equates with the loss of ovarian function before age 40. The problem of POI overall is associated with a host of gene defects, all of which set the stage for genetic testing in patients in the reproductive age group with amenorrhea in association with hypergonadotropic state. Genes are also involved with cumulus expansion (GDF9 and BMP15) and endometriosis, and most recently serve as predictors of oocyte quality and successful embryo implantation and development. Specific follicular cell receptors bind growth factors, which are locally synthesized with the ultimate effect of intracellular signaling and protein kinase activation. This activity affects transcription of targeted genes. Gene expression is involved in follicle development, ovulation,

and corpus luteum and corpus albicans formation. Transcription factors include protooncogenes, c-Myc, and

CCAAT/enhancer binding protein.

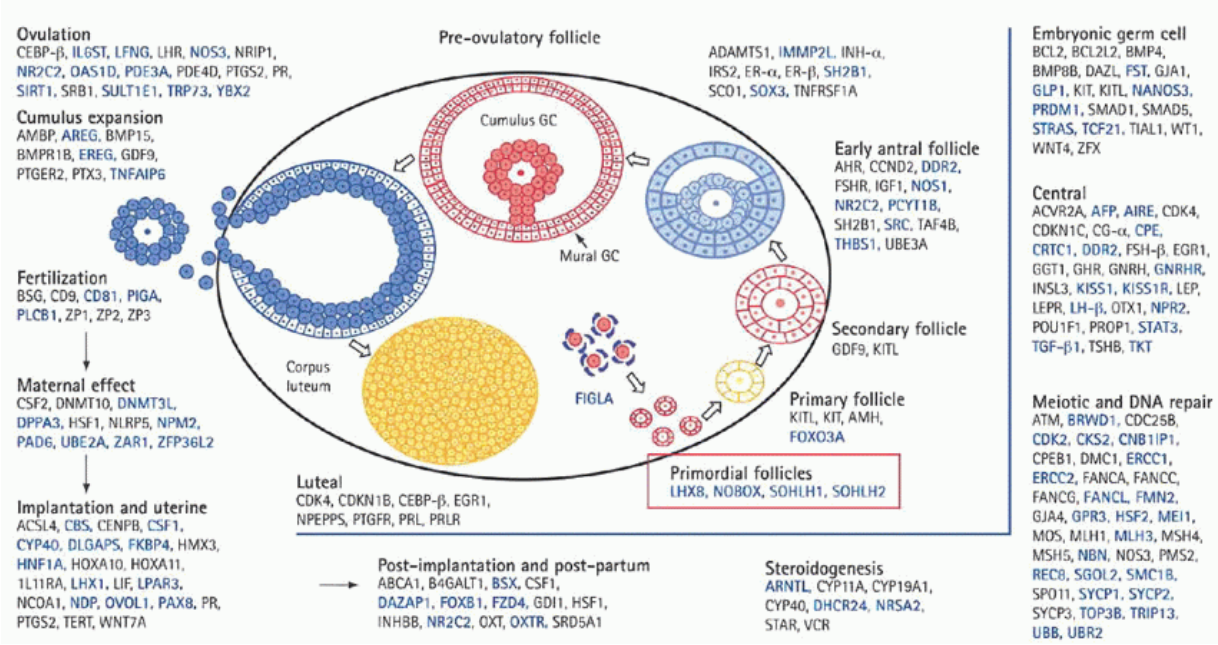

FIGURE 28.1 Model of ovarian genes recognized in 2008. (Reproduced from Fauser BC, Diedrich K, Bouchard P, et al. Contemporary genetic technologies and female reproduction. The Evian Annual Reproduction (EVAR) Workshop Group 2010. *Hum Reprod Update* 2011;17:829, with permission. Copyright © 2011 Oxford University Press.)

TABLE 28.1 Gene Mutations and Ovarian Activity

Bone morphogenetic protein receptor 1 beta (BMPR 1Beta)	Ovarian dysfunction
Fibroblast growth factor beta (FGFBeta)	Kallmann syndrome (KAL2)
Fragile X mental retardation 1 (FMR1)	Premature ovarian insufficiency
Kallmann syndrome 1 (KAL1)	Hypogonadotropic hypogonadism and insomnia X-linked Kallmann syndrome
Premature ovarian failure 1 beta (POF1Beta)	Hypergonadotropic, primary amenorrhea (POF2Beta)
Prokineticin receptor 2 (PROKR2)	Kallmann syndrome (KAL3)

FEMALE FETAL DEVELOPMENT

The ovarian surface cortex, during the early prefollicular stage, is characterized by germ cells and granulosa cells organized in cords and sheets, but the cortex lacks specific conformation. The final distinctive change to occur in the fetal ovary is the onset of meiosis at the 11th or 12th week of gestation. Meiosis is preceded by differentiation of primitive germ cells into actively dividing mitotic cells called *oogonia*. The mitotic divisions of the oogonia are associated with complete separation at telophase, leaving the daughter cells connected by intracellular bridges. After a series of mitotic divisions, there is progressive entry of cells into meiosis, beginning in the innermost cortex and gradually extending to the periphery. These cells passing through the various stages of the first meiotic prophase are then designated *oocytes*. By late gestation, all surviving oocytes have advanced to the diplotene stage. Further differentiation of the oocytes is arrested at this stage and does not resume until ovulation begins at menarche, approximately 12 years later.

Follicular formation begins at 18 to 20 weeks gestation and continues throughout the remaining weeks of fetal development.

All the surviving oocytes are surrounded by adjacent granulosa cells; oocyte and follicular growth are well established by the late fetal and early neonatal period. The constant degeneration and loss of oocytes before their incorporation into the follicles reduces their numbers to only 1 to 2 million (follicles) in the newborn ovary.

ANATOMY

The dimensions of the adult ovary vary from individual to individual but average 3 to 5 cm in length, 2 to 3 cm in width, and 1 to 2 cm in diameter, with a weight of 3 to 8 g. The ovarian capsule is smooth in childhood, but its surface becomes pitted from follicular maturation and atresia.

The size, shape, and position of the ovary in the pelvis are somewhat variable, and both the consistency and the follicular changes taking place within the ovary vary with stage of the menstrual cycle. The ovary typically is anchored to the sidewall of the pelvis in the shallow peritoneal fossa of Waldeyer formed between the angles of proximity of the ovary to the ureter. This knowledge is important before dissecting the ovary off the pelvic sidewall.

The ovary is connected to the uterus by the utero-ovarian ligament, to the posterior aspect of the broad ligament by the mesovarium ligament, and to the lateral pelvic sidewall by the infundibulopelvic ligament (Fig. 28.2). The

mesovarium ligament attaches to the mesentery of the ovary. The other two ligaments are attached at the hilum of the ovary.

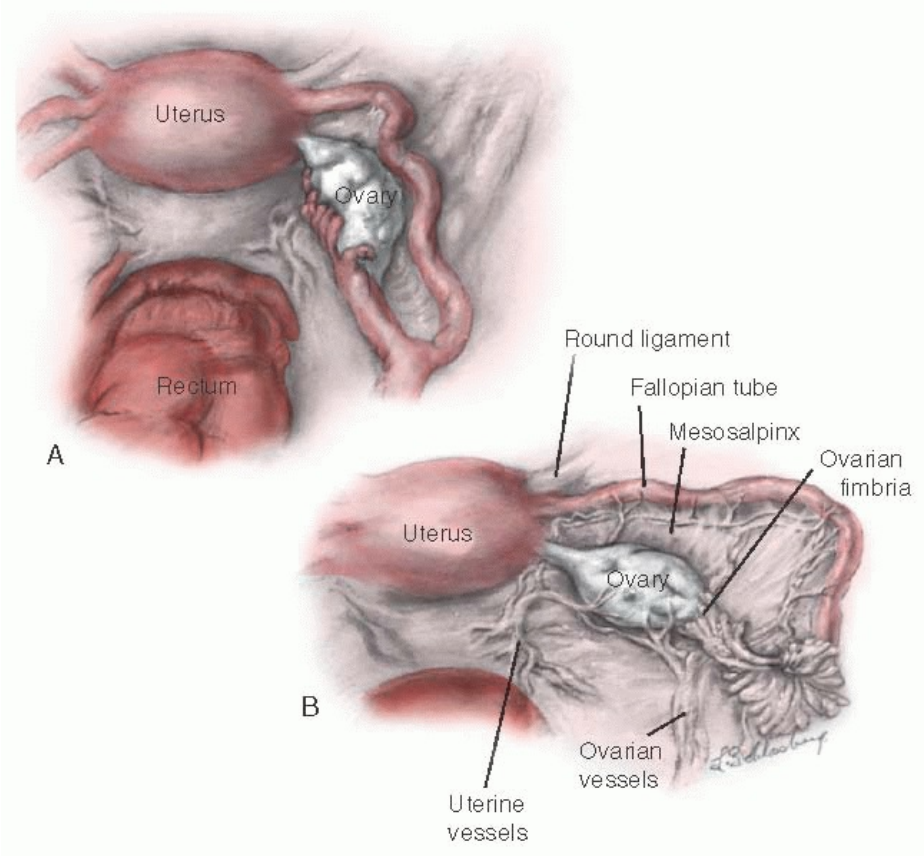

FIGURE 28.2 Normal anatomy of the ovary. **A:** Anatomic relations of the uterus, tube, and ovary. **B:** The infundibulum of the oviduct extends onto the ovary and is attached at its most distal pole (ovarian fimbria). The mesovarian suspends the ovary. Each ovary is attached at the hilum.

The ovary migrates downward from high in the abdomen during embryonic life. The infundibulum of the fallopian tube extends onto the ovary and is attached to it at its most distal pole by the fimbria ovarica. The relation of the ovary to the fimbria ovarica and to the utero-ovarian ligament is crucial, and they should be carefully maintained during ovarian reconstruction.

During embryogenesis, the ovary may assume an unusual appearance (i.e., it may be septate) or assume an unusual position (Fig. 28.3). An accessory ovary (Fig. 28.3A) usually is close to or is connected to a normally placed ovary. An accessory ovary also may be attached to the broad, utero-ovarian, or infundibulopelvic ligaments. Unlike the accessory ovary, a supernumerary ovary (Fig. 28.3B) must have an independent embryologic origin. It may develop from a primordium such as arrested migrating gonadocytes. A supernumerary ovary consists of typical ovarian tissue but has no direct or ligamentous

connection with a normally placed ovary. A supernumerary ovary is thus a true third ovary that has independent function and is located at a point that is distant to a normally placed ovary. Ovarian malposition (**Fig. 28.3C**) also may occur when the ovary fails to descend into the pelvis to assume its normal location. In ovarian malposition, the ovary is attached as it should be to the uterus by the utero-ovarian ligament and to the fallopian tube by the fimbria ovarica, but it may lie adjacent to the liver or spleen. The ovary is elongated and may measure up to 15 cm in length. The fallopian tube attaching to such a malpositioned ovary may be 20 to 26 cm in length, almost twice its normal length.

The normal ovary has a surface covering composed of a single layer of flattened, germinal epithelial cells. This layer is contiguous at the ovarian hilum, with the peritoneal epithelium of the posterior leaf of the broad ligament. Beneath the germinal epithelium is a second layer of condensed ovarian stroma that forms a fibrous capsule, the tunica albuginea. The area through which the vessels and nerves enter and exit is the hilum of the ovary. Immediately around the hilum and extending into the substance of the ovary is an area known as the medulla, which is covered by the cortex. The medulla is composed of fibrous tissue unlike the condensed stroma of the ovarian cortex. The medulla contains no follicles; it has only blood vessels and the remnants of the tubular structure that would have developed into a testis (i.e., the rete ovarii) had the fetus been male.

The ovarian artery arises from the renal arteries. The artery descends from the aorta and crosses the ureter obliquely to enter the infundibulopelvic ligament on its course to the ovary. When it reaches the broad ligament, the ovarian artery branches to supply the fallopian tube and ovary before it finally anastomoses directly with the uterine artery to form a continuous arcade in the broad ligament. The ovarian veins are situated mainly in the mesosalpinx, where they give rise to the pampiniform plexus. At the outer end of the broad ligament, this plexus coalesces to form a single, large ovarian vein. The ovarian vein runs adjacent to ovarian artery to terminate in the inferior vena cava on the right and the renal vein on the left.

The lymphatic vessels of the ovary drain in three directions. The main group accompanies the ovarian vessels in the infundibulopelvic ligament and eventually reaches the periaortic nodes in the vicinity of the kidney. Other lymphatic channels communicate with channels of the opposite ovary by crossing the fundus of the uterus through the ovarian ligament. Some channels drain through the ovarian and round ligaments into the superficial inguinal lymph nodes in the groin. The ovary is supplied by both motor and sensory parasympathetic and sympathetic nerves,

which accompany the ovarian vessels from the abdomen as they pass into the infundibulopelvic ligament to reach the hilum of the ovary. The segmented nerves supply the ovary from T10 and T11.

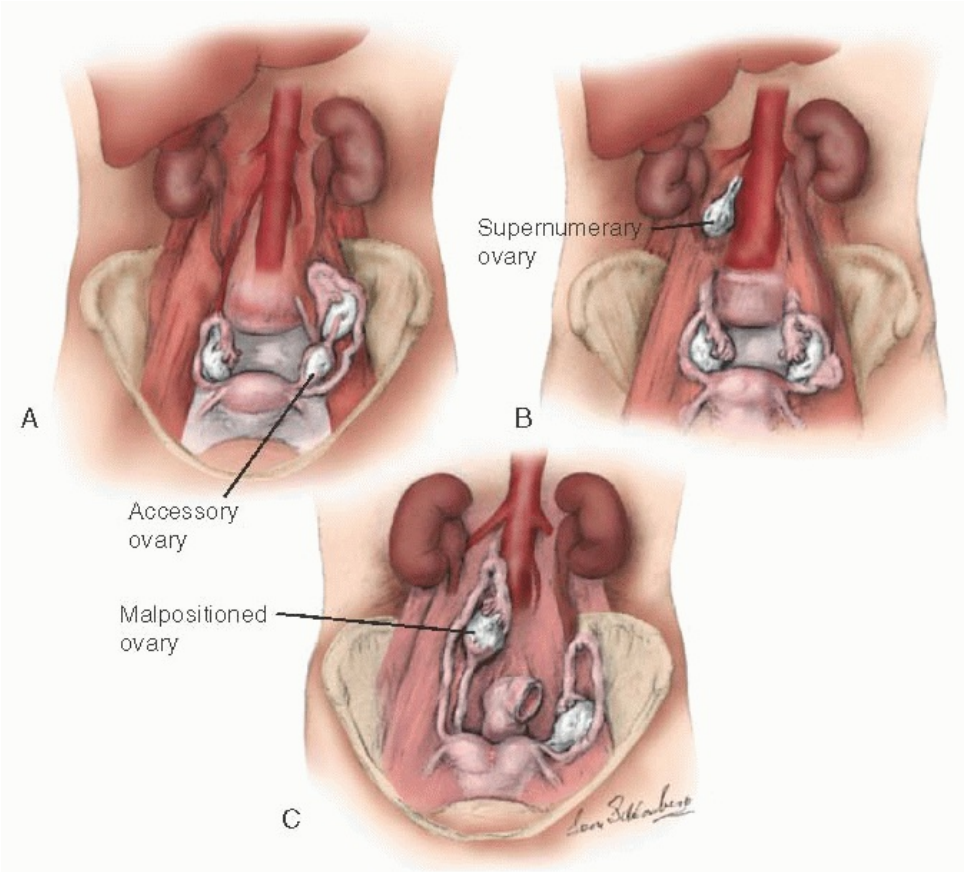

FIGURE 28.3 Ovarian anomalies. **A:** Accessory. **B:** Supernumerary. **C:** Malpositioned.

ADNEXAL MASS

The uterine adnexa (gynecologic origin) consist of the ovaries, the fallopian tubes, and the uterine ligaments. Although adnexal pathology often involves one of these structures, contiguous tissue of nongynecologic origin also may be involved. Adjunctive diagnostic techniques such as sonography, magnetic resonance imaging (MRI), and computed tomography (CT) may help delineate the nature of adnexal enlargement. Pelvic ultrasonography, especially three dimensional, is an accurate means of determining the location, size, extent, and consistency of pelvic masses and is also useful for detecting obstructive uropathy, ascites, and metastasis. Other more specialized diagnostic procedures also may be necessary for the evaluation of an adnexal mass (**Table 28.1**).

Computed tomography scanning has been particularly useful in gynecologic oncology because it helps define the extent of paracervical and parametrial involvement and allows a reasonable determination of the resectability of malignant neoplasms. Magnetic resonance imaging has surpassed CT in the precision of measurement of adnexal masses. Magnetic resonance imaging also allows a clear definition of the relationship of adjacent organs.

In a study conducted by Timmerman and coworkers, assessment was made of the use of both ultrasound and circulating levels of CA-125 antigen. Multivariate logistic regression analysis algorithms were used to distinguish benign adnexal masses from a malignant process. Transvaginal ultrasonography with color Doppler imaging was recorded in the 191 patients evaluated, aged 18 to 93 years. Of interest, 26.7% of the cohort of patients studied had malignant tumors. The authors believed that regression analysis could be used to accurately discriminate malignant from benign adnexal masses preoperatively.

An intriguing aspect of ultrasound assessment is the prediction of malignancy in adnexal masses using an artificial neural network. Taylor and colleagues reported generating a neural network algorithm that enabled computing of a probability of malignancy score for preoperative discrimination between malignant and benign adnexal masses. A retrospective analysis that included training in artificial neural network assessing transvaginal B-mode ultrasonography and color Doppler imaging was determined. The variables that were put into the artificial neural network included age, menopausal status, maximum diameter of the neoplasm, tumor volume, and papillary projections. The results identified four primary variables that were most effective in distinguishing benign versus malignant processes. These variables included age, time-averaged maximum velocity, papillary projection score, and maximum tumor diameter. The authors concluded that artificial neural networks are a useful clinical parameter to distinguish benign from malignant ovarian masses.

Surgical intervention ultimately may be necessary to determine the nature of the adnexal mass. Minimally invasive surgery is useful to exclude benign ovarian or nonovarian neoplasms. Indications for visualization and as indicated to obtain a tissue diagnosis of an adnexal mass with laparoscopy or exploratory laparotomy include the following:

- Ovarian mass greater than 6 cm in diameter
- Adnexal mass greater than 10 cm in diameter
- Any solid mass first developing after menopause
- Failure to discover the nature of the mass (e.g., leiomyoma) with radiologic or sonographic imaging techniques

One of the major goals of evaluation of the adnexal mass is to rule out malignancy. There is an age-dependent risk for a malignant adnexal mass. The incidence of malignant neoplasm increases significantly after age 50 years. Increased size of the adnexal mass is associated with an increased risk of malignancy.

Granberg and colleagues found that less than 1% of masses smaller than 5 cm were malignant, less than 11% of masses 5 to 10 cm were malignant, and 72% of masses larger than 10 cm were malignant. Sassone and associates, in an evaluation of women of all ages (mean age 41 years) by transvaginal sonography, found that 3% of masses smaller than 5 cm and 7% of masses 5 to 10 cm were malignant; the incidence of malignancy for masses larger than 10 cm was 13%.

Endometriosis is a common cause of an adnexal mass. An endometrial cyst of the ovary may develop into an endometrioma. Leakage of blood from the cyst may cause peritoneal irritation, pelvic adhesions, and pelvic organ fixation.

Tubo-ovarian inflammatory complex usually is the result of incompletely treated or unresolved subacute, chronic pelvic inflammatory disease (PID) in the walled-off area surrounding the pelvic structure.

Uterine leiomyomata cause nodularity and consequent irregular conformation of the uterus. The uterus may become enlarged

and may present as an abdominal mass. The inability to distinguish a leiomyoma from an ovarian tumor on pelvic examination is an indication for further diagnostic evaluation.

Adnexal enlargement may be the result of carcinoma of the rectum, appendix, or bladder. Patients present with a variety of symptoms according to the organ involved. A complete and thorough evaluation is necessary to delineate the etiology of a neoplasm.

An adnexal mass may be noted in cases of acute abdomen. The differential diagnosis should include adnexal torsion, ruptured hemorrhagic cyst, degenerating leiomyomata, ectopic pregnancy, unruptured tubo-ovarian abscess, acute appendicitis with or without abscess formation, and diverticular disease of the sigmoid colon. A careful history, pelvic examination, and appropriate imaging studies often allow a prompt diagnosis.

Although every adnexal mass requires individual evaluation and management, it is possible to make a number of useful general recommendations. Expectant management is justified only when an asymptomatic physiologic cyst is suspected. Most cysts greater than 6 cm in diameter require a thorough evaluation. Imaging techniques are invaluable for characterizing the nature of the adnexal enlargement, but these procedures do not replace a careful medical history and thorough physical and pelvic examination.

ADNEXAL MASS DURING PREGNANCY

The incidence of adnexal mass in pregnancy requiring surgical intervention has been reported to occur at 1 in 81 to 2,500 pregnancies. When an adnexal mass is noted incidentally on ultrasound during pregnancy, the majority of small, simple cysts do not pose a risk to the pregnancy. Furthermore, most large or sonographically complex masses spontaneously resolve, as reported by Bernhard and colleagues; this study evaluated 18,391 ultrasound studies done in an obstetric population for which 432 women were identified with an adnexal mass. The incidence of adnexal masses was 2.3% in the pregnant population evaluated. In addition, the rate of torsion of the adnexal mass was 1%, and the rate of malignancy was also reported as 1%.

The majority of patients in one other study involving 320 pregnant patients with an adnexal mass were noted to have a simple cyst less than 5 cm, specifically 76%; the cysts were

more commonly asymptomatic. The remaining patients were noted to have complex cycsts greater than 5 cm; of interest, of the complex cysts, 69% resolved spontaneously. The concern always remains regarding the potential for malignancy. Masses with increased blood flow or decreased resistance index and greater than 10 cm or a growth rate greater than 3.5 cm per week were noted to have a higher risk for malignancy.

Hoover and Jenkins addressed the incidence and differential diagnosis, benign cystic teratoma (7% to 37%), serous cystadenoma (5% to 28%), mucinous cystadenoma (3% to 24%), endometrioma (0.8% to 27%), paraovarian cyst (<5%), and leiomyoma (91% to 25%). Ovarian malignancy accounted for 1% to 8%, most of which were low malignant potential (LMP).

Other risks related to adnexal mass in pregnancy include rupture and obstruction regarding labor. Randomized prospective data focused are lacking with regard to pregnant patients with adnexal masses addressed surgically versus expectant management. Complications that include preterm labor and spontaneous abortion must be included in the overall assessment and management. Evaluation of oncofetal antigens includes alpha-fetoprotein, human chorionic gonadotropin (hCG), lactate dehydrogenase, estradiol, and testosterone.

Before operative intervention, a complete assessment of the fetus—including ultrasound to rule out a lethal anomaly and to document cardiac activity—is in order. The optimal time for elective surgery is during the second trimester. The patient should be informed of the increased risk of preterm labor and delivery. The patient should be placed in the left lateral tilt position to avoid inferior vena cava compression and associated uteroplacental insufficiency. Postoperatively, the fetus should be placed on continuous fetal heart rate monitoring.

The most effective approach in the management of adnexal masses during pregnancy remains a point of controversy (i.e., laparoscopy vs. laparotomy). In a series of 88 pregnant women who underwent 93 surgical procedures for suspected adnexal pathology, laparoscopy was performed during the first trimester in 39 patients. The remaining 54 patients underwent laparotomy, 25 during the first trimester and 29 during the second trimester. Neither intraoperative nor postoperative internal complications were reported in the series. Five of thirty-nine women undergoing the first-trimester surgery had a spontaneous abortion. During the first trimester, a Veress needle was used for insufflation, and the procedure was in essence conducted in a manner virtually identical to that in the nonpregnant state (i.e., closed laparoscopy). It was concluded that laparoscopic

gynecologic surgery is safe during pregnancy when conducted in the first trimester.

ULTRASOUND

Ultrasound is useful in predicting malignancy (**Table 28.2**). Characteristic features of benign versus malignant neoplasms have been reported. Collated data from studies of ultrasound accuracy in the prediction of malignancy have an average positive predictive value of 74% and an average sensitivity of 88% (**Tables 28.3** and **28.4**).

Weiner and coworkers have used transvaginal color flow imaging before exploratory surgery to study the impedance to blood flow in women with an adnexal mass. Intramural blood vessels consistently demonstrated low impedance to flow with a pulsatility index less than 1:16 in women with malignant tumors. The sensitivity and specificity of the preoperative pulsatility index in detecting malignant ovarian tumors were 94% and 97%, respectively. Kurjak and colleagues found that vessels with a low resistance index near the center of the mass or within papules or septa were highly correlated with malignancy. Therefore, transvaginal color flow imaging may be a useful clinical tool in the preoperative evaluation of ovarian masses.

TABLE 28.2 Special Diagnostic Procedures for the Evaluation of an Adnexal Mass

Nonoperative noninvasive
Abdominal and pelvic radiography
Barium enema
Excretory urography
Gastrointestinal series with small-bowel follow-through
Computed tomography scan
Magnetic resonance imaging
β-hCG
CA-125
Nonoperative invasive
Culdocentesis
Pelvic arteriography
Operative noninvasive
Abdominal and pelvic examination under anesthesia
Operative invasive
Culdoscopy
Laparoscopy
Exploratory posterior colpotomy
Exploratory laparotomy

Doppler resistance index has been used as a “vascular” scoring system. Color Doppler ultrasonography appears to be a reliable method in presurgically evaluating ovarian neoplasms.

Transvaginal color Doppler sonography has identified the following parameters as useful in determining malignant versus benign ovarian masses: number of vessels detected in each tumor, tumor vessel location (central vs. peripheral), peak systolic velocity, lowest resistance index, mean resistance index,

lower pulsatility index, and mean pulsatility index. Color Doppler signals were detected in 100% of malignant masses and 75% of benign masses, with the difference being statistically significant as reported by Alcazar and associates. Tumor vessel

location appears to be central in virtually all malignant masses. Overall, the receiver operating characteristic curves generated can be used to predict malignant processes. The lowest resistance index was associated with the majority of malignant tumors.

TABLE 28.3 Ultrasound Characteristics of the Ovary

Benign pattern
Simple cyst without internal echoes
Simple cyst with scattered echoes
Polycystic echoes
Polycystic echoes with thick septum
Sessile or polypoid smooth mural echoes
Central dense round echoes
Thin or thick multiple linear echoes
Thin or thick multiple linear echoes with dense part
Malignant pattern
Cystic echoes with papillary or indented mural part
Polycystic echoes with irregular thick septum and solid part
Solid pattern (50%) heterogeneous component with irregular cystic part
Completely solid with homogeneous component
Low impedance to flow (color Doppler)

TABLE 28.4 Ultrasound Accuracy in Prediction of Malignancy

AUTHOR	PATIENTS (*n*)	MALIGNANCY PREVALENCE	POSITIVE PREDICTIVE VALUE (%)	NEGATIVE PREDICTIVE VALUE (%)	SENSITIVITY	SPECIFICITY
Kobayashi (1976)	406	15	31	93	71	73
Meire et al. (1978)	51	35	83	91	83	91
Pussell (1980)	26	48	83	91	83	84
Herrmann et al. (1987)	241	21	75	95	82	93
Finkler et al. (1988)	102	36	88	81	62	95
Benacerraf et al. (1990)	100	30	72	91	80	87

Granberg et al. (1989)	180	21.5	74	95	82	92
Sassone et al. (1991)	143	10	87	100	100	83

Three-dimensional ultrasonographic technology has been used to evaluate adnexal masses. Images are dissected in *XYZ* planes and can be focused especially on areas suggestive of malignancy. Three-dimensional ultrasonography facilitates real-time analysis of acquired image data and allows reassessment of the findings at the time of the original ultrasound. Three-dimensional transvaginal ultrasonographic technology appears to enhance and facilitate morphologic assessment of benign as well as malignant ovarian masses.

The appearance on ultrasound provides clinically useful information. Up to 95% of endometriomas exhibit diffuse homogenous low-level internal echoes. They can vary in appearance to include large cystic and solid components; thus, hemorrhagic cysts must be included in the differential. Teratomas on ultrasound demonstrate hyperechoic nodules with distal acoustic shadowing, often termed a “dermal plug.” Hair and sebaceous contents are visualized as hyperechoic lines and dots, termed a “dermoid mesh.” With regard to cystadenomas, serous are more common than mucinous and the former are noted to have thin septations; occasionally, papillary projections may be noted. Mucinous cysts are multilocular with varying amounts of fluid content; low-level internal echoes with multiple thin septa are commonly noted. Cystadenocarcinoma is characterized by thicker septations, papillary projections greater than 3 mm, and irregular walls. Tumors of LMP demonstrate an “ovarian crescent sign,” equated with a rim of normal-appearing ovarian tissue adjacent to the tumor mass. Vascular mural nodules and papillary projection may be present. Paraovarian masses include paraovarian cysts and hydrosalpinx. Ovarian torsion is associated with a “ground-glass” appearance on ultrasound; a characteristic “whirlpool sign” is consistent with the appearance of vessels coiling in a twisted vascular pedicle on color Doppler studies. The latter may demonstrate arterial or venous flow, only arterial flow, or no flow at all to the torsed ovary.

In addition to the role of Doppler ultrasonography with regard to identifying a malignancy, it is also useful in following the progression or regression of the adnexal mass.

MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging is a “second-line imaging modality.” It is important that patients fast 4 hours before the planned MRI examination as this limits artifact from bowel peristalsis. Scanning in left lateral decubitus position may be necessary during pregnancy. A body array coil is frequently used over the pelvis in pregnant women undergoing MRI. Gadoliniumbased contrast is a pregnancy category C drug.

TUMOR MARKERS

Tumor markers are substances that are identified in higher than normal amounts in blood, urine, or body tissues of patients with specific malignancies. Tumor markers are not unique to malignant processes and can be elevated with benign conditions. Tumor markers are not elevated in every patient with malignancy, especially in the early stages of the disease. Many tumor markers are not specific for a particular type of cancer; therefore, there are limitations to the use of tumor markers.

CA-125 is a tumor-associated antigen to an antibody expressed by approximately 80% of patients with epithelial ovarian cancer. It can be increased by nongynecologic malignancies with involvement of the pleura or peritoneum and by benign conditions that result in ascites. Because of the many medical diagnoses that give false-positive CA-125 results, CA-125 cannot be used for general population screening for ovarian cancer in either premenopausal or postmenopausal women. However, in menopausal women who present with a pelvic mass, CA-125 can help differentiate benign from malignant masses.

Because menopausal women have fewer gynecologic diseases that give false elevation of CA-125, the test is more sensitive and specific in this age group. Several authors have

demonstrated that a panel of assays can improve both sensitivity and specificity in the detection of ovarian malignancies. For example, Soper and associates demonstrated 100% specificity and predictive value for CA-125 with TAG 72 or CA-15-3. **Table 28.5** provides specific markers and their clinical application.

TABLE 28.5 Tumor Markers: Adnexal Masses

MARKER	COMMENTS
CA-125	80% nonmucinous ovarian carcinomas have elevation of CA-125. Decreasing levels generally indicate response to therapy. Used to identify recurrences.
CEA	Primary use is to monitor recurrence of colon cancer. Oncofetal antigen-Ag complex glycoprotein, 20,000 d associated with plasma membrane of tumor cells. Increased with ovarian cancer and with melanoma, breast, pancreatic, stomach, cervical, bladder, kidney, thyroid, and liver cancer. Inflammatory bowel disease and smoking elevate CEA.
c-Myc	Amplified in 30%-50% of ovarian tumors. The protein is simultaneously overexpressed.
c-MycRA	Associated with aneuploidy in ovarian malignant cell progression.
BRCA1	Associated with mutations of breast tumor-related antigen. BRCA1 tumor suppressor gene has been identified; 63% risk of developing ovarian cancer with positive BRCA1 gene.

TABLE 28.6 Classification of the Adnexal Mass

GYNECOLOGIC ORIGIN	NONGYNECOLOGIC ORIGIN
Nonneoplastic	Nonneoplastic
Ovarian	Appendiceal abscess
Physiologic cysts	Diverticulosis
Follicular	Adhesions of bowel and omentum
Corpus luteum	
Theca lutein cyst	Peritoneal cyst
Luteoma of pregnancy	Feces in rectosigmoid
Polycystic ovaries	Urine in bladder
Inflammatory cysts	Pelvic kidney
Urachal cyst	Anterior sacral meningocele
Nonovarian	Neoplastic

Ectopic pregnancy	Carcinoma
Congenital anomalies	Sigmoid
Embryologic remnants	Cecum
Tubal	Appendix
Pyosalpinx	Retroperitoneal neoplasm
Hydrosalpinx	Presacral teratoma
Bladder	
Neoplastic	
Ovarian	
Nonovarian	
Leiomyomata	
Paraovarian cyst	
Endometrial carcinoma	
Tubal carcinoma	

Adapted from Hall DJ, Hurt WG. The adnexal mass. *J Fam Pract* 1982;14:135, with permission.

TABLE 28.7 Clinical Findings Suggesting Benign or Malignant Adnexal Mass

BENIGN	MALIGNANT
Unilateral	Bilateral
Cystic	Solid
Mobile	Fixed
Smooth	Irregular
No ascites	Ascites
Slow growth	Rapid growth
Younger patient	Older patient

The clinical findings listed in **Tables 28.5** 28.6 and **28.7** are often helpful in differentiating a malignant from a benign neoplasm. All ovarian neoplasms larger than 6 cm in diameter with a solid component should undergo investigation. The postmenopausal ovary is usually small and nonpalpable. Enlargement of the postmenopausal ovary requires appropriate investigation. Symptoms of ovarian neoplasms usually depend on their size, rate of growth, and position in the pelvis or abdomen. Symptoms may include vague lower abdominal fullness or pressure discomfort. Larger masses rise out of the true pelvis and may cause abdominal enlargement with varicosities and edema of the lower extremities. Most ovarian neoplasms are asymptomatic until they enlarge or affect adjacent organs and structures.

MINIMALLY INVASIVE APPROACH TO AN ADNEXAL MASS

STEPS IN THE PROCEDURE

Laparoscopic Excision of Adnexal Mass

- Preoperative assessment: Imaging studies and tumor markers as appropriate
- Intraoperative management:
  - Lithotomy position, Foley catheter in the bladder, drape perineum into sterile field
  - Laparoscopic placement of secondary trocar ports
  - Evaluation of the upper abdomen and pelvis
  - Identification of adnexal mass
  - Determine the most appropriate procedure
  - Obtain pelvic washings if appropriate
  - Restore normal anatomy
  - Identify ureter(s) in pelvis
  - If cystectomy, plan resection to preserve normal ovarian tissue
  - If adnexectomy, elevate adnexa; identify, isolate, and secure infundibulopelvic vasculature
  - Divide uterine tube at isthmus
  - Secure hemostasis along mesosalpinx/mesovarium
  - Extirpate adnexa
  - Reduce insufflation, and check for hemostasis
  - Remove adnexa using Endo Catch bag or other techniques for removal

The pelvic (adnexal) mass may be of gynecologic or nongynecologic origin (**Table 28.6**). Specific clinical findings are helpful to differentiate a malignant from a benign neoplasm (**Table 28.7**). It is important to establish whether the mass is of ovarian origin and to understand that a solid mass causing an ovary to enlarge to greater than 6 cm in diameter should be considered potentially malignant until proven otherwise. The most common ovarian mass is the physiologic ovarian cyst, which is caused by failure of a follicle to rupture or to regress. Physiologic ovarian cysts normally are less than 6 cm in diameter, smooth, mobile, and may be slightly tender to palpation. They usually contain straw-colored fluid and may be associated with menstrual irregularity. Physiologic ovarian cysts smaller than 6 cm usually regress by absorption of the fluid or spontaneous rupture. The premenopausal patient may be managed conservatively over two menstrual cycles. If regression fails to occur over two periods of observation or if enlargement is noted, reassessment is indicated.

Oral contraceptives have been suggested as an alternative treatment for functional cysts. The combination-type oral contraceptives send negative feedback to the pituitary gland to decrease gonadotropin stimulation of the ovary, which causes regression of the cyst. Steinkampf and colleagues noted that the rate of disappearance of functional ovarian cysts was not affected by estrogen-progestin treatment; nevertheless, a patient taking oral contraceptives with an adnexal mass should be thoroughly investigated.

Failure of the corpus luteum to regress (in the nonpregnant patient) may cause development of a corpus luteum cyst. The size of the corpus luteum cyst varies according to the amount of blood contained within the cyst. A large corpus luteum may rupture and cause intraperitoneal hemorrhage. Amenorrhea or irregular uterine bleeding may accompany the development of a corpus luteum cyst. A sensitive pregnancy test, ultrasonography, and laparoscopy can be used to differentiate an ectopic pregnancy from a persistent corpus luteum.

A theca lutein cyst, which may be associated with gestational trophoblastic disease or pregnancy, is the result of luteinization of the ovary by hCG. Many of these cysts are bilateral and multicystic. A reduction in hCG levels usually leads to their spontaneous regression.

Polycystic ovarian (PCO) disease is associated with bilaterally enlarged ovaries with a smooth surface. The ovaries contain multiple follicular cysts; many patients are obese and hirsute and have accompanying anovulation (see below).

Congenital anomalies of the müllerian system and vestigial remnants of the wolffian system are of gynecologic, if not strictly ovarian, origin. Müllerian anomalies should be considered in the differential diagnosis of an adnexal mass. Uterine anomalies with outflow tract obstruction oftentimes are associated with cyclic pain from development of hematometra, whereas an enlarged paraovarian cyst may be asymptomatic.

OVARIAN REMNANT SYNDROME

The ovarian remnant occurs in patients who have had previous oophorectomy with or without hysterectomy. The patient may present with symptoms with or without a palpable mass or with a palpable pelvic mass but no symptoms. Pathologic investigation confirms the presence of ovarian tissue when there should be none.

The ovarian remnant syndrome differs from the residual ovarian syndrome in that with the latter, the ovary is purposely saved, and a pathologic process subsequently develops in the ovary. The ovarian remnant syndrome follows attempted oophorectomy.

Minke and associates demonstrated that devascularization of ovarian tissue can occur with reimplanting on intact or abraded peritoneal surfaces, where it may resume endocrine function. Thus, the authors suggest that great care should be exercised to remove all ovarian tissue, particularly when oophorectomy is performed through the laparoscope.

Ultrasonography remains a valuable tool in establishing the diagnosis of ovarian remnant syndrome. The use of both transabdominal sonography and transvaginal sonography with use of color Doppler identification of the mass acquires information with respect to both arterial and venous flow. This facilitates identification of ovarian tissue.

Symmonds and Petit identified three major factors that may complicate the initial surgery and make it difficult or impossible for the surgeon to ascertain whether all ovarian tissue has been removed: increased pelvic vascularity, which renders hemostasis difficult; adhesions, which distort the anatomy and make dissection difficult; and neoplasms, which also distort the anatomy. The most common preexisting disease is endometriosis, followed in frequency by PID. Patients with ovarian remnant syndrome often present with both pelvic pain and a mass. The quality of the pain varies, often cyclically, and ranges from a sensation of pressure or dull aching to a severe stabbing pain.

The clinical diagnosis of ovarian remnant syndrome can be difficult. A finding of premenopausal levels of follicle-stimulating hormone (FSH) may facilitate the diagnosis. Sonography (especially vaginal) may be of value, and a CT scan or MRI may be useful for defining the physical relation of the ovarian remnant to surrounding structures.

The treatment of choice is adequate excision of the ovarian remnant with removal of contiguous adherent tissue such as pelvic peritoneum, bowel serosa, the underlying involved ligament, and alveolar and vascular tissues (**Fig. 28.4A**, **B**). Excision of ovarian tissue may require a retroperitoneal dissection to define the relation of the ureter to the bowel and ovary.

Magtibay and colleagues addressed the surgical management of patients with ovarian remnant syndrome at the Mayo Clinic. All operations for residual ovary syndrome were performed by laparotomy. Of 186 patients who underwent a wide dissection and removal of the remnant, a moderate risk of bowel, bladder, or ureteral injury was noted; however, 90% of patients had complete resolution or marked improvement of symptoms after surgery.

Laparoscopic excision of ovarian remnant ovaries is feasible. A retroperitoneal approach that allows dissection of the course of the ureters with coagulation and dissection of the infundibulopelvic ligament and the uterine vessels can be accomplished. There is potential for ureteral injury as well as cystotomy and bowel injury.

RESIDUAL OVARY

Based on the clinical circumstance, the gynecologic surgeon should consider the value of ovarian conservation at the time of hysterectomy for benign disease. Some authors have noted the incidence of malignant neoplasm in retained ovaries as a reason for prophylactic oophorectomy, and others have noted

the presence of “residual ovary syndrome,” characterized by either recurrent pelvic pain or a persistent pelvic mass (sonogram image) (**Fig. 28.5**). However, Funt followed 992 patients after conservation of one or both ovaries at the time of hysterectomy and reported that none developed ovarian malignancy, and only 1.4% required subsequent surgical intervention for adnexal pathology. The benefits of preserved ovarian function thus appear to substantially outweigh the risk of subsequent ovarian pathology requiring further surgery. Before surgery, the gynecologic surgeon should discuss the various risks and benefits of bilateral oophorectomy and should encourage the patient to participate in any decision concerning the fate of her ovaries.

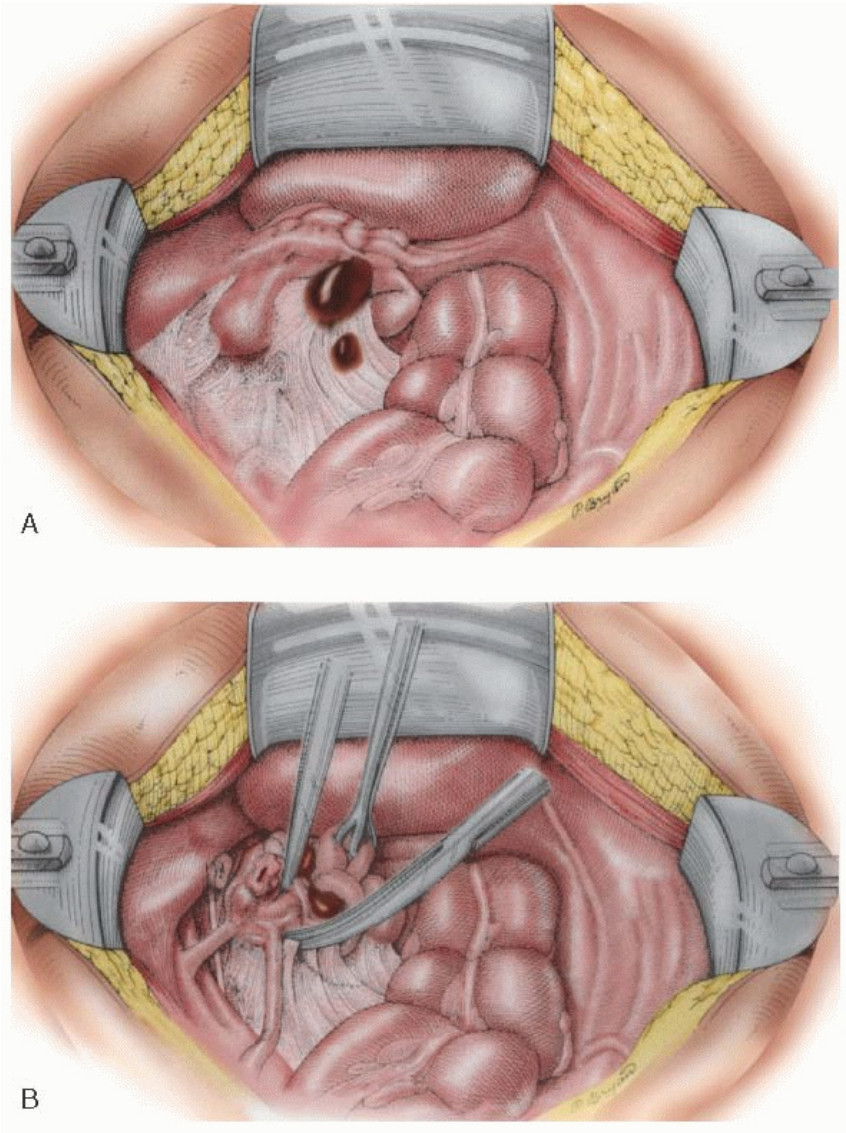

FIGURE 28.4 A: Not infrequently, the ovarian remnant may adhere to the bowel and the pelvic sidewall peritoneum. **B:** The ureter must be visualized and its relation to the bowel and ovarian remnant established. This may require development of the pararectal and rectovaginal spaces.

Gonadotropin-releasing hormone (GnRH) agonists have been used to assess response of residual ovaries with chronic pelvic pain followed by surgical intervention to remove the residual ovarian tissue. Resolution of pelvic pain in six treated patients occurred with the analogize GnRH agonist and persisted with surgical extirpation of the ovarian tissue. Suppression of ovarian function by GnRH agonists allows differentiation of pelvic pain caused by residual ovary from other sources and thus should be a prerequisite to surgical intervention.

In a retrospective report of 20 years of experience with residual ovary syndrome in which 2,561 hysterectomies were performed, the incidence of residual ovary syndrome was 2.85%. Thus, 1 in 35 women who undergo hysterectomy with ovarian preservation become symptomatic—that is, they experience pelvic pain often with the presence of a benign cyst. Patients should be counseled preoperatively with respect to the potential for residual ovary syndrome when the initial surgical intervention is anticipated. In addition to chronic pelvic pain, a pelvic mass and dyspareunia include the “cluster of symptoms” that can occur in patients who have undergone previous hysterectomy.

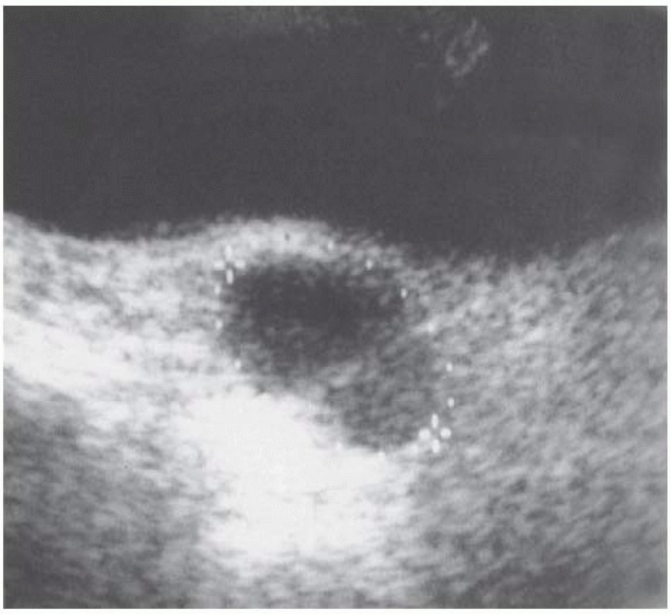

FIGURE 28.5 Abdominal sonogram showing a residual ovary with presumed follicular activity.

ADNEXAL TORSION

Torsion of the adnexa is an infrequent cause of pain in the lower abdomen. However, torsion is a common gynecologic surgical emergency, with a prevalence of 2.7%. Treatment of adnexal torsion is considered an emergency because peritonitis and death can result. Any portion of the adnexa (tube or ovary) may undergo torsion. It may occur in neoplastic ovaries or as a consequence of hyperstimulation.

The clinical findings of torsion are nonspecific. For this reason, delay in diagnosis and surgical intervention is common. The classic presentation is the acute onset of abdominal pain with clinical evidence of peritonitis and an adnexal mass. However, according to Bayer and Wiskind, the presenting findings in most patients are nonspecific and unimpressive. Torsion is more likely to occur during ovulation or as a premenstrual event associated with increased pelvic congestion; the authors found no correlation between the phase of the cycle and the onset of the symptoms.

Historically, the adnexa usually were removed because some authors suggested that untwisting the adnexa could increase the risk of thromboembolism. This has not been well substantiated. There is growing evidence that unwinding the involved adnexa to observe for tissue reperfusion and viability is safe. Nevertheless, a significant delay in surgical intervention may result in irreversible necrosis, requiring removal of the tube, ovary, or both.

The minimally invasive surgical management of adnexal torsion has been increasing in efficacy. Mage and colleagues found that untwisting the adnexa was possible in most patients in their series, and no further intervention was required. Likewise, Shalev and Peleg demonstrated that laparoscopic detorsion of the adnexa is safe and reliable as a primary treatment of this condition. Thus, the weight of evidence warrants conservation of the adnexa if there is evidence of reperfusion and if significant delay has not resulted in irreversible tissue necrosis. In most instances, detorsion may be accomplished through the laparoscope.

SURGERY OF THE OVARIAN SURFACE

Surgery to remove adhesions or endometriosis from the ovarian surface is not unusual and primarily accomplished via minimally invasive surgery. De novo adhesions or adhesions between the medial surface of the ovary and the broad ligament may be filmy and vascular (**Fig. 28.6A**) and may be excised by fine electrocautery or vaporized with the use of a laser (**Fig. 28.6B**). More extensive adhesions that completely cover the ovarian surface may be thick and avascular (**Fig. 28.6C**, **D**). The plane of dissection between the broad ligament or pelvic sidewall and the adherent ovarian surface must be developed with care so as not to remove or damage the peritoneum while excising the adhesion (**Fig. 28.6D**). Multiple, small adhesions distributed over the ovarian surface, once coagulated, can be gently removed from the ovary without trauma to the ovarian cortex.

If the lateral aspect of the ovary is densely adherent to the broad ligament, it may be necessary to dissect the ovary free.

Some cases require that a large area of the sidewall or the broad ligament be denuded; reperitonealization can be accomplished with nonreactive absorbable suture material.

Small endometrial implants can be fulgurated or vaporized. The resulting small ovarian defect usually does not require closure. Care should be taken to ensure that the endometriosis is superficial and that the implant is not actually the tip of a large endometrioma within the substance of the ovary.

RECONSTRUCTION OF THE OVARY

Before ovarian reconstruction is begun, it is important that proper mobilization of the ovary be accomplished for reestablishment of normal anatomy. Once complete excision of the involved ovarian pathology has been accomplished, the main objectives of ovarian reconstruction are atraumatic closure of the stroma and cortex and prevention of adhesion formation. The principles for accomplishing this goal include gentle tissue handling, hemostasis, the use of fine (and ideally minimally reactive) suture material, and an effort to “bury knots” for the prevention of adhesions.

The restoration of normal-appearing anatomy is the most logical approach for creating maximal ovarian surface, which facilitates ovum pickup by the fallopian tube. Controversy continues as to whether it is more appropriate to completely excise or lyse paraovarian and peritubal adhesions.

The most important aspect of ovarian reconstruction whether done via laparotomy or with a minimally invasive, including robotic surgical, approach is excellent reapproximation of the cortex with the use of atraumatic techniques, including fine absorbable suture material and minimizing suture exposure on the cortex. On completion of the procedure, intraabdominal lavage should be used, ideally with a physiologic substance such as lactated Ringer solution. Every effort should be made to remove all blood from the peritoneal cavity, preferably with the patient taken out of the Trendelenburg position.

The approach to resection of an ovarian cyst should be planned so as to minimize adhesion formation. The incidence of de novo adhesion formation appears to be decreased when the initial approach is through laparoscopy. The Operative Laparoscopy Study Group assessed the issue of frequency and severity of adhesion reformation and of de novo adhesions after operative laparoscopy. In a multicenter collaborative approach that included early second-look intervention, 68 patients underwent operative laparoscopic procedures, including adhesiolysis as well as ovarian cystectomy. The scoring of adhesions noted during the second-look laparoscopy occurred at nine sites (each ovary, each fallopian tube, omentum, culde-sac, pelvic sidewall, and large and small bowel). The study concluded that adhesion reformation is a frequent occurrence and that de novo adhesion formation occurred less frequently after initial operative laparoscopy.

A number of agents have been advocated for preventing adhesions, including oxidized regenerated cellulose (Interceed [TC7], Johnson & Johnson Medical, Arlington, TX), which is an absorbable barrier that promotes reepithelialization of the affected area. Pagidas and Tulandi compared Interceed with lactated Ringer solution for adhesion prevention. Lactated Ringer solution was as effective as Interceed in decreasing adhesion formation. Haney and colleagues compared oxidized regenerated cellulose with expanded polytetrafluoroethylene (Gore-Tex surgical membrane). The results indicated that expanded polytetrafluoroethylene was associated with fewer postsurgical adhesions. Other agents include sodium hyaluronate carboxymethyl cellulose (Seprafilm). A number of adhesion barriers are currently being evaluated and include Hyalobarrier, SprayShield, Prevadh, and INTERCOAT. Further research may well provide clinicians with an extended armamentarium for adhesion prevention.

Functional Ovarian Cysts

Physiologic cyst enlargement of the ovary may occur as a sequela of failure of either follicular rupture or corpus luteum regression. The latter is termed Halban syndrome. The former has been associated with luteinized unruptured follicle syndrome, in which “intraovarian ovulation” is thought to occur; this is a diagnosis usually established with ultrasound. In general, functional ovarian cysts regress spontaneously; however, they may persist and become symptomatic, reaching dimensions as large as 10 cm in diameter. The obvious and most feasible approach is observation, because most such cysts are

self-limited. The cyst, however, may prove to be a source of continued pelvic pain or may adhere to the posterior broad ligament, producing persistent symptoms. The potential for adnexal torsion always exists with an ovarian cyst.

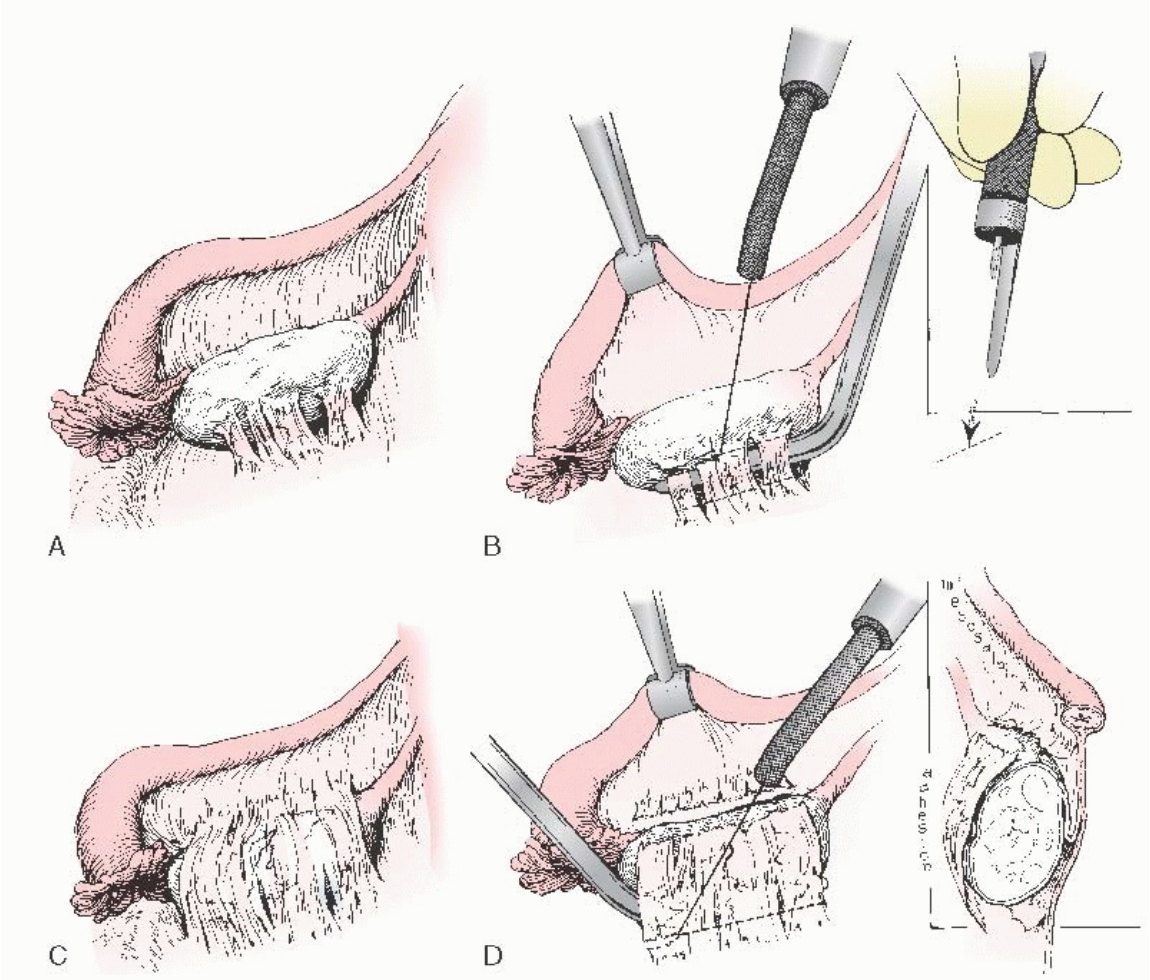

FIGURE 28.6 Ovarian adhesions. **A:** Filmy adhesions between the medial aspect of the ovary and the pelvic sidewall. **B:** These may be removed with laser or fine electrocautery with use of a quartz or glass rod, respectively, as a backstop. **C:** The ovary may be enveloped by adhesions. **D:** Care should be taken to tent up the adhesions so that the peritoneum is not damaged or incised.

RESECTION OF BENIGN CYSTS

Surgical intervention often is initiated with a laparoscopic approach, which permits completion of fenestration of the nonneoplastic ovarian cyst. The cyst lining is stripped from the remaining "normal ovary," and ovarian reconstruction takes place. In several series of laparoscopic management of ovarian cysts, a simple follicular or luteal cyst was identified in most patients evaluated for pelvic pain. In a series by Kleppinger, 31 of 64 ovarian cysts were noted to fall into this category.

Surgical Techniques

Laparotomy

An elliptic incision is made through the thin ovarian cortex of a benign cyst (Fig. 28.7). The end of the knife handle is then inserted and a plane developed over the cyst wall. Alternatively, fine-needle electrocautery can be used to develop a plane, and microsurgical scissors can be used to separate the cyst wall from the ovarian cortex. Low-power magnification (i.e., surgical loupes) often assists the surgeon in identifying the correct plane between the cyst wall and the ovarian parenchyma. After the cyst wall has been completely separated from its adherent attachments to the thin ovarian cortex, it can be shelled out without rupture. However, even with the gentlest technique, rupture can occur because of the friability of the cyst wall. Before the cyst is shelled out, it is important to pack the culde-sac with moist, lint-free pads so that, if rupture does occur, spillage does not contaminate the pelvic cavity. After the cyst has been removed, the dead space can be obliterated with a purse-string suture of fine-gauge nonreactive material. Alternatively, nonreactive vertical mattress sutures or figure-of-eight, or both, can be placed to approximate the lateral walls of the ovary. The ovarian surface is then neatly reapproximated with a subcortical running suture of fine-gauge nonreactive material (Fig. 28.7A). If the cortex is quite friable, it may be necessary to place interrupted fine-gauge sutures to achieve adequate approximation. Some authors advocate leaving the ovary open after cystectomy. To date, there have been no controlled trials evaluating postoperative adhesion formation when the incised

ovarian surface is or is not reapproximated.

In some instances, there is excessive redundant thin cortex, which may present a special problem in ovarian reconstruction. The amount of cortex removed depends on the position of the cyst as well as its overall size. Careful assessment of the ovary is necessary before the initial incision is made. The incision in the ovarian cortex facilitates symmetric reconstruction. The redundant cortex can be removed and the dead space obliterated with an internal closure, with care taken to prevent suture material from penetrating the ovarian cortex. This prevents ischemia and adhesion formation. The infolding technique recommended by Kistner and Patton may result in anatomic distortion and puckering of the ovarian cortex. The

"baseball" closure allows careful approximation of cortical edges when redundancy is noted (**Fig. 28.8**).

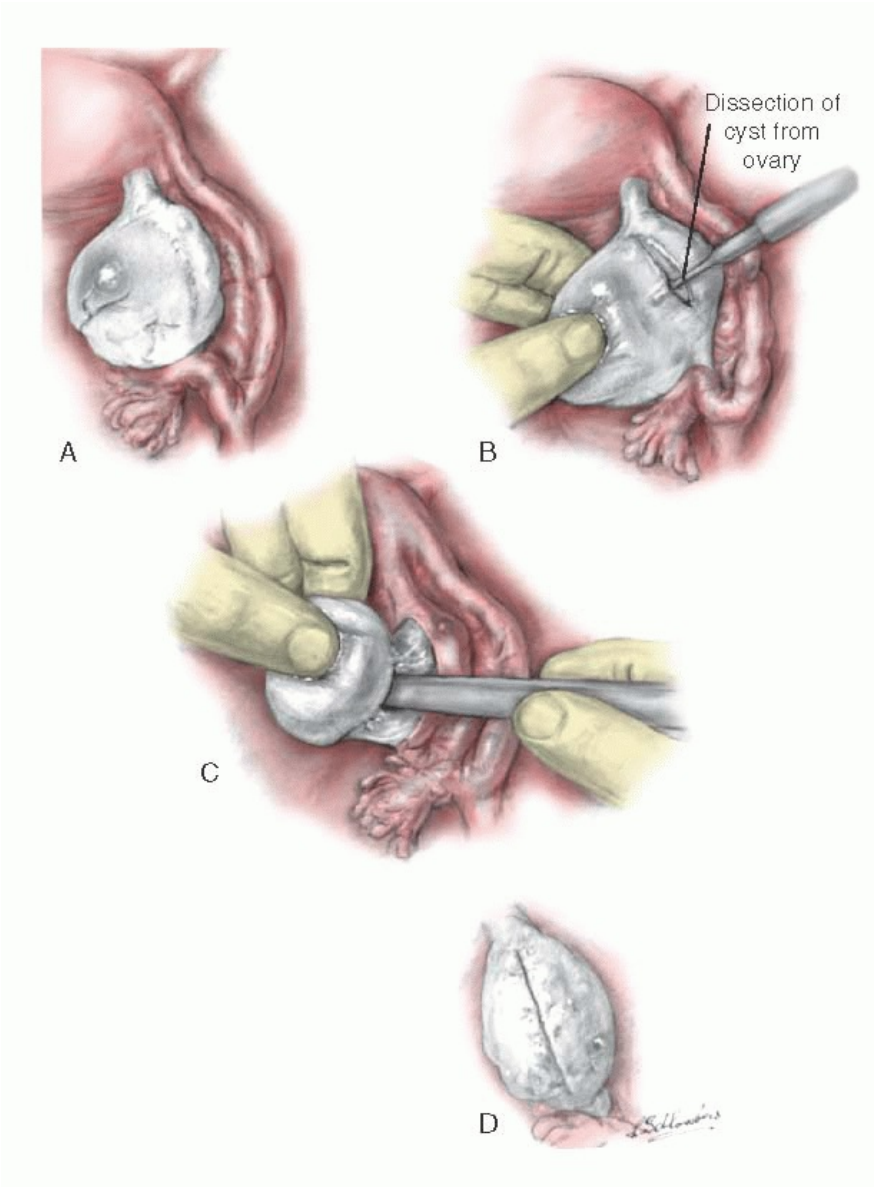

FIGURE 28.7 Resection of benign cyst. **A:** Thin-walled ovarian cyst. **B:** An incision is made through the cortex. **C:** A plane is developed by the use of blunt dissection. The inner ovarian stroma may be approximated with a purse-string suture of 5-0 nonreactive material. **D:** The ovarian cortex is approximated with 7-0 nonreactive suture material.

Concern over ovarian surgery via laparotomy has been reported. In an older reference of 36 young women operated on for an ovarian cyst, 45% were noted subsequently to be infertile. The author, Van der Watt, conveyed the importance of not interfering with functional cysts in "normal ovaries," because resulting adhesion formation could compromise fertility. It was advocated that benign ovarian cysts should not be removed at the time of surgery for other indications unless they are sufficiently large to interfere with tubal function or cause discomfort to the patient.

Minimally Invasive and Robotic-Assisted Surgery Overview

Specific skill levels reflecting both the degree of operator expertise and appropriate instrumentation provide clinicians with four

levels of training. Level I stands for equipment needs and potential surgical procedures for basic operative laparoscopy, including such entities as diagnostic laparoscopy, tubal sterilization, lysis of filmy adhesions, and biopsy. Level II reflects the clinician's ability to perform linear salpingostomy for ectopic pregnancy, salpingectomy, lysis of vascular adhesions, and elimination of endometriotic implants. Level III includes the ability to perform salpingo-oophorectomy, lysis of extensive adhesions (including bowel adhesions), ovarian cystectomy, appendectomy, myomectomy, laparoscopic-assisted hysterectomy, and neosalpingostomy,

as well as the ability to treat tubo-ovarian abscess and uterine suspension. Level IV includes bowel resection, anastomosis, pelvic lymphadenectomy, presacral neurectomy, tubal reanastomosis, and excision of deep, infiltrating vaginal, paravaginal, and rectal endometriosis.

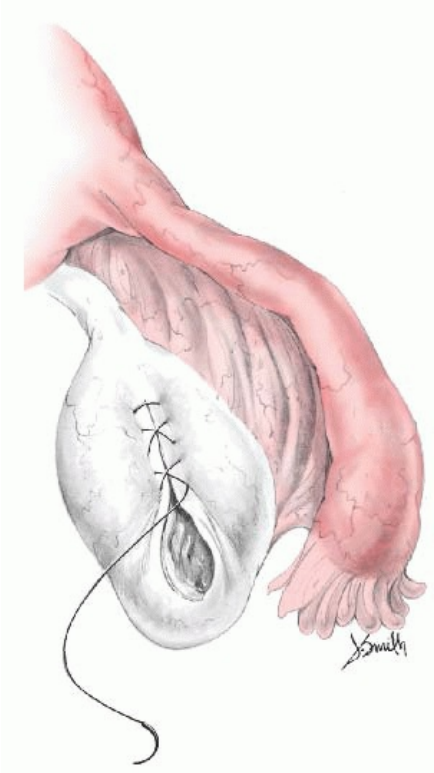

FIGURE 28.8 Closure of the ovary with a baseball stitch.

A number of principles should be followed as surgeons proceed with the correction of pelvic abnormalities that are amenable to a laparoscopic approach. The first is to restore normal anatomy. Once the ovary is stabilized, ideally with an atraumatic forceps, an appropriately planned ovarian incision can be made to correct the pathology encountered. Every effort should be made not to spill the contents.

Large amounts of irrigation solution should be used. In some instances, the cyst wall can be stripped, electrocoagulated, or vaporized. The ovarian incision can then be either left open to heal by primary intention or reapproximated with sutures with either extracorporeal or intracorporeal suture-tying techniques. When this procedure is completed, the pelvis is irrigated with large amounts of irrigation solution (Ringer lacate), and the patient is taken out of the Trendelenburg position to facilitate removal of any blood products that remain in the peritoneal cavity.

One alternative to suturing is to reapproximate incised segments of ovarian cortex with the use of bipolar coagulation to provide coaptation of the incised segment of the ovary. There is continued debate regarding the use of adhesion prevention materials.

A number of potential pitfalls continue to be of concern in the laparoscopic approach to ovarian lesions. These have been addressed by Seltzer and colleagues and include the following:

- The potential for disruption of an ovarian malignancy
- Whether observation-recommended surgical intervention would be the most feasible alternative
- Potential for increased duration of the surgical procedure if done endoscopically

- Total cost
- Potential for incomplete resection of an ovarian lesion laparoscopically

One can view laparoscopic approach to the adnexal mass based on age. Specifically, in the pediatric patient, problems such as torsion, hemorrhagic cysts, benign neoplasm (e.g., teratoma), as well as oophorectomy have been reportedly addressed via the laparoscope. One advantage over laparotomy is the ability to better visualize the entire lower abdomen and pelvis, including the opposite ovary. In the adult, depending on the clinical circumstance, cyst aspiration, cystectomy, or oophorectomy can be accomplished laparoscopically.

Predictors of clinical outcomes in the laparoscopic management of adnexal mass have been addressed by Havrilesky and coauthors. The authors noted that adnexal mass thought to be benign preoperatively were successfully managed laparoscopically in three fourths of the patients. Adverse events were attributable to concurrent hysterectomy rather than removal of the adnexal mass. Malignancy occurred in 2%, and laparoscopic management was not associated with adverse outcomes.

Concern is expressed for an ovarian neoplasm subsequently noted to be malignant. In a countrywide survey in Austria, Wenzl and colleagues reported on 54,198 laparoscopies; 16,601 were performed for adnexal masses, and 108 cases of ovarian tumors were subsequently found to be malignant. Of the 108 cases, 20 were managed laparoscopically, 22 by immediate laparotomy, and the rest by delayed laparotomy (3 to 1,415 days). The authors concluded that laparoscopic surgery with the finding of an ovarian malignancy is rare: 0.65% of all endoscopic surgical procedures.

The extent of damage to ovarian reserve associated with laparoscopic excision of endometriomas was studied by Ragni and coauthors. A reduced number of dominate follicles, oocytes, embryos, and high-quality embryos were observed in the operated gonad. Fertilization rate and rate of good-quality embryos were similar in operated and control groups. Laparoscopic excision of endometriomas is associated with a quantitative but not a qualitative damage to ovarian reserve.

Robotic-assisted intervention brings a 3D perspective to surgical procedures. Wrist movement of the surgeon at the console provides seven degrees of freedom (movement) and can provide an added dimension to pelvic surgical procedures. Nezhat and coworkers assessed robotic surgical intervention in 15 patients undergoing gynecologic surgery. These clinicians concluded that robotic-assisted laparoscopic surgical intervention had advantages in providing a 3-dimensional visualization of the operative field, decreasing operator fatigue and tension tremor, and added wrist motion for improved dexterity and greater surgical precision. The disadvantages include additional expense and added operating time for assembly (docking) and disassembly (undocking) and the bulkiness of the equipment.

MANAGEMENT OF POLYCYSTIC OVARIAN DISEASE

Signs and symptoms of PCO syndrome (PCOS) begin at puberty. Polycystic ovary is a sign, not a diagnosis. In a consensus meeting held in Rotterdam, the American Society for Reproductive Medicine (ASRM) and the European Society of Human Reproduction and Embryology (ESHRE) agreed that two of the following criteria must be met once other endocrinopathies have been ruled out (i.e., Cushing, adrenal hyperplasia):

- Oligomenorrhea
- Clinical and/or biochemical evidence for hyperandrogenemia
- Polycystic-appearing ovaries on ultrasound

The polycystic ovary may result from a virilizing ovarian or adrenal neoplasm or from congenital adrenal hyperplasia, or it may result from suboptimal hypothalamic-pituitary function at puberty. The exact mechanism for the development of ovulatory failure has been attributed to androgen overproduction and its effect on the hypothalamic-pituitary-ovarian axis.

Stein and Leventhal, during the period 1902 to 1935, noted that a group of women had evidence for what is currently called polycystic ovaries at the time of laparotomy. Specifically, in 1935, Stein and Leventhal reported seven patients with the hallmarks of PCO.

The histologic findings in a polycystic ovary cover a broad spectrum, ranging from the originally described typical “Stein-Leventhal” type of polycystic ovary with a large number of follicular cysts and few atretic cysts in which there is marked stromal hyperplasia and hyperthecosis to a smaller ovary with a few follicular cysts and atretic follicles. The polycystic ovary may exhibit microscopic islands of luteinized thecal cells, that is, hyperthecosis, scattered in the stroma, but usually, there is a

thickened, fibrosed tunica with a large number of cystic follicles beneath this thickened capsule.

Methods of management of ovulation induction include use of clomiphene citrate, controlled ovarian hyperstimulation with gonadotropins-follicle-stimulating hormone, and the option of assisted reproductive technology (ART). With select indications use of metformin, in off-label indication, as management of associated insulin resistance-hyperinsulinemia. Ovarian drilling remains one additional option for management of PCOS in select patients. There are several hypotheses regarding the mechanism by which ovarian drilling (wedge

resection) of the polycystic ovary resolves ovulatory failure. The theory stating that the fibrous capsule acts as a mechanical barrier to the ovulatory follicle has been refuted. Evidence against this theory consists of the observation that if one ovary is removed, ovulation occurs from the remaining ovary. In addition, the use of clomiphene citrate of letrozole results in ovulation through an intact capsule. Some have stated that neonatal androgens may cause an abnormal hypothalamic-pituitary axis, resulting in abnormal gonadal patterns. This theory is not widely accepted. Neonatal androgen treatment in rats is associated with masculinization of the hypothalamus and with ovulatory failure with polycystic ovaries.

The most popular theory explaining how ovarian drilling results in the resumption of ovulatory cycles notes that the removal of androgen-secreting stroma and theca reduces the amount of abnormal steroid production in the ovary. After wedge resection, there is usually a decrease in the mean level of 17α-hydroxyprogesterone, dehydroepiandrosterone, androstenedione, and testosterone, as well as a transitory decrease in estradiol. This reduction in the steroidogenesis of androgens, allowing normalization of the luteinizing hormone (LH) to follicle-stimulating hormone (LH:FSH) ratio, results in the resumption of ovulatory cycles. Ovarian renin-angiotensin activity is enhanced with PCO. This system— renin-angiotensin—remains unaltered following ovarian electrocautery (i.e., ovarian drilling), even though serum levels of LH, testosterone, and androstenedione decline.

Sex hormone-binding globulin (SHBG) concentrations following electrocautery with PCO have been evaluated. Whereas there were significant decreases in serum androgens and gonadotropins, the concentration of SHBG increased in the serum. Gjonnaess has reported that there is no change with respect to dehydroepiandrosterone sulfate with ovarian drilling. This is indicative of neural alteration in the pituitary-adrenal axis in comparison to the pituitary-ovarian axis.

A consensus (2007) regarding PCOS focused on treatment. The results noted better pregnancy rates with use of clomiphene citrate or clomiphene citrate plus the insulin sensitizer metformin in comparison to metformin alone. They also felt that there is a role for ovarian drilling.

There is some debate as to the amount of ovarian mass that should be removed at the time of wedge resection. Halbe and coworkers attempted to clarify this question by removing different amounts of ovarian cortex and medulla from a random selection of patients with PCO disease. Thirty-eight of sixty-two patients were interested in conception. The 38 patients were divided into three groups, the first of which underwent removal of not more than one fifth of the original ovarian size. The second group had one third of the ovarian mass removed, and the third group had one half to three fourths of the original ovarian size reduced. The resumption of ovulatory cycles was recorded at 53%, 71%, and 91%, respectively. The authors concluded that the best ovulatory rate and the best pregnancy rate resulted after removal of at least half of the ovarian medulla.

The introduction of clomiphene citrate and the oral antihyperglycemic drug and insulin sensitizer metformin has changed the management of PCO syndrome in patients who desire pregnancy. Depending on the clinical circumstance, the conception rate with clomiphene citrate has been reported at 50% to 60%. The incidence of post-clomiphene citrate birth defects (3.1%) is not increased over commonly quoted rates for populations at large. Some patients may not want to accept the risks of multiple births or hyperstimulation with administration of pure FSH or FSH and LH ovulation induction.

Antidiabetic agents have been advocated to reduce insulin resistance with PCO. Metformin has been shown to decrease insulin levels with resultant diminishing of circulating androgens. Hirsutism often improves. Metformin may enhance the efficacy of clomiphene and gonadotropin therapy with PCO. Metformin may also promote weight loss. Baseline and periodic liver function tests are recommended. Metformin is contraindicated with renal or hepatic disease. Patients have shown a response at dosages of 500 mg three times per day.

Surgical Technique of Laparoscopic Treatment of Polycystic Ovaries

STEPS IN THE PROCEDURE

Polycystic Ovaries-Minimally Invasive Surgical Approach-Ovarian Drilling

- Lithotomy position, Foley catheter in the bladder, prepped, and draped
- Laparoscope and secondary ports placed
- Inspection of upper and lower abdomen
- With monopolar 20 to 30 W cutting current (or analogous setting for bipolar), vaporize all visible subcapsular follicles
- Place 2 to 4 mm depth punctures over capsule, caution must be addressed at stroma
- Place 5 to 10 punctures in each ovary

The laparoscopic approach incorporates the use of monopolar cautery with a needlepoint applicator or bipolar cautery to drill holes several millimeters apart through the ovarian cortex (**Fig. 28.9**). Care should be exercised to avoid the hilum because bleeding could result if it is penetrated. It is important to achieve hemostasis over the drilled areas.

The ovarian drilling technique includes a 5-mm second puncture placed suprapubically, through which suction irrigation or grasping of tissues can be performed. All visible subcapsular follicles are vaporized, and a 2- to 4-mm-diameter crater is made randomly in the ovarian stroma. Hemostasis is accomplished with bipolar forceps.

Ovarian coagulation can be accomplished with unipolar electrode. The power setting is 20 to 30 W in a cutting mode. The cortex is usually penetrated at 10 to 15 sites for a depth of 3 to 5 mm. No study has correlated the number of drilling sites and incidence of ovulation or pregnancy. Different studies have recommended 5, 10, or 15 perforations per ovary. In general, 5 to 10 punctures are made in each ovary at a 40-W power setting for each puncture over a 2- to 3-second time frame. Caution is exercised to minimize thermal damage. Smaller ovaries may require fewer cauterization sites.

As noted above, the PCOS Consensus Workshop Group provided support for ovarian drilling in patient's refractory to medical methods of ovulation induction. The procedure has also been termed multiperforation as well as laparoscopic ovarian diathermy. Monopolar and laser techniques have been described.

Overall, ovarian drilling is a second-line treatment for PCOS patients who desire fertility. Benefits of ovarian drilling include low probability of multiple births and avoidance of ovarian hyperstimulation syndrome as is more common with gonadotropin ovulation induction. Preoperatively, patients should be apprised of the potential consequences of ovarian drilling, which include adhesion formation and damage to

ovarian reserve. Incidence of ovulation with ovarian drilling is reported at 70% and pregnancy rates as high as 40% after three monitored cycles.

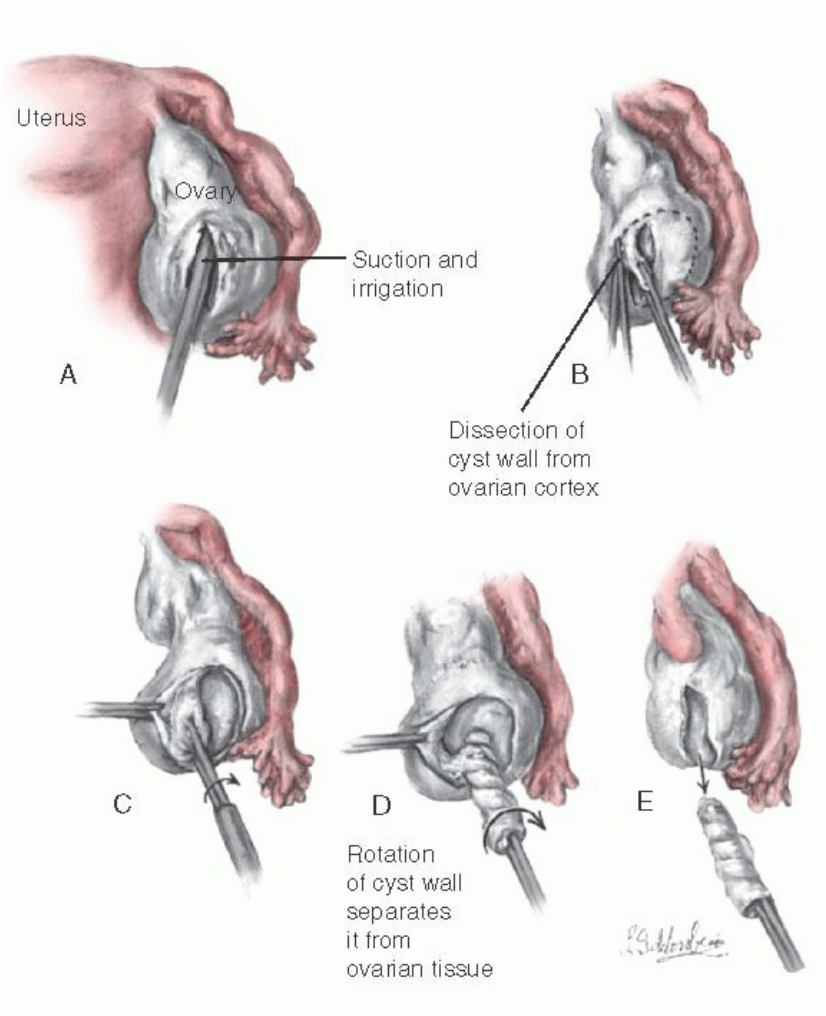

FIGURE 28.9 Removal of a small ovarian endometrial cyst through the laparoscope. **A:** After incision of the ovarian cortex, the contents of the endometrioma are removed with suction and irrigation. **B:** The plane between the ovary and the cyst wall is developed by using traction and twisting the forceps clockwise. **C:** The endometrial cyst wall is grasped with forceps. **D:** The cyst wall separates from the ovarian tissue by use of a twisting motion. The ovarian defect may be left open to heal by secondary intention or may be closed with vertical mattress sutures. **E:** The cyst wall is removed.

There are no randomized controlled studies addressing the efficacy of the laparoscopic approach to ovarian drilling. Twenty-seven studies were evaluated by Donesky and Adashi and involved a total of 729 patients. The ovulation rate was 84.2%, and the pregnancy rate was 55.7%. These authors emphasized that well-designed studies are needed in this area, which would encompass the PCO population proposed for laparoscopic drilling. This cohort of patients would require a well-documented clinical and biochemical finding of PCO, documented long-standing infertility (2 years or more), evidence for failure of clomiphene citrate, absence or correction of other infertility factors, randomization into a treatment group, and standardized documented follow-up, with particular attention to postovulatory patterns.

As noted above with regard to complications, the major concern is that of adhesion formation after either wedge resection or laparoscopic drilling. Toaff and associates noted extensive peritubular and periovarian adhesions in a small series (seven) of patients who did not conceive after bilateral wedge resection. One other concern is that of bilateral ovarian atrophy as a reflection of aggressive ovarian resection. This is a rare complication of the procedure. Thus, iatrogenic consequences of the surgical approaches must be discussed with the patient preoperatively (**Fig. 28.10**).

INCIDENTALOMA

Incidental adnexal masses (incidentaloma) are more common in postmenopausal women with a prevalence of 3% to 18% among asymptomatic women. More commonly, these present as unilocular, benign-appearing ovarian cysts noted on ultrasonographic studies. Overall, 80% resolve spontaneously over several months. Persistent adnexal masses should be assessed which evaluation specific to the clinical circumstance, patient's age, sonographic findings, Doppler studies, etc. Masses greater than 10 cm should have a histopathologic diagnosis.

There does not appear to be consensus regarding methods of ovarian screening among major medical societies; ongoing studies continue to address this question from a costeffective perspective. This includes use of CA-125 and pelvic sonography.

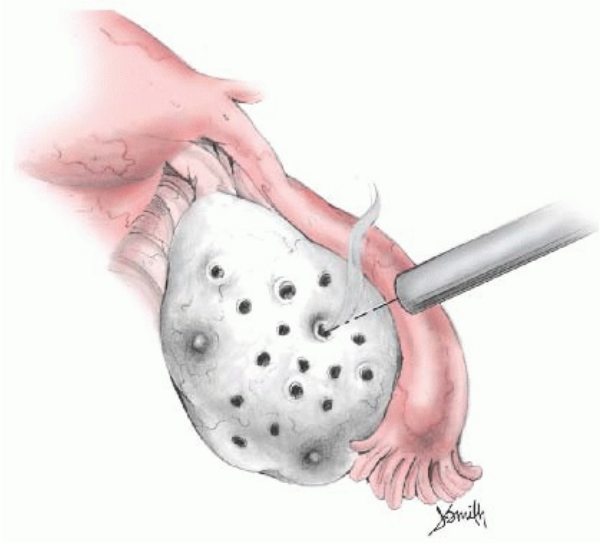

FIGURE 28.10 Laser drilling of ovary for surgical treatment of PCO disease.

PARADOXICAL OOPHORECTOMY

Paradoxical oophorectomy is the removal of severely pathologic adnexa to improve fertility in patients with strictly unilateral tubal disease. Consideration of removal of the contralateral ovary when there is single tubal patency (i.e., paradoxical oophorectomy) has perhaps taken on a new perspective with the advent of ART. From a historical point of view, it has been advocated that a patient with one functional tube would benefit from paradoxical oophorectomy, thus ensuring that ovulation would occur repeatedly on the appropriate side. Scott and coworkers reported a series of 24 patients with unilateral tubal patency diagnosed by retrograde injection at laparotomy. Contralateral oophorectomy or salpingo-oophorectomy was performed on all patients, and 16 women subsequently had 21 pregnancies, for a pregnancy rate of 67%. The authors suggested that the frequency with which transperitoneal migration occurs may be a factor. Hallet noted that one in five tubal ectopic pregnancies has a corpus luteum on the contralateral side; Jansen noted an intrauterine pregnancy rate of 18.7% (n = 91), contrasted with bilateral salpingostomy for hydrosalpinges in the presence of only one ovary wherein the pregnancy rate was 43.8% (n = 16). With unilateral salpingostomy or bilateral division of adhesions, pregnancy rates were comparable to those after bilateral salpingolysis. The mean surgery-pregnancy interval was longer after unilateral salpingostomy (104 weeks) than after bilateral salpingolysis (45 weeks). The author suggested that salpingooophorectomy may be preferable to salpingoneostomy for unilateral hydrosalpinx. With the provision of ART/in vitro fertilization (IVF), the management of tubal obstruction, especially in the absence of a hydrosalpinx, has led to a more conservative surgical approach.

Perhaps the major concern is for the patient who presents with tubal ectopic gestation in which the opposite (i.e., normal-appearing) adnexa appears to be unaffected. The paradoxical salpingo-oophorectomy approach has been advocated with this circumstance by Scott and coworkers. It has been advocated to wait at least 2 years after diagnostic laparoscopy reveals extensive unilateral disease before proceeding with paradoxical oophorectomy. From the other perspective, if the patient plans to proceed with IVF, the presence of two functional ovaries usually results in more oocytes recovered.

Randomized, carefully controlled clinical trials are necessary to further evaluate the efficacy of paradoxical oophorectomy. The risks and benefits must be carefully considered both preoperatively and intraoperatively, especially if the patient is a candidate for ART. There is clear evidence that increased numbers of ova can be recovered when both ovaries are in situ. Increased pregnancy success after superovulation is a reflection of the number of ovaries (one vs. two)—the total number of follicles available for stimulation.

Minimally Invasive Oophorectomy

The general principles of laparoscopic oophorectomy include placing the patient in the Trendelenburg position, with appropriate planning of ports for the proposed procedure and planning for removal of the affected adnexa. Pelvic washings

and use of frozen section may be germane to the task at hand. After restoration of normal anatomy and adhesiolysis as indicated, the adnexa are gently placed on stretch. They are approached from either the infundibulopelvic ligament or the insertion of the round ligament. Regardless of the approach chosen, identification of the ureter is of paramount importance. The infundibulopelvic ligament is identified and coagulated. The broad ligament is incised, beginning at the round ligament, and further dissection is performed into the retroperitoneal space. Every effort must be made to completely remove all ovarian tissue to prevent ovarian remnant syndrome.

With regard to tissue removal, once the adnexa have been completely freed, if benign disease is extremely likely, desiccation of the tissue and thus segmental removal are appropriate. However, if there is concern for the pathology, use of an endoscopic pouch is appropriate. In this circumstance, every effort is made to remove the ovary intact. Careful inspection of the operative site and a check for any bleeding are recommended. In addition, the end-point pressure of CO_2 insufflation should be reduced with suctioning of some of the CO_2 to check for any tamponade effect. As with all laparoscopic procedures, the patient should be monitored after surgery for any signs of intraperitoneal bleeding.

FERTILITY PRESERVATION WITH CANCER

As responses to both medical and surgical therapies continue to result in increasing numbers of cancer survivors, gynecologic surgeons must be kept abreast of current thinking in this field. Cryopreservation of ovarian tissue—nonfertilized, immature germ cells—is receiving increased attention including in prepubertal girls. Medical agents, including letrozole and tamoxifen, have been used prior to cryopreservation in women with breast cancer. Tamoxifen resulted in two to five times higher embryo yield than natural cycle IVF. The best prognosis for fertility appears to preserve gametes before initiation of chemotherapy for cancer. Ovarian transplantation with subsequent embryo generation has been reported after restoration of ovarian function by heterotopic transplantation. Ovarian transplantation remains an experimental technique at this point in time. Ovarian cortical tissue strip retrieval is amenable to a laparoscopic approach. Autologous, orthotopic transplantation after cryopreservation has been successfully used to restore fertility. Ovarian tissue banking and autografting of ovarian cortex are promising therapies for patients with ovarian failure. Kim and coauthors have verified the correlation between ischemic tissue damage and the duration of ischemia. The authors noted the ovarian cortex could tolerate ischemia for at least 3 hours. Thus, it appears that the future of ovarian transplantation depends on the postgrafting ischemia time by effective revascularization techniques.

Specific chemotherapeutic agents are proven to be toxic to the ovary. Resultant amenorrhea and infertility are the consequences. Patient age, drug dose, and dose and extent of disease are contributing factors (**Table 28.8**).

Fertility-sparing surgery includes oophoropexy-ovarian transposition (**Table 28.9** and **Fig. 28.11**). This procedure temporarily relocates the ovaries as when pelvic radiation is planned. Cancers of the spine and colon and gynecologic cancers may require pelvic irradiation. The procedure of ovarian transposition (**Fig. 28.11**) can be done via a minimally invasive surgical approach. In general, such procedures reduce the ovarian exposure to radiation by 90% to 95%. On occasion, ovaries have been reported to migrate back to the pelvis.

Ovarian function remains intact in 60% to 89% of patients who undergo radiation therapy, while in the reproductive age, scattering of radiotherapy may account for the failures. Spontaneous pregnancies have been reported following oophoropexy. In addition, access for IVF has been successful in providing pregnancies following ovarian transposition. Complications include pelvic pain secondary to the ovarian relocation.

Tumors of LMP diagnosed in the reproductive age group can be managed, depending on the clinical circumstance, with unilateral salpingo-oophorectomy to preserve fertility (**Table 28.9**).

TABLE 28.8 Chemotherapy and Medical Diagnosis

AGENT	CANCERS IN THIS CATEGORY
High risk	
Cyclophosphamide	Leukemia lymphoma

Busulfan	
Intermediate risk	
Cisplatin	Breast cancer
Carboplatin	Ovarian endometrial
	Cervical
Low risk	
Doxorubicin	Hodgkin lymphoma
Bleomycin	Lymphoma
Vinblastine	Acute myelogenous leukemia
Dacarbazine	Breast cancer
Anthracycline	Multiple myeloma
Cytarabine	GI tract cancers
Methotrexate	
Dactinomycin	
Mercaptopurine	

Simultaneous administration of gonadotropin-releasing hormone agonists (GnRHa) with chemotherapy has been advocated in women in the reproductive age group but remains an area of controversy, the theory being to prevent or decrease the rate of ovarian damage. This may be more effective in the category of low-risk chemotherapeutic agents; however, there is a paucity of prospective studies assessing the efficacy of simultaneous GnRHa therapy with chemotherapy and ultimate effect on pregnancy rate. Detailed discussion of each option and specific indication is beyond the objective of this chapter. Suffice to say, it is important that patients be apprised of options prior to proceeding with chemo- and/or radiation therapy.

OVARIAN TRANSPOSITION BEFORE RADIOTHERAPY

Lemevel and coworkers reported laparoscopic transposition in a patient being treated for Hodgkin disease before receiving radiotherapy. The ovaries were laparoscopically suspended out of the field of radiation. Iatrogenic menopause did not occur in the four patients for which this was reported. Other authors have reported similar recommendations. Bisharah and Tulandi have recommended transection of the ovarian ligament and transposition of the ovaries without affecting the fallopian tubes. This is associated with positioning of the ovaries laterally and anteriorly at the level of the anterosuperior iliac spines.

Gonads are sensitive to irradiation. Whole-body, abdominal, or pelvic irradiation can cause ovarian damage and adversely affect uterine function. It is estimated that the sensitivity of oocytes to radiation is an LD50 (the lethal dose required to eliminate 50% of the oocytes) of 2 Gy.

TABLE 28.9 Options for Fertility Sparing

Fast-track ART/IVF
Embryo cryopreservation
Oocyte cryopreservation
In vitro maturation of oocytes
Donor oocyte
Donor embryo
Gestational carrier
Ovarian cortex cryopreservation and transplantation

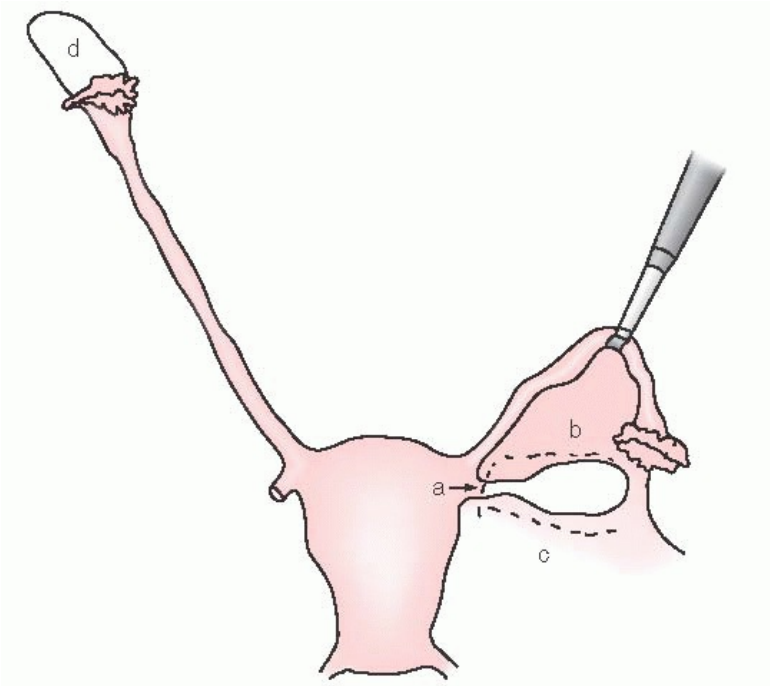

FIGURE 28.11 Laparoscopic ovarian transposition. Ovarian ligament (a) and mesovarium (b) are divided. If mobility is inadequate, relaxing incision on peritoneum inferior to ovary (c) may be needed. Final location of ovary is shown (d). (Reprinted from Bisharah M, Tulandi T. Laparoscopic preservation of ovarian function: an underused procedure. *Am J Obstet Gynecol* 2003;188:367. Copyright © 2003, with permission from Elsevier.)

As noted in **Table 28.8,** cytotoxic drugs are classified as follows:

High risk: Cyclophosphamide, ifosfamide, chlormethine, busulfan, melphalan, procarbazine, and chlorambucil

Intermediate risk: Cisplatin and carboplatin

Low risk: Vincristine, methotrexate, dactinomycin, bleomycin, mercaptopurine, and vinblastine

Attempts have been made to assess ovarian function and “ovarian reserve.” This has included evaluation of ovarian volume, serum inhibin B secreted by antral developing follicles, and antimüllerian hormone, a glycoprotein expressed in fetal tissue and preantral and small antral follicles, but in the adult, when levels are lowered (i.e., in cancer survivors), the ovarian reserve is decreased.

One alternative to oophoropexy is oocyte retrieval, fertilization, and cryopreservation—that is, ART/IVF. Preserving unfertilized oocytes remains an area of increasing success, as technology advances in cryopreservation continues to unfold.

Fertility outcome following ovarian transposition and pelvic irradiation for pelvic cancer has been addressed in a total of 37 consecutive cases by Morice and colleagues. Patients were treated for clear cell adenocarcinoma of the vagina or cervix, ovarian dysgerminoma, and sarcoma. The pregnancy rate was 15% (4/27) in patients attempting pregnancy with clear cell adenocarcinoma of the vagina or cervix. In the dysgerminoma and sarcoma group, 80% pregnancy occurred (8/10). Thus, the prognosis for future fertility following ovarian transposition and irradiation should be considered for discussion in selected patients before radiotherapy. The subject of fertility preservation in cancer survivors has been addressed by the Ethics Committee of the American Society for Reproductive Medicine, the main

focus of which is that physicians should inform cancer patients before treatment of their alternatives and include them in pretherapy discussion of alternatives before initiation of treatment.

PROPHYLACTIC OOPHOECTOMY IN ASSOCIATION WITH INCREASED CANCER RISK

Patients with a personal or family history that leads to assessment of genetic defects that include BRCA1 and BRCA2 mutation carrier status may benefit from prophylactic bilateral salpingo-oophorectomy (BSO), especially if childbearing is completed. No effective ovarian cancer screening exists. Tumor markers that include CA-125 and pelvic imaging done on a screening basis, as noted above, lack sensitivity and specificity. Overall, they are inefficient as a screening tool. Retrospective data support prophylactic BSO and lower occurrence of breast cancer in BRCA1 carriers (OR = 0.44, 95% CI: 0.28 to 1.15). Average interval between BSO and diagnosis of breast cancer was 7.2 years in those affected. The problem of primary peritoneal cancer remains a concern despite BSO. Thus, BSO does not completely eliminate the possibility of ovarian cancer. Primary peritoneal origin is associated with diffuse involvement of tumor on peritoneal surfaces and resembling papillary serous carcinoma of the ovary. This can occur with BRCA1 and BRCA2 mutations after BSO has occurred. Occult either ovarian or fallopian tube carcinoma has been noted at time of prophylactic BSO in 2% to 10% of patients with BRCA1 and BRCA2 mutations. Of note, use of hormone therapy following prophylactic BSO did not alter the reduction in breast cancer risk in BRCA1 and BRCA2 mutation carriers.

OVARIAN CYSTS IN NEONATE AND PREPUBERTAL CHILD

In a retrospective study of 65 fetal ovarian cysts noted by ultrasound, 57% were located on the left, 36% were on the right, and 7% were bilateral. In 17 patients, intervention was required after delivery because of persistence and/or enlargement. The histologic results included follicular cysts in 12 cases, a lymphangioma, and one teratoma; the remaining were amenable to aspiration. The authors, Mittermayer and colleagues, conclude that lack of regression requires intervention in the neonatal period. Ovarian cysts in the neonate greater than 5 cm in diameter have an increased chance of torsion.

Ovarian surgery in the premenarchal girl has been evaluated in a study from the University of Michigan in 52 patients, 50% of whom were less than 1 year old and 31% between 1 and 8 years of age. The most common presentation was abdominal/pelvic mass (*n* = 24), and the postoperative diagnoses included torsion in 18 and malignancy in 5 patients. Histopathologic evaluation included hemorrhagic infarction, dysgenetic gonads, simple cysts, teratoma, theca lutein cyst, fibroma, neuroblastoma, germ-cell tumor, gonadoblastoma, and metastatic Wilms tumor.

A general statement is that pathologic cysts in a newborn are equated with greater than 2 cm. There is no exact guideline for monitoring or management of neonatal ovarian cysts. Torsion of the intrauterine ovary can occur. Other problems to be considered included intracystic hemorrhage, rupture, and dystocia. A complex cyst is equated with increased chance of ovarian vascular dysgenesis or of a neoplasm. In general, neonatal ovarian cysts are predominately benign and self-limiting. There is a frequency of up to 5% of all abdominal masses in the 1st month of life. Overall, the earliest identification of neonatal ovarian cyst formation is 19 weeks of gestation and more often noted at 32 to 26 weeks gestational age.

Aspiration of a neonatal ovarian cyst can be considered if the concern for interference with spontaneous delivery exists. Postnatal percutaneous aspiration of a large ovarian cyst may reduce the rate of torsion and other sequela. Separation of fetal-neonatal cysts into simple versus complex allows the clinician options for management, the former being of less concern. In general, cysts less than 5 cm may be observed especially if they have a simple cyst appearance. Laparoscopic approach and, when feasible, an ovarian cortex-preserving approach are advised, especially when it is thought to be a benign process. Expectant management over a 4- to 6-month period is acceptable especially if the cyst appears to be “simple.” Malignancy of the neonatal ovary is rare. In childhood during the second decade, ovarian malignancy becomes of higher probability than in the neonate. In a series from Children’s Hospital of Philadelphia reported by Brown and associates, one malignancy in 34 adnexal masses in children less than 8 years of age was noted (2.9%) in comparison to a 33% incidence in children greater than 8 years of age (18 of 58). Treatment options in large part depend on the clinical circumstance, whether the mass is simple, complex, symptomatic, etc. Surgical intervention should include the possibility of minimally invasive approach if feasible.

LAPAROSCOPIC OVARIAN SURGERY IN THE PEDIATRIC OR ADOLESCENT PATIENT

STEPS IN THE PROCEDURE

Laparoscopic Surgical Procedures in Pediatric and Adolescent Patient

- In pediatric patient, Crede bladder, prep, and drape abdomen
- Place Veress needle, and introduce 2- to 3-mm laparoscope and secondary ports
- CO_2 is introduced at 0.5 L/min with an end-point pressure of 6 to 8 mm Hg depending on age/size of patient
- In the adolescent, the pressure setting is 10 to 12 mm Hg; depending on age/size of patient, closed or open technique for abdominal insufflation and laparoscope placement is appropriate
- Port closure in the pediatric patient may require use of Steri-Strips
- In the adolescent, skin approximation at secondary ports can be accomplished with sutures

As noted above, a number of gynecologic problems from the neonatal period through adolescence can be addressed laparoscopically. Entities such as ovarian torsion, acute PID (diagnosis and treatment complementing antimicrobial therapy), torsion, and benign neoplasms must be considered in the latter age group. In addition, gonadectomy for problems such as male pseudohermaphroditism is amenable to a laparoscopic approach.

Follicular cysts appear to be of particular concern in both the pediatric and adolescent patient because they present with abdominal pain. An abdominal or pelvic mass can be identified on physical examination. The clinician must always keep in mind

the importance of appropriate preoperative assessment (with the use of ultrasound and other clinical parameters) in deciding which patients are candidates for operative intervention. Depending on the clinical circumstance, a conservative approach in this age group is advocated; concern must be given (especially in the pediatric patient) to the potential for malignancy with ovarian masses, particularly if a solid component is identified.

The literature attests to operative intervention of ovarian cysts that appear to be nonfunctional. One of these was reported in a 1.5-month-old infant in whom ultrasound showed evidence of an ovarian mass. At laparotomy, the mass proved to be consistent with right ovarian torsion and necrosis, and it required adnexectomy. In one other reported case, a follicular-appearing cyst seen on ultrasound was associated with rapidly progressive virilization and a markedly elevated plasma testosterone level (289 ng/dL); histologic evaluation identified a granulosa cell tumor with mild luteinization.

The feasibility of aspirating an ovarian cyst continues to be controversial. In two case reports, laparoscopic puncture and aspiration of a malignant ovarian cyst were performed. Preoperative ultrasound indicated that the involved adnexal mass had a benign nature. Cytologically negative fluid was obtained from the aspirate. Eight weeks after operation, extensive disseminated ovarian carcinoma was noted at laparotomy.

Endoscopic surgery continues to broaden its horizon with expansion into laparoscopic surgical care beginning with the neonate. The use of 2-mm laparoscopes with the addition of 2- to 3-mm instrumentation has facilitated the diagnostic and therapeutic aspects of laparoscopy in this age group. Miniaturized video camera systems are necessary when one uses the 2-mm laparoscope telescope. When a decision is made to proceed with laparoscopy in a neonate or infant, general endotracheal anesthesia is used. Ideally, prophylactic antibiotics are administered preoperatively. The stomach is emptied with a suction catheter when the patient is asleep, and the bladder is emptied by use of the Crede maneuver. The abdominal wall is thinner and more elastic in the child than in the adolescent or adult. One must take this into consideration when introducing instrumentation, because it may be easier to insufflate in the subcutaneous space of the child than in the subcutaneous space of an adult. A Veress needle can be used with insufflation of carbon dioxide at 0.5 L/min. In infants, the end point of peritoneal-distending pressure should be set at 6 to 8 mm Hg; in the pediatric patient, 8 to 10 mm Hg; and in the older child or adolescent, 10 to 12 mm Hg.

After surgery, the trocar sites can be sutured in children, whereas in neonates and infants, the use of Steri-Strips (3 M, St. Paul, MN) or other wound closure bandages is usually adequate for reapproximation of the incised skin edges. Waldschmidt and Schier reported a series of 136 laparoscopic surgical procedures in neonates and infants. The most frequent indications were lysis of adhesions, abdominal cysts and neoplasms, gonadectomy, appendectomy, and cholecystectomy. A 1,400-g preterm infant was the only one in the series who suffered a complication (hernia at the incision site). Thus, adnexal pathology in this age group appears to be amenable to a laparoscopic approach.

Procedures such as transposition of an ovary before radiotherapy, bilateral gonadal excision in a male pseudohermaphrodite

(i.e., Y-bearing chromosomal analysis), adnexal torsion, suspected salpingitis, and endometriosis all have been identified in this age group. The authors concluded that because the morbidity is low, a laparoscopic approach should be considered.

Although certain procedures in the child do not differ significantly from those in the adult, the early diagnosis of ovarian pathology (e.g., adnexal torsion) can result in a significant advantage in terms of managing the patient and preserving ovarian tissue.

BEST SURGICAL PRACTICES

- Minimally invasive surgery can be used to evaluate and manage ovarian masses ≥6 cm and adnexal masses ≥10 cm.
- Before operative intervention in a pregnant patient with a symptomatic adnexal mass, complete assessment of the fetus—including ultrasound to rule out any fetal anomalies—is recommended. The optimal time for elective intervention is during the second trimester. The patient should be informed regarding preterm labor and delivery. The surgical procedure ideally is performed in the left lateral decubitus position.
- Transvaginal color Doppler sonographic assessment of ovarian malignant masses includes vessels detected, location of tumor vessels (central vs. peripheral), determination of peak systolic velocity, low resistance index, mean resistance index, and lower pulsatility index.
- The major goal of the evaluation of a pelvic mass is to rule out malignancy. All ovarian neoplasms greater than 6 cm with a solid component should undergo a thorough evaluation to rule out cancer.
- In management of ovarian remnant syndrome, treatment of choice is adequate excision of the remnant ovarian tissue and contiguous adherent tissues: pelvic peritoneum, bowel serosa, and underlying involved alveolar and/or vascular tissues. Retroperitoneal dissection may be required.
- Prior to cancer therapy, whether it be chemo- or radiation therapy, patients should be counseled regarding option for fertility preservation.

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