Chapter 20
The Impact of Assisted Reproductive Technology on Gynecologic Surgery

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DEFINITIONS

Controlled ovarian hyperstimulation—Administration of exogenous gonadotropins to induce growth of multiple ovarian follicles within a single menstrual cycle.

Developmental states—*Morula*—The stage between 72 and 96 hours after insemination, from the 16-cell stage to formation of the blastocyst. *Blastocyst*—The stage consisting of an inner cell mass from which the fetus develops and a trophectoderm from which the placenta develops. It is distinguished from the morula by the presence of a fluid-filled cavity.

Embryo transfer—The delivery of viable embryos to the uterine fundus for implantation. This is traditionally done transcervically or less commonly by laparoscopic cannulation of the fallopian tubes.

Intracytoplasmic sperm injection (ICSI)—Procedure by which a single sperm is injected directly into a mature oocyte assisted fertilization.

Mature oocyte—An oocyte at metaphase II of meiosis. Fertilization may occur at this stage of development.

Noncommunicating hydrosalpinx—Accumulation of distal tubal fluid that is unable to pass into the peritoneal cavity.

Oocyte—The immature female gamete.

Oocyte retrieval—The removal of oocytes after controlled ovarian hyperstimulation by ultrasound-guided needle aspiration. In rare instances, laparoscopic retrieval may be necessary.

Ovarian hyperstimulation syndrome (OHSS)—A complication of assisted reproductive technology that occurs almost exclusively with the use of gonadotropin stimulation. It is a condition of vascular hyperpermeability secondary to the release of vasoactive substances (vascular endothelial growth factor, tumor necrosis factor-alpha, interleukins) from the overstimulated ovaries. The transudation of proteinrich fluid from the intravascular to the extravascular compartment can lead to ascites, hemoconcentration, electrolyte imbalance, or hepatic and renal dysfunction. Severe OHSS can lead to vascular collapse, acute respiratory distress syndrome (ARDS) and even death.

Prezygote—The stage of pronuclear formation after penetration of the mature (MII) oocyte by spermatozoon. At this stage, male and female pronuclei are evident as well as the second polar body. This is the stage immediately preceding syngamy, the fusion of two nuclei to form a single nucleus of the zygote.

Zona pellucida—The glycoprotein membrane surrounding the plasma membrane of an oocyte.

Zygote—Single cell stage after pronuclear breakdown (syngamy) but before first cleavage.

ASSISTED REPRODUCTIVE TECHNOLOGY

Assisted reproductive technology (ART) is inclusive of any procedure involving fertilization of the oocyte outside the body. The first live birth from ART was reported in 1978 by Patrick Steptoe and Robert Edwards following laparoscopic retrieval of a single oocyte from a naturally stimulated ovary. The most frequently practiced ART

procedure is in vitro fertilization (IVF). It involves a sequence of events beginning with controlled ovarian hyperstimulation, harvesting of oocytes, fertilization with spermatozoa, culturing of embryos, and replacement into the uterine cavity. Also under the umbrella of ART are laparoscopic tubal transfer of gametes (gamete intrafallopian transfer; GIFT), zygotes (zygote intrafallopian transfer; ZIFT), and embryos (tubal embryo transfer; TET). These techniques have largely been supplanted by IVF in light of their requirement for laparoscopy and considerable technical advances in both IVF and embryo culture conditions.

Assisted Reproductive Technology and the Expectations of Pregnancy

Consideration should first be made to the success rates of ART without surgical intervention. If this is deemed reasonable, it may be prudent to forgo surgery—and the inherent risks therein—and proceed directly to IVF. The decision to proceed with surgical intervention also requires detailed knowledge of its impact on subsequent pregnancy rates and should only be entertained if pregnancy rates could be significantly improved or the need for ART eliminated altogether.

Data on ART outcomes are collected every year to provide information to prospective patients as well as clinicians. The 2010 data from the Society for Assisted Reproductive Technology (SART) report pregnancy rates for fresh and frozen nondonor oocytes per cycle of IVF (**Table 20.1**). Success rates are clinic specific, and this information is available through http://sart.org.

Female age is the single most important predictor of IVF success rate due to the direct relationship between advancing female age and genetic instability of the oocyte. Over 90% of maternally derived aneuploidy stems from meiosis I chromosomal segregation errors. Two main mechanisms for oocyte aneuploidy have been described by Fragouli and colleagues. The first occurs exclusively during meiosis I with premature division of a chromosome into its two sister chromatids, followed by their random segregation. The second error is nondisjunction of entire chromosomes during meiosis I and meiosis II leading to hyperhaploid (n = 24) and hypohaploid (n = 22) gametes. As a result, advancing age of the female partner is inextricably

coupled with a decline in pregnancy and live birth rates. Coincidental with age, ovarian reserve also plays a major role in a woman's reproductive potential. Thus, any discussion of prognosis should be made in the context of ovarian reserve assessment.

TABLE 20.1 2010 Success Rates of IVF Cycles[a] Using Fresh Embryos from Nondonor Oocytes

	AGE RANGES				
	<35	**35-37**	**38-40**	**41-42**	**>42**
Number of cycles	39,473	20,250	20,706	9,650	5,546
Percentage of cycles resulting in pregnancies	47.7	38.8	29.9	20.1	8.9
Percentage of cycles resulting in live births	41.7	31.9	22.1	12.5	4.1
Reliability range	(41.2-42.1)	(31.3-32.6)	(21.5-22.7)	(11.8-13.1)	(3.6-4.7)

Percentage of retrievals resulting in live births	44.6	35.5	25.4	14.9	5.3
Percentage of transfers resulting in live births	47.8	38.4	28.1	16.8	6.3
Percentage of cycles with elective single embryo transfer	9.6	5.3	1.7	0.6	0.5
Percentage of cancellations	6.6	10.0	12.9	16.5	22.0
Implantation rate	36.9	27.0	17.7	9.6	3.7
Average number of embryos transferred	2.0	2.2	2.6	3.0	3.1
Percentage of live births with twins	32.4	27.2	22.1	16.9	9.6
Percentage of live births with triplets or more	1.5	1.5	1.1	1.1	0.9

[a]Data collected from Society for Assisted Reproductive Technology (SART) member clinics.

ASSISTED REPRODUCTIVE TECHNOLOGY AND ENDOMETRIOSIS

Endometriosis is endometrial tissue found outside the uterus. This ectopic tissue responds to the hormonal changes of a menstrual cycle and can be a significant cause of morbidity. The precise pathophysiology of endometriosis and its impact on fertility depend upon the degree of endometriosis present in the ovaries and pelvis. Proposed mechanisms include distortion of pelvic anatomy and abnormal peritoneal environment characterized by increased inflammatory cytokines and oxidative stress, which may interfere with follicular development, ovum pickup, fertilization, and embryo development.

For patients who are infertile and have no other cause for infertility, it can be tempting to explore the pelvis via laparoscopy to diagnose and ultimately ablate lesions from endometriosis. There are two randomized prospective trials evaluating the efficacy of laparoscopic ablation of mild-to-moderate endometriosis and postoperative natural fecundity. The Canadian Collaborative Group on Endometriosis (ENDOCAN) randomized 341 patients with unexplained infertility for 2 years or more to diagnostic laparoscopy versus ablation and followed patients for 36 months. They found a modest increase in fecundity rates in those whose endometriosis was ablated, from 2.4% to 4.7%. Ultimately, eight women required surgery to achieve one additional pregnancy. The second, an Italian study led by Parazzini, randomized 96 women to diagnostic laparoscopy versus ablation followed for 1 year and found no increase in spontaneous conception rates. However, when adjuvant GnRH agonist was used postoperatively over a brief time interval, spontaneous conception was increased from 18% to 39%.

In the context of ART, pregnancy rates in patients with mild-to-moderate endometriosis who forgo surgery are comparable to patients with unexplained infertility. The conception rates after ART are significantly higher compared to those who are managed expectantly for up to 24 months following ablative surgery. In a study by Suzuki et al., even patients with more advanced endometriosis experienced monthly fecundity rates of 22% to 25%, questioning the need for laparoscopic intervention prior to ART. Thus, surgery can marginally improve spontaneous conception rates in individuals with infertility and stage I—II endometriosis but does not approach success rates achieved with ART.

There are several considerations to be made in women with asymptomatic severe endometriosis and fertility. If there is significant anatomic distortion, surgery vis-à-vis fimbrioplasty or lysis of adhesion, in instances where adnexa are adherent to surrounding structures, can improve fertility. Reports on postoperative natural pregnancy rates are sparse and in the range of 7% to 15% over 12 months.

Garcia-velasco and Arici demonstrated that with respect to ovarian endometriomas, laparoscopic cystectomy prior to IVF does not appear to improve pregnancy rates. Since endometrias can be destructive to the ovarian reserve of young women, surgical intervention may be appropriate for this patient group. Rapidly growing endometriomas may indicate an underlying malignancy or borderline tumor. Therefore, any adnexal structure with a documented increase in size over a short time interval should be investigated for pathologic diagnosis. Depending on its size and location within the ovary, endometriomas may

present structural impedance at oocyte retrieval. Each scenario provides a legitimate reason to favor removal prior to IVF.

ASSISTED REPRODUCTIVE TECHNOLOGY AND TUBAL INFERTILITY

Tubal factor infertility accounts for 30% of cases of female infertility and 9% of diagnoses among couples who underwent ART treatments in the United States in 2010. Tubal health is evaluated by hysterosalpingogram (HSG). In this procedure, contrast is placed into the uterine cavity and the fallopian tubes are visualized using fluoroscopy. The luminal diameter should be less than 1 mm at the isthmic portion of the fallopian tube and typically increases to 2 to 3 mm at the ampullary end. Free spill of contrast should be visualized to confirm tubal patency. Assisted reproductive technology was originally devised as a method to overcome tubal factor infertility. Statistically, current success rates after IVF exceed that of surgical repair. However, IVF can be financially and emotionally burdensome, and there are some instances when surgical correction can restore normal reproductive anatomy and should be considered before proceeding to IVF.

The optimal candidate for tubal reconstruction is young (<30) with a history of voluntary surgical sterilization without coexistent infertility factors. She should be counseled regarding postrepair conception rates, which range from 18% to 45% over a 12-month period, as well as ectopic pregnancy rates of 7% to 25%, as reported by Collins. Postoperative fecundity rates are subject to patient selection, technical skill of the surgeon, as well as the final length of the repaired fallopian tube.

Proximal Obstruction

The final diagnosis of proximal tubal disease by HSG should be reserved until confirmed with further testing. Tubal spasm or failure to produce adequate anterograde pressure of dye can be misinterpreted as proximal occlusion. Procedural options permitting simultaneous diagnosis and correction of proximal obstruction are fluoroscopic cannulation, laparoscopic chromotubation, and hysteroscopic catheterization. Each of these is sufficient to assign a final diagnosis of proximal tubal obstruction. If proximal obstruction is confirmed and efforts to establish patency are unsuccessful, IVF is the treatment of choice for these patients.

Hysteroscopic Catheterization—This procedure begins with appropriate distention media. A hypoosmotic media

like glycine is ideal because it is immiscible with blood, ensuring clear visualization of the tubal ostia. First, standard chromopertubation of the fallopian tubes is done to confirm the diagnosis of proximal obstruction. The hysteroscope is then introduced through the cervical os, and tubal ostia are visualized. A soft flexible catheter with a metal introducer is directed through the obstructed side to a depth of 1 to 2 cm, and the inner metal introducer is removed while the outer sheath is advanced further into the isthmic portion of the fallopian tube. Indigo carmine is introduced through the operator's end of the catheter. A concurrent laparoscopy confirms spill of dye through the fimbriated end, and the catheter is removed. Laparoscopy also ensures prompt recognition of bleeding or tubal perforation.

Distal Obstruction/Hydrosalpinges

Surgical correction of mild tubal disease may be appropriate for young women. Correction may involve lysis of peritubal adhesions or fimbrioplasty. In fimbrioplasty, every effort should be made to use a laparoscopic approach to reduce the risk of adhesion formation. If tubal caliber is normal and the fimbriated end agglutinated, the closed tip of a pair of fine forceps is introduced through the distal end and gently separated. The procedure should be repeated to reduce the rate of reocclusion. Care should be taken to avoid bleeding, as this increases the risk of scarring the delicate fimbria. Peritubal adhesions should be filmy and clear and separated without the use of cautery. Patton reported fecundity rates of parous women after this procedure in the range of 63% over 24 months, with a 5% ectopic pregnancy rate. However, women with severe distal disease and those over 37, who have diminished of ovarian reserve and increased aneuploidy rates, should forego surgery and proceed directly to IVF.

The study of ART outcomes has altered our management of hydrosalpinx. Patients with dilated, fluid-filled fallopian tubes may experience decreased pregnancy rates with IVF. The theories behind such observations include embryo toxicity and alterations in endometrial receptivity markers from exposure to tubal fluid. An interruption in embryo-endometrial cross talk could result from retrograde flow of tubal fluid. In fact, a recent survey of reproductive endocrinologists conducted by Omurtag and colleagues reported increased consideration of salpingectomy for hydrosalpinx without evidence of spill into the peritoneal cavity by HSG, presuming a greater degree of retrograde flow. In general, when the decision has been made to intervene surgically prior to ART, proximal tubal occlusion with bipolar cautery or surgical clips has comparable benefit to salpingectomy in patients with challenging access to adnexa.

Most studies support removal of ultrasound-visible hydrosalpinges prior to IVF; however, individual consideration should be made in women who are poor surgical candidates secondary to adhesive disease. Some of these patients may benefit from hysteroscopic placement of coiled tubes passed anterograde into the tubal ostia. In this procedure, flexible inserts containing polyethylene terephthalate fibers are guided by the hysteroscope and passed directly into the fallopian tubes. The inserts induce a fibrotic reaction that will permanently occlude the tube and thereby prevent retrograde flow of fluid into the uterine cavity. A follow-up HSG 3 months after insertion will confirm complete occlusion.

Because the current success rate of IVF in women with tubal disease exceeds that of surgical repair, it remains the treatment of choice. However, American Society for Reproductive Medicine (ASRM) practice guidelines state that tubal reconstructive surgery is a reasonable treatment option for young women with mild tubal disease and for those with ethical, religious, or financial restrictions that preclude IVF.

ASSISTED REPRODUCTIVE TECHNOLOGY AND SURGICAL MANAGEMENT OF UTERINE MYOMAS

Advising the infertile female on the management of an asymptomatic fibroid is a frequent clinical dilemma. It is unclear whether the presence of fibroids without cavitary involvement can be considered the sole cause for infertility. Theories behind adverse sequelae of myomas include mechanical obstruction of tubal ostia, chronic

intracavitary inflammation, and increased uterine contractility.

There exist very few randomized trials to guide the gynecologic surgeon on the reproductive benefit of surgery in this situation. Metwally and colleagues identified that only three randomized clinical trials exist evaluating the effect of surgical intervention on subfertility, and a vast number of retrospective and observational studies make up the remaining body of literature. Two of the RCTs compare laparoscopic versus abdominal myomectomy and find they appear to have similar outcomes in miscarriage, pregnancy, and live birth rates.

Only one RCT evaluates surgical intervention versus no intervention and subsequent fertility. Casini et al. randomized 181 young women with myomas less than 4 cm and unexplained infertility to surgical intervention or expectant management for 1 year. Women with submucous myomas benefited from intervention with an increase in pregnancy rate of 27% in the expectantly managed group to 43% in the operative group ($P < 0.05$). Improvement after surgery in women with intramural myomas without cavitary involvement ($n = 76$) did not reach significance but trended higher in the operative group.

It is generally accepted that subserous myomas do not adversely affect pregnancy or live birth rates, thus removal is rarely warranted. Pritts' review showed agreement among studies on the topic: submucous myomas decrease pregnancy rates and increase the incidence of miscarriage. For the majority of patients with submucous myomas, surgical resection restores pregnancy rates to match those with a normal uterine cavity.

The management of intramural myomas not distorting the uterine cavity has become the focus of much debate in the ART world. Large intramural myomas appear to diminish pregnancy and live birth rates in infertile women; however, there is no conclusive evidence that surgical removal restores these rates. Therefore, the decision must weigh risks versus potential benefit of myomectomy. Risks for morbidity include bleeding necessitating hysterectomy or transfusion; postoperative adhesions, especially involving the fallopian tubes; and infection. When the potential obstetric complication of uterine rupture and an increased likelihood of cesarean section are considered, it is clear that there is reason for caution about recommending myomectomy for unproven benefit.

ASSISTED REPRODUCTIVE TECHNOLOGY AND THE INDICATION FOR HYSTERECTOMY

Prior to ART, it was standard practice to remove the uterus and bilateral adnexa in cases of pelvic pain from endometriosis or adnexal mass. The uterus was considered a vestigial organ without the accompanying adnexa and a source for carcinoma of the cervix or endometrium later in life. Now, patients with these conditions achieve pregnancies through the use of donor oocytes. The uterus should also be conserved for premenopausal women who have the opportunity and desire to cryopreserve oocytes/embryos prior to surgery.

ASSISTED REPRODUCTIVE TECHNOLOGY AND THE PRESERVATION OF FERTILITY AFTER SURGICAL MENOPAUSE

Improved survival rates for women with cancer have led to the pursuit of fertility preservation. As such, recent years have witnessed the development of methods for gamete, embryo, and ovarian tissue cryopreservation from the prepubertal girl to the adult woman. Although it is beyond the scope of this chapter to describe the technical aspects of cryopreservation, the fundamental principles of cryopreservation and success rates upon thaw will be reviewed. The purpose of this section is to provide the gynecologic surgeon with appropriate options that should be offered to the patient about to undergo bilateral oophorectomy or gonadotoxic therapy.

Ovarian Tissue Cryopreservation

This method offers the ability to cryopreserve thousands of primordial follicles without a delay in cancer treatment. In the majority of diagnosed cancers, chemotherapy is initiated soon after diagnosis. Because gonadotropin stimulation and oocyte retrieval usually require 2 to 3 weeks, it may be timeprohibitive to freeze

embryos for potential future use. Breast cancer patients may have a brief window between surgery and chemotherapy, but supraphysiologic estrogen levels seen with IVF—especially in those with ER/PR+ tumors—risk stimulation of the primary tumor.

Strips of ovarian cortical tissue are surgically removed by laparoscopy or laparotomy and immediately frozen through slow cooling or vitrification. The tissue can later be thawed and the primordial follicles matured in vitro or can be autotransplanted back into the patient. Returning the tissue at or near the original location is referred to as orthotopic transplantation, while placing the tissue in a separate site such as the forearm or abdominal wall is heterotopic transplantation. With a forearm graft, the ovarian tissue is grafted into the subcutaneous space located above the brachioradialis fascia. The patients then must undergo gonadotropin stimulation, harvest, and uterine embryo transfer to conceive.

There have been approximately 20 reports of human live births using ovarian cortical tissue cryopreservation with autotransplantation, the first one reported in 2004. Thus, this technique should be considered experimental. Of note, this is the only treatment option for prepubertal girls. The potential drawbacks to be discussed are potential reseeding of tumor cells, especially in systemic cancers such as in leukemia, and in cases of high tumor potential as in BRCA gene carriers.

Oocyte Cryopreservation

Candidates for oocyte cryopreservation include premenopausal women scheduled for prophylactic oophorectomy for BRCA gene mutation, severe pelvic pain for endometriosis, or oncologic patients requiring gonadotoxic therapy. Oocyte cryopreservation necessitates a minimum delay in treatment for the primary disease of 2 to 3 weeks, and toleration of a transient rise in estrogen levels up to 4,000 pg/mL. In breast cancer patients with ER/PR+ tumors, some medical oncologists allow for one cycle of oocyte cryopreservation in the brief window between surgery and chemotherapy. It is prudent in these patients to use an aromatase inhibitor in conjunction with gonadotropin stimulation to maintain a low estradiol level.

Since the first pregnancy from frozen oocytes was described by Chen in 1986, there has been intense interest in the potential of oocyte cryopreservation. Since embryo cryopreservation using the slow-cooling method was an established technique with reasonable thaw survival and pregnancy rates, the application of slow cooling was extended to oocyte freezing. However, the oocyte has much higher water content compared to the embryo, and initial success was hampered by formation of ice crystals during cooling, causing a disruption in the meiotic spindle. In mature oocytes, metaphase chromosomes are lined up along the equatorial plate by the meiotic spindle, and this delicate spindle is easily damaged by ice crystal formation. Ultimately, changes to the sucrose and sodium concentrations were able to improve outcomes with the slow-freeze technique.

Vitrification is the solidification of a solution without formation of ice crystals. Oocytes are exposed to high concentrations of cryoprotectant followed by immersion into liquid nitrogen, creating a glass-like state. Its advantage over slow freeze is the avoidance of ice crystal formation and thus any consequent damage to the meiotic spindle. Hardening of the zona pellucida after thaw can create a challenge to successful fertilization, but is overcome by the use of intracytoplasmic sperm injection (ICSI). The majority of studies on thaw survival rates and pregnancy rates favor vitrification over the slow-freeze technique.

The ASRM reports number of live births following oocyte cryopreservation remains small but is rapidly rising. Thaw survival rates are approaching 98%, and pregnancy rate per

thawed oocyte is 4.2%. Although pregnancy rates are slowly improving with more experience, some published data touting success rates approaching that of fresh embryo transfers should be interpreted with caution given these data are derived from donor oocytes from young women without a history of infertility. Both chromosomal and congenital aneuploidy rates in thawed oocytes and live births are comparable to rates following natural

conception.

Oocyte freezing can be offered to any patient from adolescence to adulthood about to undergo bilateral oophorectomy or gonadotoxic therapy if the diagnosis will allow for the required time and hormonal stimulation necessary for oocyte harvest. Success rates as well as potential risks (OHSS, postoperative intraabdominal bleeding, and infection following oocyte retrieval) can now be reasonably quantified to allow for informed decision making.

Embryo Cryopreservation

If the patient has a stable partner at the time of diagnosis, embryo cryopreservation is the treatment of choice. This is a routine procedure in ART laboratories with reliable success rates performed through aforementioned techniques of slow freeze or vitrification. Embryos can be cryopreserved at any developmental stage, from prezygote, zygote, preembryo, morula, or blastocyst stage (**Fig. 20.1**). Decisions on the optimal

stage to freeze depend upon the experience of individual clinics. Although success rates vary by many factors—clinic experience, female age at the time of cryopreservation, and number and quality of embryos banked—a pregnancy rate of up to 60% can be reasonably achieved.

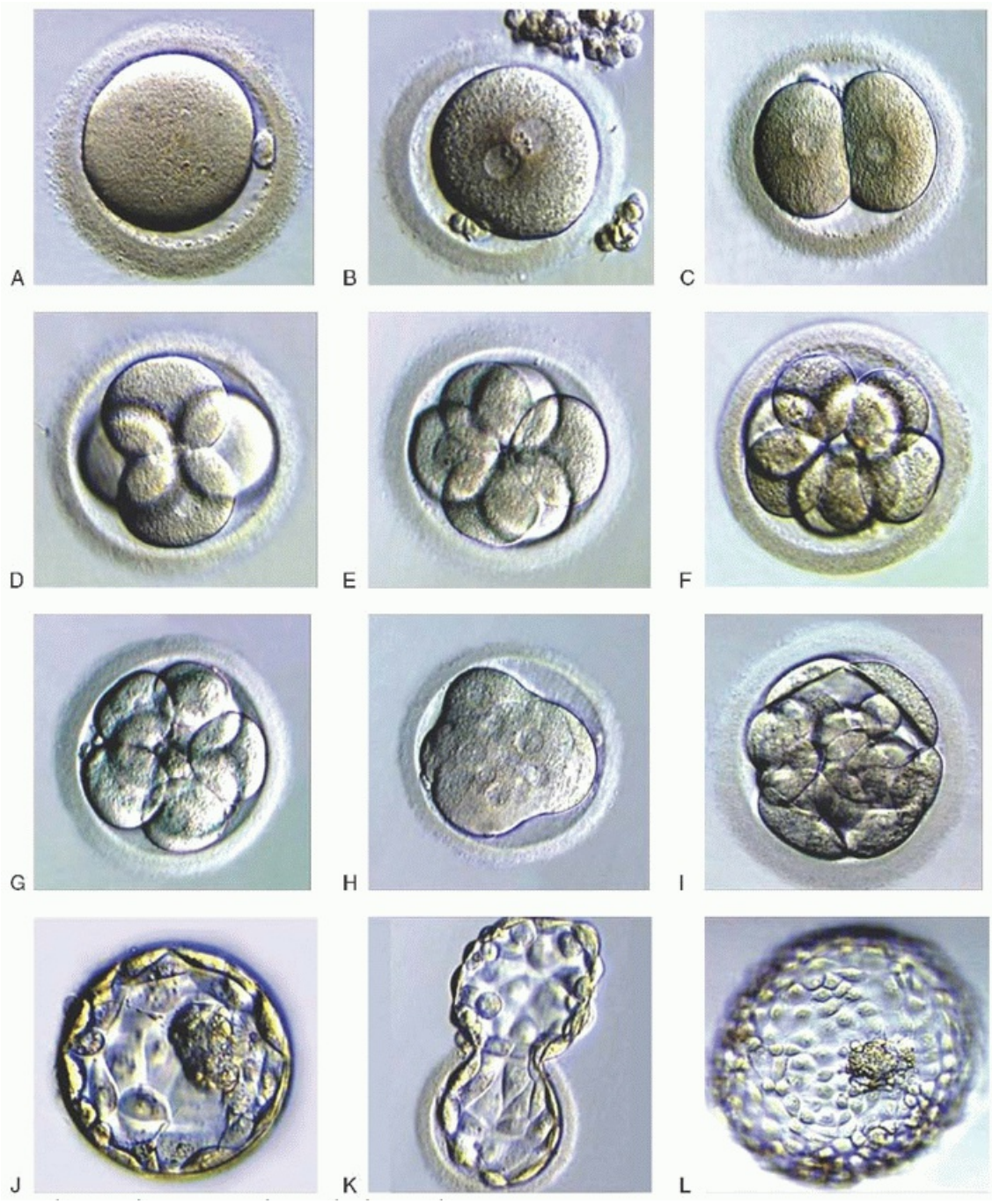

FIGURE 20.1 Embryos can be cryopreserved at any developmental stage (**A-L**).

CONCLUSION

The natural inclination of a gynecologic surgeon is to intervene in the setting of visible pathology. With regard to endometriosis, the benefit of surgical intervention varies based on degree of disease and intended fertility treatment. In cases of tubal occlusion, access to ART dictates whether surgical intervention is necessary. Each case is unique and must be considered individually. Therefore, the true challenge in treating the infertile couple in the age of ART is to understand whether surgical intervention is beneficial or an unnecessary delay to achieving pregnancy.

BEST SURGICAL PRACTICES

- The success rates of ART without surgical intervention should be considered before a recommendation for surgery is made.

- Success rates of ART are largely dependent on female age.
- Oocyte aneuploidy rates rise with advancing female age.
- For mild-to-moderate endometriosis, surgery can marginally improve spontaneous conception rates but does not approach success rates with ART.
- Patients with severe endometriosis may benefit from surgery prior to ART if lysis of adhesions is performed to restore female anatomy, thus reducing potential complications of oocyte retrieval.
- Pathologic diagnosis should be made for any rapidly expanding ovarian cyst to exclude malignancy prior to ART.
- Evidence does not support prophylactic removal of an asymptomatic endometrioma prior to ART with a goal of increasing pregnancy rates. However, removal should be considered in patients where size and location may obstruct oocyte harvest.
- Only young women (<35) with reasonable remaining tubal length and no coexistent risk factor for infertility should be considered for tubal reanastomosis. In the majority of patients with bilateral tubal disease or history of voluntary sterilization, ART should be recommended.
- Surgery for severe tubal disease should be reserved for young women who have ethical, religious, or financial restrictions that preclude IVF.
- Hydrosalpinges visible on transvaginal ultrasound should be removed prior to ART.
- Women with noncommunicating hydrosalpinges not visible on ultrasound could benefit from salpingectomy prior to ART. It is also reasonable to proceed directly to ART and reconsider salpingectomy if an initial attempt is unsuccessful.
- Subserous myomas do not adversely affect pregnancy or live birth rates, thus removal is rarely warranted.
- Submucous myomas decrease pregnancy rates and increase risk of miscarriage. Removal of submucous myomas should be advocated.
- Intramural myomas that do not distort the cavity may still reduce pregnancy rates and increase miscarriage rates. It is unclear if removal restores pregnancy rates to match rates achieved by women with unexplained infertility without myomas. Decisions made should be specific to the size, location, and coexistent conditions of the patient.
- Ovarian tissue cryopreservation can be performed without significant delay, does not require ovarian stimulation, and is the only fertility preservation option for prepubertal girls. It is currently considered experimental with a limited number of live births to date.
- Oocyte cryopreservation can be offered to adolescent and single adult women where controlled ovarian hyperstimulation and a delay in gonadotoxic treatment would not adversely affect the patient's outcome.
- Embryo cryopreservation remains the treatment of choice in fertility preservation for adult women with stable partners.

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