Tubal Factor Infertility

Diagnosis and Management in the Era of Assisted Reproductive Technology

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KEYWORDS

• Tubal factor infertility • In vitro fertilization • Microsurgery • Tubal occlusion

KEY POINTS

- Tubal factor infertility is the most common cause of female infertility.
- The diagnosis of tubal factor infertility can be established by a combination of clinical suspicion based on patient history and confirmed with diagnostic tests.
- Depending on the patient's age, location, and severity of tubal disease, tubal microsurgery or more commonly in vitro fertilization with its improving success rates are the recommended treatment options.

INFERTILITY IS A GROWING CONCERN

Approximately 85% to 90% of healthy young couples conceive within 1 year of trying, and most conceive within 6 months.[1] However, 10% to 15% of couples have difficulty conceiving and experience infertility or subfertility, which is defined as 1 year of unprotected intercourse without conception.[2] Although overall rates of infertility have remained stable during the last 30 years in the United States the overall birth and fertility rates are declining because of several social and cultural trends: women achieving advanced education and careers, delaying marriage for men and women, delaying childbearing, more frequent divorce, and reliable contraception and family planning. Comparatively, the first US census in 1790 indicated that the crude birth rate was 55 per 1000 of the total population. During the postwar "baby boom" of

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the 1950s, the fertility rate (births per 1000 women aged 15–44) peaked at 106.2 per 1000. The most recent statistics from the Centers for Disease Control and Prevention report a falling fertility rate of 66.7 per 1000 in 2009. Interestingly, although the birth rates are declining for women age 15 to 39 years, the birth rates continue to rise for women 40 to 44 years.[3]

Because of societal trends, female infertility is a growing and important issue. Much attention in the past 30 years has been focused on understanding the physiology of reproductive aging and finding treatments for all causes of infertility.

Among infertile couples, male infertility accounts for approximately 35% and female infertility approximately 65% (**Fig. 1**). The causes of male infertility arise from four major etiologies: (1) hypothalamic-pituitary disorders (1%–2%); (2) primary gonadal disorders (30%–40%); (3) disorders of sperm transport (10%–20%); and (4) idiopathic (40%–50%). Most male factor infertility is still idiopathic, reflecting a poor understanding of the mechanisms that govern testicular and sperm function. However, female infertility represents approximately 65% of the overall causes for the infertile couple. The components of female reproductive process can be divided into the following anatomic components. Dysfunction may occur at any of these steps to cause infertility: (1) the ovaries need to ovulate a mature oocyte on a regular basis (ovarian factor); (2) the cervix needs to capture and transport sperm into the uterus and fallopian tubes (cervical factor); (3) the uterus needs to allow the embryo to implant and support normal growth and development (uterine factor); and (4) the fallopian tubes need to capture the ovulated ova and transport sperm and embryo (tubal factor).

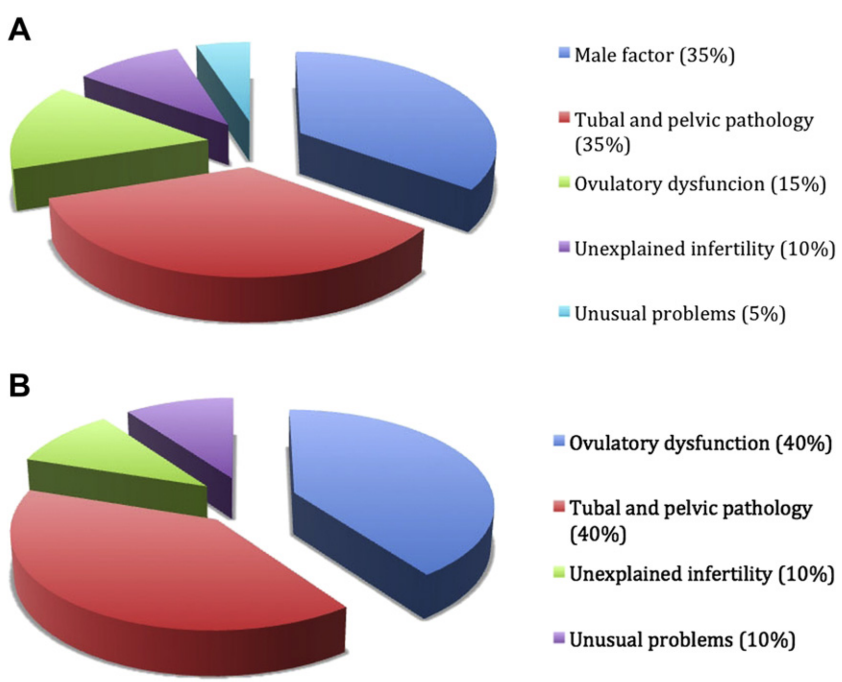

Fig. 1. (*A*) Causes of infertility among couples. (*B*) Causes of infertility in younger and older women. (*Data from* Miller JH, Weinberg RK, Canino NL, et al. The pattern of infertility diagnoses in women of advanced reproductive age. Am J Obstet Gynecol 1999;181:952–7.)

Dysfunction caused by the last component of the female reproductive pathway, tubal factor infertility, is the most common cause of female infertility and is discussed in this article.

CAUSES OF TUBAL FACTOR INFERTILITY

Tubal factor infertility due to occlusion and peritoneal pathology causing adhesions is the most common cause of female infertility and diagnosed in approximately 30% to 35% of younger and older infertile women.[4] The most prevalent cause of tubal factor infertility is pelvic inflammatory disease (PID) and acute salpingitis. *Chlamydia trachomatis*, *Neisseria gonorrhea*, and anaerobic organisms are the most common organisms that infect the lower genital tract and cause PID. In classic studies of women diagnosed with PID, the risk of infertility increased with the number and severity of pelvic infections. The incidence of infertility is 10% to 12% after one episode, 23% to 35% after two episodes, and 54% to 75% after three episodes.[5,6] Tubal damage from PID causes inflammation and long-term tubal changes, such as fimbrial agglutination, fimbrial phimosis, tubal obstruction, hydrosalpinx, and nodular thickening of the muscularis layer of the isthmic portion of the fallopian tube called salpingitis isthmica nodosa. The risk of ectopic pregnancy can increase sixfold to sevenfold after an episode of PID.[7]

Endometriosis is a common and chronic inflammatory disorder affecting 10% to 16% of reproductive-aged women.[8] Among women with infertility, pelvic pain, or both, it is present in 35% to 50%.[9] Although the pathophysiology of endometriosis is not completely understood, the most accepted theory is retrograde menstruation of debris from the uterus through the fallopian tubes that attach to the peritoneal surfaces. Women who develop endometriosis are unable to clear the disseminated endometrial cells, and may have altered humoral and cellular immune systems. Chronic inflammation from the reactive cytokines and chemokines produced by the ectopic endometrium results in scarring similar to that observed in PID. The long-term consequence of the inflammation is often distal tubal adhesive disease and occlusion. Among women with tubal factor infertility, endometriosis accounts for 7% to 14% (**Fig. 2**).[10]

Although uncommon in the United States, worldwide tuberculosis is reported to infect 9.4 million new people each year.[11] Among patients with pulmonary tuberculosis, the incidence of pelvic tuberculosis is between 10% and 20%.[12] The most common clinical symptoms of pelvic tuberculosis are pelvic pain, general malaise, menstrual irregularity, and infertility. Both fallopian tubes usually develop salpingitis,

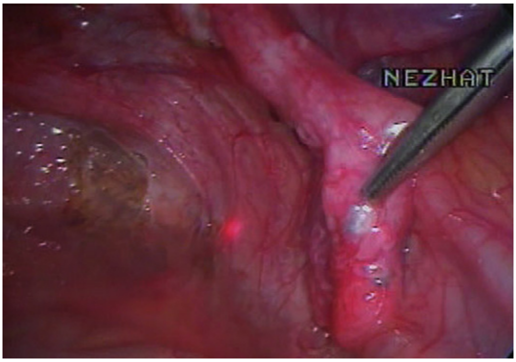

Fig. 2. Laparoscopy of a patient with endometriosis present on the fimbriae of the fallopian tube.

which in later stages resembles PID. Large, caseous pyosalpinges are characteristic of tuberculosis infection, but the pyosalpinges may also contain the exudate of a secondary infection with other urogenital organisms. Before effective multiregimen antibiotics, the treatment of pelvic tuberculosis was surgical, but was frequently complicated by fistula formation and persistent draining sinuses. Currently, surgery is reserved for women who have failed medical therapy and either have a persistent adnexal mass after 4 to 6 months of antituberculosis antibiotic therapy or unrelieved pelvic pain while on medical therapy.[13]

Other causes of tubal factor infertility include scarring from abdominal and pelvic surgeries. Ruptured appendix increases the risk of tubal infertility (relative risk = 4.8; 95% confidence interval, 1.5–14.9).[14] Inflammatory bowel disease was once thought to decrease fertility, but population-based studies of women with Crohn disease reported infertility rates between 5% and 14%, which are similar to the general population.[15,16] Women with ulcerative colitis have similar rates of fertility.[17] However, after surgery for both inflammatory bowel diseases, fertility rates decreased possibly because of surgery in the pelvis and subsequent adhesions and damage to the reproductive organs.[18]

Myomas near the tubal ostium can occlude the cornua and interstitial portion of the fallopian tube, causing or creating the appearance of proximal fallopian tube blockage. Depending on the degree of anatomic distortion, myomectomy can be complicated because removal of the fibroid may not restore fallopian tube patency. Meticulous surgical repair of the cornual with intraoperative chromopertubation can determine if the tube is patent at the end of the procedure (**Fig. 3**).

Bilateral tubal ligation is an iatrogenic cause of tubal occlusion. The traditional postpartum tubal ligation consists of ligating a knuckle at the midisthmic portion of the fallopian tube. Laparoscopic tubal ligation methods include monopolar and bipolar cautery, Hulka Clips, Fallope Rings, and Filshie Clips. Essure and Adiana are permanent hysteroscopic methods of proximal tubal occlusion. The microinsert is placed into the interstitium, scarring the fallopian tube, and occluding the proximal portions of the tubes over 3 months. A hysterosalpingogram (HSG) is performed after the 3 months to document occlusion.

PATIENT HISTORY

The patient's medical history can provide valuable information to assess the risk for tubal disease. A history of the risk factors, such as PID, septic abortion, ruptured

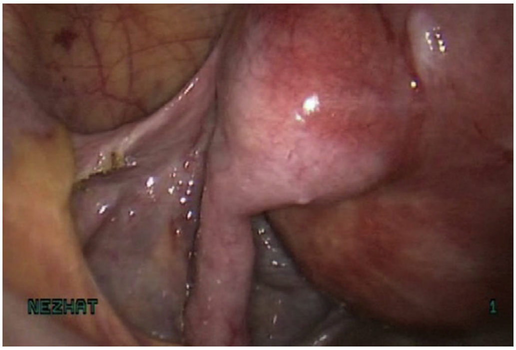

Fig. 3. Laparoscopy revealing a uterus with cornual myoma compressing the tubal ostium and causing proximal tube occlusion.

appendix, tubal surgery, or ectopic pregnancy is highly suggestive of tubal damage and dysfunction. Chronic medical conditions including endometriosis, or multiple abdominal and pelvic surgeries increase the amount of inflammation and scarring in and around the fallopian tubes and ovaries. A history of permanent sterilization by tubal ligation is a clear indicator of tubal occlusion. Gathering a thorough review of symptoms is essential to elicit symptoms of pelvic and abdominal pain, dyschezia, and dyspareunia.

PHYSICAL EXAMINATION

Evaluation of the infertile female patient should include a complete physical examination. Weight and body mass index should be noted. Thyroid enlargement, tenderness or nodularity, breast secretions, signs of androgen excess, such as facial and body hair and acne, or insulin resistance suggest some common endocrine causes of infertility (ie, thyroid dysfunction, hyperprolactinemia, and polycystic ovarian syndrome). In women with infertility and history of risk factors for tubal disease, the abdominal and pelvic examination is particularly important and assists in the diagnosis. Pelvic or abdominal tenderness, organ enlargement or masses on examination, vaginal or cervical abnormalities, secretions, and abnormal discharge help to differentiate anatomic abnormalities, neoplasia, or infection. A Pap smear and cervical cultures should be performed during the pelvic examination. The bimanual examination can provide information regarding uterine contour irregularity. Lack of uterine mobility indicates potential scarring from previous surgeries or disease processes. A rectovaginal examination should be performed to diagnose tenderness, nodularity, or masses in the adnexa or cul-de-sac suggestive of endometriosis.

IMAGING AND ADDITIONAL TESTING TO DIAGNOSE TUBAL FACTOR INFERTILITY

Laparoscopy and Chromopertubation

Laparoscopy with chromopertubation is considered the definitive test for evaluating tubal disease. Laparoscopy is performed under general anesthesia, and is often combined with chromopertubation (injection of a dilute blue dye though a cannula that passes through the cervix into the uterus, allowing the dye to enter the uterine cavity and fallopian tubes) to evaluate tubal patency and hysteroscopy to evaluate the interior of the uterus. Laparoscopy provides a panoramic view of the abdomen and pelvis and allows surgeons to diagnose and treat various pathologies, such as distal tubal occlusive disease, endometriosis, and adnexal and pelvic adhesions. Intraoperative chromopertubation is a better test for diagnosing tubal patency than HSG because there is less observer variability. However, cornual spasms, which are uterine contractions that transiently close the interstitial segment, can confound the results if the dye is injected too quickly. The cornual spasm causes the false appearance of proximal tube occlusion. Nevertheless, information obtained from laparoscopies tends to be more accurate than HSG, and is a better indicator of future fertility (**Fig. 4**).[19]

Hysterosalpingography

HSG is an outpatient radiographic procedure that examines fallopian tube patency. It is ideally performed 2 to 5 days immediately after the end of menses to minimize the interference from blood clot and menstrual debris, to prevent the chance that the procedure may be performed after conception, and to minimize the risk of infection. *C trachomatis* has been cultured in up to 3.4% of women scheduled to undergo an HSG.[20] Postprocedure PID is uncommon, occurring in less than 1.4% of women

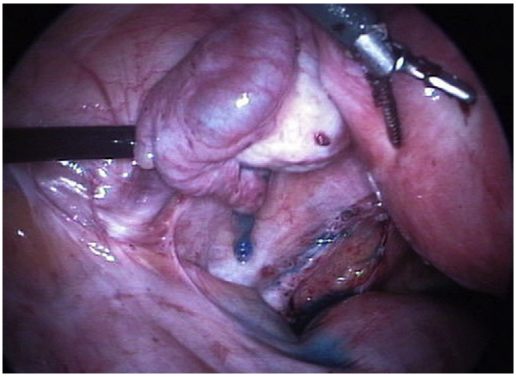

Fig. 4. Laparoscopy with chromopertubation demonstrating a patent fallopian tube with dilute methylene blue dye emanating from the fimbriae.

undergoing an HSG. Women with dilated fallopian tubes had a significantly higher risk (11%) of postprocedure PID.[21] However, it is a potentially devastating postprocedure complication, especially in a group of women undergoing infertility evaluation. Consequently, because of the risk of lower genital tract infection at the time of the procedure, doxycycline, 100 mg twice a day for 5 days, beginning 1 to 2 days before the procedure is recommended[22] to prevent postprocedure PID. If a woman has had an episode of PID, the HSG should be delayed at least several weeks after the infection has resolved.

The HSG procedure is standard and preprocedure preparation is simple and involves the doxycycline regimen outlined previously and ibuprofen 30 to 60 minutes before the procedure to minimize discomfort during the procedure. The patient is in a supine position on a fluoroscopy-read table and a metal “acorn” cannula or a balloon catheter is placed into the cervix and lower segment of the uterus. Water-soluble or oil-soluble contrast media is injected into the cannula or catheter, which directs the contrast media into the uterine cavity and fallopian tubes. Fluoroscopy guides the imaging over the patient’s pelvis. Three basic films are required for documenting an adequate study: (1) a scout film of the lower abdomen and pelvis, (2) a film to document the uterine contours and tubal patency, and (3) a postevaluation film to detect areas of contrast loculation that may indicate peritubal adhesive disease. Additional oblique films may be needed if the uterus obscures the tubes or if the uterine cavity seems abnormal.

Although traditional laparoscopy with chromopertubation is the gold standard for investigating tubal patency, HSG has moderate sensitivity (65%) but excellent specificity (83%) in the infertile population. However, if the HSG indicates occlusion, there may be a good chance (60%) that the tubes are actually patent, and if the HSG demonstrates patency there is a little chance (5%) that the tubes are occluded.[23,24] The primary reason for the moderate sensitivity is twofold: injection of the HSG contrast material causes cornual spasm more commonly than the dilute dye used in laparoscopic chromopertubation and the interpretation of the HSG is subject to intraobserver variability.[25] Nevertheless, HSG is a valuable, less-invasive method of examining tubal patency. HSG has advantages over laparoscopy aside from being a faster, less invasive, and less expensive procedure. It can delineate the contours of the uterine cavity and the lumen of the fallopian tubes. An incidental but important finding with the use of oil-soluble contrast media is that it has been shown to increase fertility in the months immediately after the procedure in women with patent tubes.[26] The thought is the oil-soluble contrast material flushes tubal debris from the tubal lumen (**Fig. 5**).[27]

Sonohysterosalpingography

Sonohysterosalpingography (SHG) is an alternative imaging technique to the HSG. SHG is an ultrasound-based imaging modality that permits an accurate evaluation of tubal patency and uterine and ovarian pathology. Use of a sonographic contrast medium (eg, sterile saline, air, Echovist, Albunex, and Infoson) injected into the uterine cavity enhances visualization of the uterine contours and fallopian tubes. If at least one fallopian tube is patent, then fluid accumulates in the posterior cul-de-sac during the procedure. Use of three-dimensional imaging to generate coronal images and Doppler to highlight fluid movement through the fallopian tubes can further improve the diagnostic capabilities of the SHG.

There are several advantages of the SHG. It is a fast, low-cost test that can be performed in an outpatient setting without anesthesia or sedation. There is no exposure to radiation. It is better tolerated than the HSG,[28] with fewer side effects rated as moderate to severe pain, vasovagal symptoms, nausea, and vomiting. Serious post-procedure complications (eg, fever and peritonitis) occurred in only 0.95% of the procedures.[29,30] Although the sonographic images are inferior to fluoroscopy, SHG is more sensitive and specific than the HSG when evaluating tubal patency. In fact, a meta-analysis comparing the accuracy of HSG, SHG, and laparoscopy found that SHG was superior to HSG and comparable with laparoscopic chromopertubation to demonstrate tubal patency (**Fig. 6**).[31]

Chlamydia serology

Chlamydia antibody tests (CAT) are a simple and noninvasive method of assessing tubal disease. They are blood tests that can detect previous infection with *C trachomatis*, an obligate intracellular bacteria that causes PID and subsequent fallopian tube injury and dysfunction.[32] Four commercial assay methods for detecting *Chlamydia* are currently available: (1) immunofluorescence, (2) microimmunofluorescence, (3) enzyme-linked immunosorbent assay, and (4) immunoperoxidase. The microimmunofluorescence test is the most specific for *C trachomatis*, detecting its type-specific

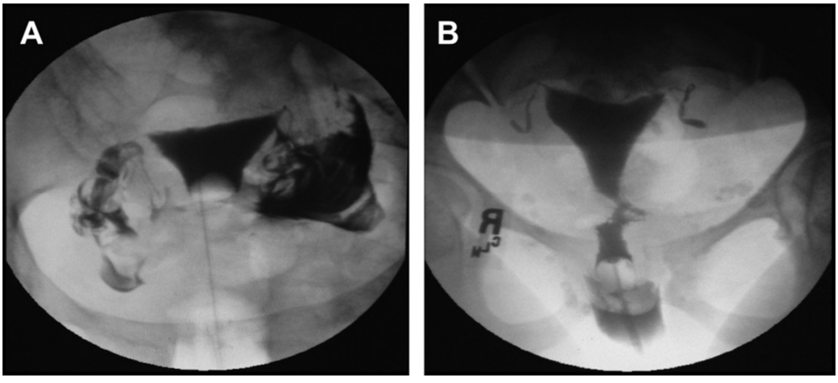

Fig. 5. (*A*) Normal HSG with patent fallopian tubes. The contrast material has moved through both fallopian tubes and spilled into the cul-de-sac, indicating bilateral tubal patency. (*B*) Abnormal HSG showing bilateral distal tubal occlusion. The contrast material fills the uterine cavity and flows through most of the fallopian tubes, but there is no spill of the contrast material into the cul-de-sac, indicating a distal tubal occlusion.

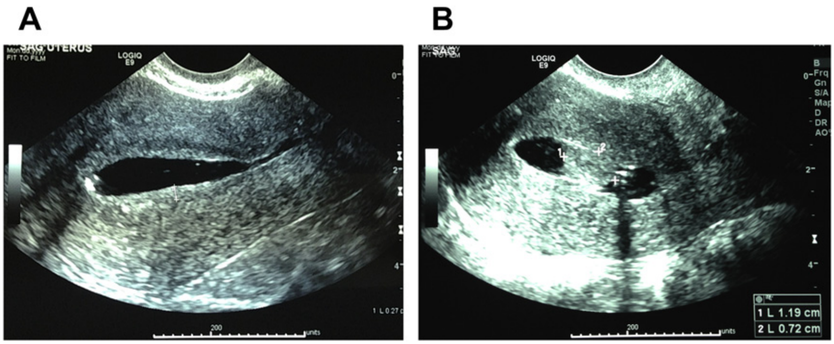

Fig. 6. (*A*) A normal SHG. The uterine cavity is distended, and the endometrium is smooth and without intracavitary defects. The myometrium is homogeneous. (*B*) A SHG demonstrating an intracavitary myoma.

immunoglobulin G antibodies. Other methods are not as specific, and do not distinguish between *C trachomatis* and the antibodies of other *Chlamydia* species, *Chlamydia pneumonia* and *Chlamydia psittaci*. Mol and colleagues[33] performed meta-analysis comparing CAT with HSG for the diagnosis of tubal occlusion using laparoscopic chromopertubation as the standard. The microimmunofluorescence test has a sensitivity less than 75%, but a specificity greater than 75%. Several limitations cloud the use of this test, including false-positive results caused by cross-reactivity with some gram-negative bacterial lipopolysaccharides and false-negative results in women with mild *Chlamydia* infections.[32] Thus, the role for CAT in the evaluation of infertile women has not been clearly defined. These serologic tests may be most suitable as a screening test to classify women into low- or high-risk groups for tubal disease warranting further investigation with more invasive tests, such as HSG, SHG, or laparoscopy.

MANAGEMENT OF TUBAL FACTOR INFERTILITY

Fallopian tube disease can roughly be divided into proximal tube and distal tube obstruction. Proximal tubal obstructions prevent sperm from reaching the distal fallopian tube where fertilization normally occurs. Distal tubal occlusion prevents ovum capture from the ovary, but can exhibit a range of disease from mild (fimbrial agglutination); moderate (varying degrees of fimbrial phimosis); and severe (complete obstruction). Damage to internal tubal mucosal structures cannot be detected easily and normal tubal function is difficult to assess.

Tubal Surgery

After diagnostic testing has indicated tubal occlusion, interventional radiology and microsurgical techniques can restore fallopian tube anatomy and function.

Proximal tubal occlusion

Proximal tubal blockage accounts for 10% to 24% of tubal disease.[34] Selective salpingography is a radiographic procedure similar to HSG in which the fallopian tube is directly opacified under fluoroscopic guidance. A catheter is placed in the tubal ostium, and a radiopaque dye is injected into the fallopian tube to determine patency. The procedure is usually performed by interventional radiologists and has been used to differentiate tubal spasm from true tubal obstruction. The advantage of this procedure is that if an obstruction is identified, a subsequent fallopian tube recanalization can be performed during which a smaller catheter is placed to clear the obstruction. The recanalization procedure is simple and successfully completed in 71% to 92% of cases.[35] Recanalization is possible but less successful in women who have occluded tubes after surgical anastomosis for reversal of a tubal ligation. Reported success rates per fallopian tube are related to amount of postoperative scarring and range from 44% to 77%.[36] Of the women who had successful fallopian tube recanalization, the average pregnancy rate was 30%.[37–40] Complications from the procedure are rare and include perforation in 3% to 11% of cases without clinical sequelae[34] and an ectopic pregnancy rate of 3%, which is comparable with the general population.[41] If the obstruction is not resolved by tubal cannulation, then in vitro fertilization (IVF) is preferred to proximal tube resection and microsurgical proximal tube anastomosis. Microsurgical proximal tube anastomosis has been largely relegated to historic surgical interest, because it is associated with very low success rates and risk of cornual rupture in pregnancy. It should only be considered if IVF is not an option for the patient.

Distal tubal occlusion

Distal tubal occlusion accounts for most tubal occlusion and infertility. Microsurgery can treat most cases depending on the degree of occlusion. A successful outcome with tubal surgery is associated with no more than limited filmy adnexal adhesions; mildly dilated tubes (<3 cm in diameter) with thin and pliable walls; and a lush endosalpinx with preservation of the mucosal folds.[42] Salpingostomy involves creating an opening in a completely obstructed tube, and historically was performed at laparotomy with microscopic assistance. More recently, laparoscopic salpingostomy has been performed with equivalent results.[43] Unfortunately, salpingostomy yields low long-term pregnancy rates of approximately 20% to 30% 1 to 2 years after surgery[43,44]; rates vary considerably depending on the extent of tubal damage and other clinical factors. Ectopic pregnancy rates after salpingostomy range from 4% to 25%.[44]

Varying degrees of fimbrial disease can be laparoscopically treated with fimbroplasty and fimbriolysis. Fimbriolysis refers to the separation of adherent fimbria. Fimbrioplasty describes the correction of phimotic but patent fimbria. Surgical success is inversely related to the severity of disease. For mild forms of distal tubal occlusion, pregnancy rates have been reported up to 60%,[45] but success rates are lower at 10% to 35% for women with severe tubal disease.[46,47] Most of the pregnancies occur within the first 2 years after surgical treatment of distal tubal disease. There is almost no role for surgical intervention in patients with proximal and distal disease because live birth rates are invariably lower than 10%.[45]

Hydrosalpinges

Distal tubal occlusion from salpingitis or extrinsic causes may lead to formation of hydrosalpinges either in one or both fallopian tubes. Numerous studies have shown that hydrosalpinges have a negative effect on pregnancy and IVF success rates. In a large meta-analysis of retrospective cases, women with hydrosalpinx had half the pregnancy, implantation, and delivery rates, and up to twice the incidence of spontaneous abortions after IVF and embryo transfer (IVF-ET).[48,49] Although the hydrosalpingeal fluid does not have direct toxic effects on the human embryos,[50,51] leakage of the fluid into the uterine cavity may compromise implantation through decreasing endometrial receptivity[52,53] and mechanically washing the blastocyst from the endometrial surface.[54] Treatment options for hydrosalpinges include drainage, neosalpingostomy, salpingectomy, and proximal tubal occlusion.

The least invasive of these options is transvaginal needle aspiration of a hydrosalpinx under ultrasound guidance before an IVF-ET cycle or at the time of oocyte retrieval. Therapeutic aspirations of hydrosalpinges have been reported[55,56]; however, there is often rapid reaccumulation of fluid. Nonrandomized study results were conflicting and conclusions weak.[55,57] One randomized controlled trial (RCT) reported improved pregnancy outcomes,[58] but this study was underpowered, leaving the need for more studies to assess the benefits and outcomes of hydrosalpinx aspiration. Laparoscopic neosalpingostomy for draining hydrosalpinges before IVF-ET theoretically should improve pregnancy rates, but there are no confirmatory studies to date.[59]

Randomized clinical trials comparing pregnancy rates and outcomes with IVF in women with and without prior laparoscopic salpingectomy have consistently reported that salpingectomy restores pregnancy rates and live birth rates to those similar to women without hydrosalpinx.[60–62] The multicenter, prospective RCT by Strandell and colleagues[60] found significantly increased pregnancy and live birth rates of 37% and 29%, respectively, in the salpingectomy group compared with rates of 24% and 16%, respectively, in the nonintervention group. A Cochrane analysis of the three RCTs concluded that laparoscopic salpingectomy should be considered before IVF for women with communicating hydrosalpinges.[63] Meta-analysis of two laparoscopic proximal tubal occlusion studies[62,64] also found improved odds of clinical pregnancy.[63] Thus, both salpingectomy and proximal tubal occlusion are recommended for the treatment of hydrosalpinx before IVF-ET.

Sterilization reversal

Approximately 1 million women in the United States have tubal ligations each year. Up to 7% regret the permanent sterilization, and about 1% request tubal reversal.[65] For those women who want to conceive, there are two treatment options: IVF or tubal reanastomosis. The advantages of surgical tubal reanastomosis are the chance for natural conception and lower risk for multiple gestations, but the disadvantages are the potential tubal scarring from the surgery itself, delay in attempting conception, higher risk of ectopic pregnancy, and need for future contraception.

Tubotubal reanastomosis is traditionally achieved by laparotomy after laparoscopic assessment of the fallopian tubes. If one or both fallopian tubes are judged to be repairable, then the occluded ends of the proximal and distal segments are opened and the ends are anastomosed with a fine nonreactive suture. Koh and Janik[66] reported the first case of laparoscopic tubal reanastomosis in 1992, but only laparoscopists skilled in microsurgical reanastamosis have been able to successfully replicate the procedure. More recently, more surgeons are using the da Vinci Robotic Surgical System for laparoscopic tubal reanastamosis with good results.[67,68] Women with tubal occlusion caused by tubal ligation are typically fertile and have better success rates after tubal surgery than women with tubal pathology. They also have good success rates with IVF. A preoperative HSG may be useful to assess the proximal segment of the tube. Less than 5% of fallopian tubes are irreparable. The prognosis for achieving live birth after tubal reversal depends on the patient's age, type and location of the sterilization procedure, and the final length of the repaired fallopian tubes. Better success rates are reported in younger women with no other infertility factors, and sterilization performed with rings or clips.[69] In appropriately selected candidates, overall conception rates are good (62%–83%) after microsurgical sterilization reversal.[46,70–72] The risk for ectopic pregnancy after tubal reanastomosis is up to 6%, and higher after isthmic-ampullary anastomosis than after isthmic-isthmic anastomosis.[46] Sterilization reversal after hysteroscopic placement of the microinserts Essure and Adiana is very difficult to achieve because of the placement of the coils, which scar and occlude the isthmic portions of the fallopian tubes. Sterilization reversal of this type requires tubouterine implantation in which a new opening is created through the uterine muscle and the remaining tubal segment is inserted into the uterine cavity. During the same procedure the microinserts are removed. Data on the success rate of tubal reversal after intratubal microinserts are limited. Three case reports of successful tubouterine implantation after intratubal microinserts have been described.[73,74]

Advancements in reproductive surgery with the da Vinci Surgical System

The da Vinci Robotic Surgical System developed by Intuitive Surgical (Sunnyvale, CA) pioneered one of the first integrated three-dimensional viewing systems for minimally invasive surgery. The system was approved for laparoscopic hysterectomies in 2005, but since that time has expanded to include myomectomy, complex resections of endometriosis, sacral colpopexy, and tubal reanastomosis. The high-definition video system and three-dimensional viewer have tremendously enabled surgeons to perform laparoscopic microtubal surgery with good results.

Gargiulo and Nezhat[75] reported their experience with a variety of robotic-assisted gynecologic surgeries including robotic-assisted tubal reanastomosis and tubal reconstructive surgeries citing the three-dimensional visualization of the operative field, decreased surgeon fatigue, and the seven degrees of motion provided better dexterity and surgical precision.[76–80]

Logically, using the da Vinci Surgical System for the technically challenging and microscopic procedures in reproductive surgery has been a natural progression for this surgical tool. Techniques for the robot-assisted tubal reanastomosis and other complex surgical procedures are described in recent publications.[75,81] A series comparing outcomes between women undergoing robotic-assisted tubal anastomoses and open microsurgical tubal anastomosis demonstrated that the robotically assisted laparoscopic microsurgical tubal anastomosis was feasible and cost effective with results equivalent to the traditional open approach.[82] In a series of 10 women with prior bilateral tubal ligation, 19 fallopian tubes were reanastomosed using the robotic-assisted laparoscopy technique. Chromopertubation at the end of the surgery demonstrated patency in all tubes. At 6 weeks after surgery HSGs were performed, and 17 of 19 tubes were patent. Five intrauterine pregnancies were reported.[83] The advantages of the da Vinci Surgical System are clear, and it has the potential to revolutionize the field of reproductive surgery.

In Vitro Fertilization

As assisted reproductive technologies (ART) have improved over the past few decades, almost all causes of infertility, especially tubal factor infertility, have been treated though ART techniques. In the past decade alone, the percentages of transfers that resulted in singleton live births have increased from 26% in 2000 to 35% in 2009.[84] The results of IVF-ET and tubal surgery are difficult to compare because surgery and IVF-ET have variable results depending on the surgeon and IVF clinic. One prospective RCT comparing tubal surgery to infertility with IVF-ET as first-line therapy found that the former was associated with lower costs and higher overall pregnancy rates.[85] However, a Cochrane analysis concluded that the success of tubal surgery versus IVF remains largely unknown, and in the treatment of women with tubal factor infertility, there are no RCTs comparing IVF-ET with tubal surgery.[86] When a couple is deciding between IVF-ET or tubal surgery, the advantages and disadvantages of both should be discussed. The advantages of IVF-ET are good per cycle success rates, it is less surgically invasive, and attempts at conceiving can start immediately. Disadvantages of IVF are risk of multiple gestations, ovarian hyperstimulation, and high cost. Some adverse perinatal outcomes have been associated with pregnancies conceived through IVF, such as perinatal mortality, preterm delivery, low and very low birth weight infants, intrauterine growth restriction, and congenital malformations.[87,88] Nevertheless, women who are older, women with severe tubal disease, couples with male factor infertility, and couples who may only want one or two children should be counseled toward infertility management with ART. Patient preference, religious beliefs, cost, and insurance reimbursement also play a role in management.

SUMMARY

Tubal factor infertility accounts for a large portion of female factor infertility. PID and salpingitis seem to be the most common culprits causing tubal scarring and occlusion. The diagnosis of tubal occlusion can be established by a combination of clinical suspicion based on patient history and diagnostic tests, such as HSG, SHG, and laparoscopy with chromopertubation. Depending on several patient factors, tubal microsurgery, or more commonly IVF with its improving success rates, are the recommended treatment options. Many variables need to be taken into consideration when counseling patients with tubal factor infertility about their treatment options. These factors include the age of the woman and ovarian reserve, male fertility and sperm quality, number of children desired, site and extent of fallopian tube disease, risk of ectopic pregnancy, other infertility factors, cost of the treatments, and patient preference. Nonetheless, innovative and optimistic surgical and ART treatments are now available for infertile couples.

REFERENCES

1. Gnoth C, Godehardt D, Godehardt E, et al. Time to pregnancy: results of the German prospective study and impact on the management of infertility. Hum Reprod 2003;18:1959–66.
2. Gnoth C, Godehardt E, Frank-Herrmann P, et al. Definition and prevalence of subfertility and infertility. Hum Reprod 2005;20:1144–7.
3. Martin JA, Hamilton BE, Ventura SJ, et al. Births: final data for 2009. Natl Vital Stat Rep 2011;60:1–70.
4. Miller JH, Weinberg RK, Canino NL, et al. The pattern of infertility diagnoses in women of advanced reproductive age. Am J Obstet Gynecol 1999;181:952–7.
5. Westrom L. Effect of acute pelvic inflammatory disease on fertility. Am J Obstet Gynecol 1975;121:707–13.
6. Westrom LV. Sexually transmitted diseases and infertility. Sex Transm Dis 1994;21:S32–7.
7. Westrom L, Joesoef R, Reynolds G, et al. Pelvic inflammatory disease and fertility. A cohort study of 1,844 women with laparoscopically verified disease and 657 control women with normal laparoscopic results. Sex Transm Dis 1992;19:185–92.
8. Houston DE. Evidence for the risk of pelvic endometriosis by age, race and socioeconomic status. Epidemiol Rev 1984;6:167–91.
9. Sensky TE, Liu DT. Endometriosis: associations with menorrhagia, infertility and oral contraceptives. Int J Gynaecol Obstet 1980;17:573–6.
10. Patil M. Assessing tubal damage. J Hum Reprod Sci 2009;2:2–11.
11. Tubercuolsis Fact Sheet No. 104. World Health Organization. 2012.

12. Sutherland AM. The changing pattern of tuberculosis of the female genital tract. A thirty year survey. Arch Gynecol 1983;234:95–101.
13. Sutherland AM. Surgical treatment of tuberculosis of the female genital tract. Br J Obstet Gynaecol 1980;87:610–2.
14. Mueller BA, Daling JR, Moore DE, et al. Appendectomy and the risk of tubal infertility. N Engl J Med 1986;315:1506–8.
15. Mayberry JF, Weterman IT. European survey of fertility and pregnancy in women with Crohn's disease: a case control study by European collaborative group. Gut 1986;27:821–5.
16. Hudson M, Flett G, Sinclair TS, et al. Fertility and pregnancy in inflammatory bowel disease. Int J Gynaecol Obstet 1997;58:229–37.
17. Willoughby CP, Truelove SC. Ulcerative colitis and pregnancy. Gut 1980;21: 469–74.
18. Johnson P, Richard C, Ravid A, et al. Female infertility after ileal pouch-anal anastomosis for ulcerative colitis. Dis Colon Rectum 2004;47:1119–26.
19. Mol BW, Collins JA, Burrows EA, et al. Comparison of hysterosalpingography and laparoscopy in predicting fertility outcome. Hum Reprod 1999;14:1237–42.
20. Moller BR, Allen J, Toft B, et al. Pelvic inflammatory disease after hysterosalpingography associated with *Chlamydia trachomatis* and *Mycoplasma hominis*. Br J Obstet Gynaecol 1984;91:1181–7.
21. Pittaway DE, Winfield AC, Maxson W, et al. Prevention of acute pelvic inflammatory disease after hysterosalpingography: efficacy of doxycycline prophylaxis. Am J Obstet Gynecol 1983;147:623–6.
22. Antibiotic prophylaxis for gynecologic procedures. ACOG Practice Bulletin No. 104. Obstet Gynecol 2009;113:1180–9.
23. Swart P, Mol BW, van der Veen F, et al. The accuracy of hysterosalpingography in the diagnosis of tubal pathology: a meta-analysis. Fertil Steril 1995;64:486–91.
24. Mol BW, Swart P, Bossuyt PM, et al. Reproducibility of the interpretation of hysterosalpingography in the diagnosis of tubal pathology. Hum Reprod 1996;11: 1204–8.
25. Glatstein IZ, Sleeper LA, Lavy Y, et al. Observer variability in the diagnosis and management of the hysterosalpingogram. Fertil Steril 1997;67:233–7.
26. Luttjeboer F, Harada T, Hughes E, et al. Tubal flushing for subfertility. Cochrane Database Syst Rev 2007;(3):CD003718.
27. Watson A, Vandekerckhove P, Lilford R, et al. A meta-analysis of the therapeutic role of oil soluble contrast media at hysterosalpingography: a surprising result? Fertil Steril 1994;61:470–7.
28. Ayida G, Kennedy S, Barlow D, et al. A comparison of patient tolerance of hysterosalpingo-contrast sonography (HyCoSy) with Echovist-200 and X-ray hysterosalpingography for outpatient investigation of infertile women. Ultrasound Obstet Gynecol 1996;7:201–4.
29. Savelli L, Pollastri P, Guerrini M, et al. Tolerability, side effects, and complications of hysterosalpingocontrast sonography (HyCoSy). Fertil Steril 2009;92: 1481–6.
30. Dessole S, Farina M, Rubattu G, et al. Side effects and complications of sonohysterosalpingography. Fertil Steril 2003;80:620–4.
31. Holz K, Becker R, Schurmann R. Ultrasound in the investigation of tubal patency. A meta-analysis of three comparative studies of Echovist-200 including 1007 women. Zentralbl Gynakol 1997;119:366–73.
32. Mardh PA. Tubal factor infertility, with special regard to chlamydial salpingitis. Current Opinion in Infectious Diseases 2004;17:49–52.

33. Mol BW, Dijkman B, Wertheim P, et al. The accuracy of serum chlamydial antibodies in the diagnosis of tubal pathology: a meta-analysis. Fertil Steril 1997;67:1031–7.
34. Honore GM, Holden AE, Schenken RS. Pathophysiology and management of proximal tubal blockage. Fertil Steril 1999;71:785–95.
35. Thurmond AS, Machan LS, Maubon AJ, et al. A review of selective salpingography and fallopian tube catheterization. Radiographics 2000;20:1759–68.
36. Thurmond AS, Brandt KR, Gorrill MJ. Tubal obstruction after ligation reversal surgery: results of catheter recanalization. Radiology 1999;210:747–50.
37. Confino E, Friberg J, Gleicher N. Preliminary experience with transcervical balloon tuboplasty. Am J Obstet Gynecol 1988;159:370–5.
38. Maubon A, Rouanet JP, Cover S, et al. Fallopian tube recanalization by selective salpingography: an alternative to more invasive techniques? Hum Reprod 1992;7:1425–8.
39. Thurmond AS, Rosch J. Nonsurgical fallopian tube recanalization for treatment of infertility. Radiology 1990;174:371–4.
40. Kelekis D, Fezoulidis I, Petsas T, et al. Selective transcervical tubal recanalization under DSA. Rofo 1991;154:354–6 [in German].
41. Thurmond AS. Pregnancies after selective salpingography and tubal recanalization. Radiology 1994;190:11–3.
42. American Fertility Society. The American Fertility Society classification of adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, Mullerian anomalies and intrauterine adhesions. Fertil Steril 1988;49:944–55.
43. Ahmad G, Watson A, Vandekerckhove P, et al. Techniques for pelvic surgery in subfertility. Cochrane Database Syst Rev 2006;(2):CD000221.
44. Stenchever MADW, Herbst AL, Mishell D. Comprehensive gynecology. 4th edition. St Louis (MO): Mosby; 2001.
45. The role of tubal reconstructive surgery in the era of assisted reproductive technologies. Fertil Steril 2008;90:S250–3.
46. Canis M, Mage G, Pouly JL, et al. Laparoscopic distal tuboplasty: report of 87 cases and a 4-year experience. Fertil Steril 1991;56:616–21.
47. Dlugi AM, Reddy S, Saleh WA, et al. Pregnancy rates after operative endoscopic treatment of total (neosalpingostomy) or near total (salpingostomy) distal tubal occlusion. Fertil Steril 1994;62:913–20.
48. Camus E, Poncelet C, Goffinet F, et al. Pregnancy rates after in-vitro fertilization in cases of tubal infertility with and without hydrosalpinx: a meta-analysis of published comparative studies. Hum Reprod 1999;14:1243–9.
49. Zeyneloglu HB, Arici A, Olive DL. Adverse effects of hydrosalpinx on pregnancy rates after in vitro fertilization-embryo transfer. Fertil Steril 1998;70:492–9.
50. Granot I, Dekel N, Segal I, et al. Is hydrosalpinx fluid cytotoxic? Hum Reprod 1998;13:1620–4.
51. Strandell A, Sjogren A, Bentin-Ley U, et al. Hydrosalpinx fluid does not adversely affect the normal development of human embryos and implantation in vitro. Hum Reprod 1998;13:2921–5.
52. Lessey BA, Castelbaum AJ, Sawin SW, et al. Integrins as markers of uterine receptivity in women with primary unexplained infertility. Fertil Steril 1995;63:535–42.
53. Meyer WR, Castelbaum AJ, Somkuti S, et al. Hydrosalpinges adversely affect markers of endometrial receptivity. Hum Reprod 1997;12:1393–8.

54. Mansour RT, Aboulghar MA, Serour GI, et al. Fluid accumulation of the uterine cavity before embryo transfer: a possible hindrance for implantation. J In Vitro Fert Embryo Transf 1991;8:157–9.
55. Sowter MC, Akande VA, Williams JA, et al. Is the outcome of in-vitro fertilization and embryo transfer treatment improved by spontaneous or surgical drainage of a hydrosalpinx? Hum Reprod 1997;12:2147–50.
56. Aboulghar MA, Mansour RT, Serour GI, et al. Transvaginal ultrasonic needle guided aspiration of pelvic inflammatory cystic masses before ovulation induction for in vitro fertilization. Fertil Steril 1990;53:311–4.
57. Van Voorhis BJ, Sparks AE, Syrop CH, et al. Ultrasound-guided aspiration of hydrosalpinges is associated with improved pregnancy and implantation rates after in-vitro fertilization cycles. Hum Reprod 1998;13:736–9.
58. Hammadieh N, Coomarasamy A, Ola B, et al. Ultrasound-guided hydrosalpinx aspiration during oocyte collection improves pregnancy outcome in IVF: a randomized controlled trial. Hum Reprod 2008;23:1113–7.
59. Committee opinion: role of tubal surgery in the era of assisted reproductive technology. Fertil Steril 2012;97:539–45.
60. Strandell A, Lindhard A, Waldenstrom U, et al. Hydrosalpinx and IVF outcome: a prospective, randomized multicentre trial in Scandinavia on salpingectomy prior to IVF. Hum Reprod 1999;14:2762–9.
61. Dechaud H, Daures JP, Arnal F, et al. Does previous salpingectomy improve implantation and pregnancy rates in patients with severe tubal factor infertility who are undergoing in vitro fertilization? A pilot prospective randomized study. Fertil Steril 1998;69:1020–5.
62. Kontoravdis A, Makrakis E, Pantos K, et al. Proximal tubal occlusion and salpingectomy result in similar improvement in in vitro fertilization outcome in patients with hydrosalpinx. Fertil Steril 2006;86:1642–9.
63. Johnson N, van Voorst S, Sowter MC, et al. Surgical treatment for tubal disease in women due to undergo in vitro fertilisation. Cochrane Database Syst Rev 2010;(1):CD002125.
64. Moshin V, HA. Reproductive outcome of the proximal tubal occlusion prior to IVF in patients with hydrosalpinx. Hum Reprod 2006;21:i193–4.
65. Stephen EH, CA. Use of infertility services in the United States: 1995. Fam Plann Perspect 2000;32:132–7.
66. Koh CH, Janik GM. Laparoscopic microsurgical tubal anastomosis. Obstet Gynecol Clin North Am 1999;26:189–200, viii.
67. Caillet M, Vandromme J, Rozenberg S, et al. Robotically assisted laparoscopic microsurgical tubal reanastomosis: a retrospective study. Fertil Steril 2010;94:1844–7.
68. Rodgers AK, Goldberg JM, Hammel JP, et al. Tubal anastomosis by robotic compared with outpatient minilaparotomy. Obstet Gynecol 2007;109:1375–80.
69. te Velde ER, Boer ME, Looman CW, et al. Factors influencing success or failure after reversal of sterilization: a multivariate approach. Fertil Steril 1990;54:270–7.
70. Dubuisson JB, Chapron C, Nos C, et al. Sterilization reversal: fertility results. Hum Reprod 1995;10:1145–51.
71. Rock JA, Chang YS, Limpaphayom K, et al. Microsurgical tubal anastomosis: a controlled trial in four Asian centers. Microsurgery 1984;5:95–7.
72. Yoon TK, Sung HR, Kang HG, et al. Laparoscopic tubal anastomosis: fertility outcome in 202 cases. Fertil Steril 1999;72:1121–6.
73. Monteith CW, Berger GS. Normal pregnancy after outpatient tubouterine implantation in patient with Adiana sterilization. Fertil Steril 2011;96:e45–6.

74. Monteith CW, Berger GS. Successful pregnancies after removal of intratubal microinserts. Obstet Gynecol 2012;119:470–2.
75. Gargiulo AR, Nezhat C. Robot-assisted laparoscopy, natural orifice transluminal endoscopy, and single-site laparoscopy in reproductive surgery. Semin Reprod Med 2011;29:155–68.
76. Nezhat C, Saberi NS, Shahmohamady B, et al. Robotic-assisted laparoscopy in gynecological surgery. JSLS 2006;10:317–20.
77. Liu C, Perisic D, Samadi D, et al. Robotic-assisted laparoscopic partial bladder resection for the treatment of infiltrating endometriosis. J Minim Invasive Gynecol 2008;15:745–8.
78. Nezhat C, Morozov V. Robot-assisted laparoscopic presacral neurectomy: feasibility, techniques, and operative outcomes. J Minim Invasive Gynecol 2010;17: 508–12.
79. Barakat EE, Bedaiwy MA, Zimberg S, et al. Robotic-assisted, laparoscopic, and abdominal myomectomy: a comparison of surgical outcomes. Obstet Gynecol 2011;117:256–65.
80. Nezhat C, Lewis M, Kotikela S, et al. Robotic versus standard laparoscopy for the treatment of endometriosis. Fertil Steril 2010;94:2758–60.
81. Nezhat C, Nezhat FR, Nezhat C. Nezhat's operative gynecologic laparoscopy and hysteroscopy. 3rd edition. Cambridge (United Kingdom): Cambridge University Press; 2008.
82. Dharia Patel SP, Steinkampf MP, Whitten SJ, et al. Robotic tubal anastomosis: surgical technique and cost effectiveness. Fertil Steril 2008;90:1175–9.
83. Falcone T, Goldberg JM, Margossian H, et al. Robotic-assisted laparoscopic microsurgical tubal anastomosis: a human pilot study. Fertil Steril 2000;73: 1040–2.
84. Centers for Disease Control and Prevention. 2009 assisted reproductive technology success rates. National Summary and Fertility Clinic Reports. Atlanta (GA): Centers for Disease Control and Prevention; 2011.
85. Karande VC, Korn A, Morris R, et al. Prospective randomized trial comparing the outcome and cost of in vitro fertilization with that of a traditional treatment algorithm as first-line therapy for couples with infertility. Fertil Steril 1999;71:468–75.
86. Pandian Z, Akande VA, Harrild K, et al. Surgery for tubal infertility. Cochrane Database Syst Rev 2008;(3):CD006415.
87. McDonald S, Murphy K, Beyene J, et al. Perinatal outcomes of in vitro fertilization twins: a systematic review and meta-analyses. Am J Obstet Gynecol 2005;193: 141–52.
88. Jackson RA, Gibson KA, Wu YW, et al. Perinatal outcomes in singletons following in vitro fertilization: a meta-analysis. Obstet Gynecol 2004;103:551–63.