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The uterus and fertility

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Objective: To review the current understanding of the role the uterus plays in embryo implantation and to outline congenital anomalies and acquired diseases that impact normal uterine function.
Design: The publications related to the embryo implantation, Mullerian anomalies, uterine polyps, uterine synechiae, and myomas were identified through Medline and reviewed.
Conclusion(s): Congenital anomalies and acquired diseases of the uterus may negatively impact on the complex processes of embryo implantation. Hysteroscopic surgery to correct uterine septa, intrauterine synechiae, and myomas that distort the uterine cavity may benefit women with infertility or recurrent pregnancy loss. The effect of endometrial polyps on fertility is uncertain, but their removal, once identified, is justifiable. Complex congenital anomalies such as unicornuate uterus and uterus didelphys may negatively affect fertility and pregnancy outcome, and surgical treatment may benefit select patients. (Fertil Steril® 2008;89:1–16. ©2008 by American Society for Reproductive Medicine.)

Key Words: Uterus, implantation, iInfertility, Mullerian anomalies, endometrial polyps, intrauterine adhesions, uterine leiomyoma

> ". . . the womb is the field of generation; and if this field be corrupted it is in vain to expect any fruit though it be ever so well sown." Aristotle

Throughout history the uterus has been revered and reviled. It has been revered as an organ of regeneration. The Roman physician, Soranus of Ephesus (AD 98-138) wrote, "The uterus (*mētra*) is also termed *hystera* and *delphys*. It is termed *mētra*, because it is the mother of all the embryos borne of it, or because it makes mothers of those who posses it; or according to some people because it possesses a metre of time in regard to menstruation and childbirth . . . and it is termed *delphys* because it is able to procreate brothers and sisters."

The uterus, however, was also reviled as a source of disease. *Hystera*, the Greek word for uterus, extends from an ancient Greek myth that tells of the uterus wandering throughout a woman's body, causing disease as varied as wet feet and psychosis (hysteria).

In the 16th century Leonardo da Vinci dispelled much of the mystery that surrounded the uterus. Da Vinci used cadaver dissections to accurately describe the uterus, fetus, and membranes. His work forms the basis of our current understanding of the uterus (Fig. 1) (1).

Much has been learned of the uterus and its role in reproduction, yet much remains to be learned. At a fundamental level the uterus plays a role in sperm migration, embryo implantation, and fetal nourishment. Congenital uterine anomalies, acquired uterine lesions, and systemic diseases may affect such uterine functions precluding successful pregnancy.

This review will summarize our current understanding of the role the uterus plays in embryo implantation, and will outline congenital and acquired uterine diseases that adversely affect normal uterine function.

IMPLANTATION

Embryo implantation in the human is still a poorly understood process. The ovum is fertilized in the ampulla, near the ampullary–isthmic junction, where it resides for some 72 hours (2). During this time period cell division and compaction occur to form a morula. Under the influence of ovarian steroids, the autonomic nervous system, and the developing embryo itself, the morula is transported through the isthmus to the uterus (3). Following entry of the morula into the uterine cavity cell polarity is established and lineage differentiation occurs, forming a blastocyst. The blastocyst begins to express and transcribe over 500 previously dormant genes. This "activated" blastocyst hatches from the zona pellucida approximately 72 hours after entry into the uterine cavity. Hatching, as it is understood from animal models, is

Received September 10, 2007; revised and accepted September 10, 2007.
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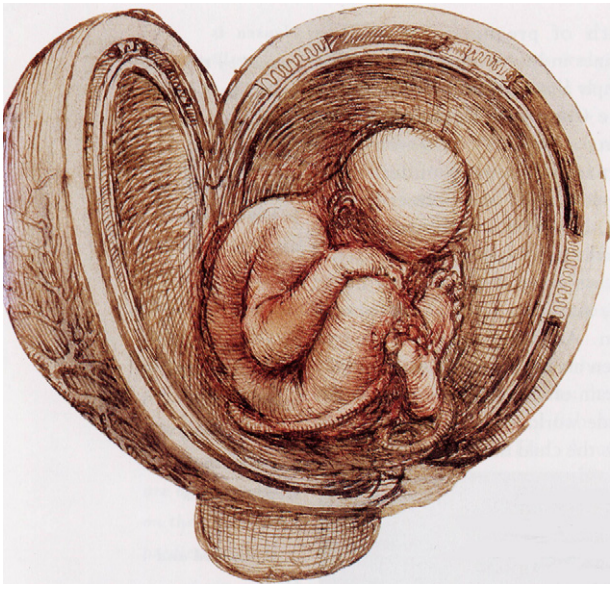
FIGURE 1

Sketch by Leonardo da Vinci of uterus with fetus, circa 1510.



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a consequence of hydrostatic pressure exerted by the expanding blastocyst and proteolytic enzymes released by the blastocyst (e.g., strypsin) and the endometrium (e.g., tryptase) that lyse the zona pellucida (4–6). A small hole is formed in the anembryonic pole of the zona pellucida from which the blastocyst escapes and begins the process of implantation (7).

Biochemical communication between the preimplantation blastocyst and the endometrium occurs prior, during, and after hatching. Chorionic gonadotropin released from the blastocyst and cytokines from both the blastocyst and endometrium begin the process of blastocyst–endometrium signaling essential for implantation. Concurrently, ovarian steroids prepare the uterus for implantation. The preovulatory increase in the secretion of 17β-estradiol stimulates proliferation and differentiation of the endometrial epithelial cells. The marked increase in progesterone production after ovulation causes endometrial stromal edema, leading to effective closure of the uterine lumen whereby the blastocyst comes into intimate contact with the endometrial epithelium.

Implantation begins 6 to 7 days after fertilization (8). Implantation has been classified into three stages: apposition, adhesion, and penetration (9). The uterus plays a role critical to the success of each stage.

At the time of apposition the embryonic pole of the blastocyst is oriented toward the endometrium. The endometrium, under the influence of progesterone, forms epithelial apical membrane projections called pinopodes. Pinopodes interdigitate with microvilli that form on the surface of the apical syncytiotrophoblast. Pinopods adhere to the trophoectoderm cells of the blastocyst through cell adhesions molecules such as E-cadherin present on the pinopode membrane (10). The location of apposition and adhesion is determined by the expression of blastocyst apposition and adhesion molecules such as integrins, laminin, fibronectin, and MUC-I under the influence of local and blastocyst-derived cytokines (11, 12).

Once adhesion of the blastocyst to endometrium is complete, invasion begins and the trophoblast penetrates the uterine epithelium. By day 10, postfertilization, the blastocyst is completely embedded in subepithelial stromal tissue and the uterine epithelium grows to cover the implantation site (13). Penetration of the trophoblast is followed by decidualization of the endometrium. Decidualization is a process of morphologic and biochemical differentiation of the endometrium. Out of the penetrating trophoblastic shell of the blastocyst mononuclear cytotrophoblasts stream to invade the entire decidualized endometrium and inner third of the myometrium as well as the maternal uterine vasculature (14). This begins the process of placentation and places fetal trophoblast in direct contact with maternal blood. Although the molecular and cellular mechanisms responsible for invasion are not well understood, it is clear that multiple signals are needed to synchronize blastocyst maturation and uterine receptivity, including sex steroid and peptide hormones, growth factors, cytokines, immunologic, and angiogenic factors (8, 15).

After implantation is complete, placental development ensues. The placenta and embryo are then supported for the remainder of the gestational period, cradled by and dependent upon the uterus and maternal circulation.

IMPLANTATION FAILURE

Implantation failure is generally related to inadequate endometrial receptivity in two-thirds of cases and abnormalities of the embryo in one-third (16). A receptive endometrium is morphologically and functionally primed for blastocyst attachment.

Since IVF began, great improvements have been made in ovarian stimulation protocols and fertililization procedures. Despite such improvements, the implantation rate has not increased dramatically. When implantation fails to occur despite the transfer of chromosomally normal good-quality embryos, other factors that may impede implantation must be affecting implantation. Endometritis, endocrine abnormalities, thrombophilias, immunologic factors, and congenital and acquired anatomic factors may contribute to implantation failure. Challenges exist in both the diagnosis and treatment of these factors.

Congenital anomalies and acquired diseases of the uterus can affect endometrial receptivity, resulting in implantation failure that manifests as recurrent pregnancy loss or infertility.

CONGENITAL UTERINE ANOMALIES

Most uterine anomalies result from a defect in the development or fusion of the paired Mullerian ducts during

embryogenesis. The American Fertility Society Classification of Mullerian Anomalies is seen in Figure 2 (17). Although familial aggregations have been reported for some uterine anomalies, it is generally accepted that uterine anomalies result from a polygenic mechanism.

Septate Uterus

The septate uterus is the most common structural uterine anomaly (18), and results from failure of the partition between the two fused Mullerian ducts to resorb. The partition between the ducts is thought to resorb in a caudal to cranial direction. Failure of complete resorption results in a fibromuscular septum that can be partial or complete—dividing the uterine cavity and cervical canal into two parts. The Buttram and Gibbons classification system, as adopted by the American Fertility Society, was developed from this traditional understanding of Mullerian duct embryology. However, recent reports have described anomalies that do not fit this model such as women with a septate uterus with cervical duplication and a longitudinal vaginal septum (19, 20) and a woman with a double cervix and vagina with a normal uterus and blind cervical pouch (21). In 1967, Musset (22) suggested that fusion occurs at the level of the uterine isthmus and simultaneously proceeds in both directions. According to this hypothesis, the dual cervix and vagina could be explained by the failed fusion of the Mullerian ducts in the caudal direction, beginning at the uterine isthmus.

Although there have been case reports documenting familial aggregation of septate uteri in families (23, 24), most are considered isolated abnormalities.

Several diagnostic modalities can assist with the diagnosis of a septate uterus. Although hysterosalpingography (HSG) may reveal two hemicavities, without visualization of the uterine fundus the septate uterus is indistinguishable from a bicornuate uterus. The diagnostic accuracy of HSG in patients with septate uteri has been reported to be between 20% and 60% (25–27). Transvaginal ultrasonography is more accurate, with a sensitivity of 100% and a specificity of 80% in the diagnosis of the septate uterus (26). Three-dimensional sonography is associated with a diagnostic accuracy of 92% (28) and hysterosonography with a 100% diagnostic accuracy in the largest series published to date (29). Magnetic resonance imaging (MRI) has been reported to detect 100% of septate uteri in two series (26, 30), but one series (31) found that MRI is not sufficiently accurate, diagnosing only 50% of septate uteri. Although combining modalities can improve diagnostic accuracy, concurrent hysteroscopy and laparoscopy is the gold standard for diagnosing the septate uterus.

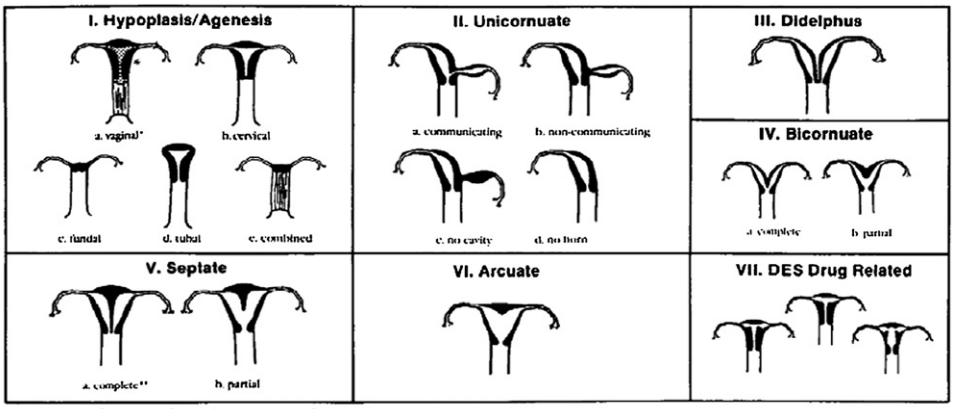
Among Mullerian abnormalities, septate uterus is associated with the highest incidence of reproductive failure. Further, the septate uterus may be associated with first- and second-trimester pregnancy loss (18) and infertility (32, 33). In a review by Homer (34), 79% of pregnancies in women with septate uteri ended in miscarriage. Such outcomes are thought to be a result of poor blood supply rendering the septum inhospitable to the implanting embryo (35).

Until the introduction of operative hysteroscopy, division of uterine septa was performed by laparotomy. Hysteroscopy revolutionized and greatly simplified the management of the septate uterus and other intrauterine lesions. Although the reproductive outcome after transabdominal and transcervical metroplasty are similar (36, 37), the transabdominal approach is associated with significantly more complications, longer hospital stay, longer recovery period, and the obvious drawbacks of hysterotomy. For this reason hysteroscopic metroplasty is the current standard of care.

Hysteroscopic metroplasty is typically performed under general or spinal anesthesia. The operative procedure is usually scheduled either in the early proliferative phase or after

FIGURE 2

American Fertility Society classification of Mullerian anomalies.



* Uterus may be normal or take a variety of abnormal forms.
** May have two distinct cervices

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pretreatment of the patients with progestins, danazol, or GnRH agonists. If a vaginal septum exists, it is incised by Metzenbaum scissors between two hemostatic clamps followed by reapproximation of the epithelial edges of the anterior and posterior vaginal mucosa. Controversy once existed as to the best management of a cervical septum. Incising the cervical septum can complicate surgery to remove a uterine septum by causing bleeding, and may predispose to cervical incompetence (38, 39). But recent studies have observed fewer intraoperative complications and good obstetric outcomes after removal of the cervical septum, which is the current practice (18, 40–42). The cervical septum is incised with Metzenbaum scissors, and incision of the corporal portion is made by hysteroresectoscopy. Hysteroscopic division of the uterine septum is performed using microscissors, electrosurgery, or laser, and may be performed under ultrasonographic or laparoscopic control. Regardless of the method of septal incision, there are two techniques: repetitive incisions across the septum's apex, causing gradual shortening, or repetitive incisions along each side of the septum alternately, thinning the septum until a short, broad notch remains that is incised from one cornual end to the other (34).

Over 20 studies have been published comparing reproductive outcome before and after hysteroscopic metroplasty for septate uterus in women with recurrent miscarriage, and all have shown significant improvement in pregnancy outcome. The miscarriage rate decreases from 88% before metroplasty to 14% after. Further, 80% of women will have a term live birth after metroplasty compared with 3% before (34).

Most studies of metroplasty for a septate uterus combine women with recurrent miscarriage and infertility, and no study has been published that randomizes infertile women to treatment versus no treatment. For this reason controversy exists as to whether infertile women should undergo metroplasty. However, women with a septate uterus and otherwise unexplained infertility may benefit from metroplasty, although the improvement in pregnancy rate is relatively modest in comparison with those who experienced recurrent pregnancy loss. In the largest series published to date 29.5% of women with otherwise unexplained infertility had a term live birth after hysteroscopic metroplasty (mean follow-up 15 months) (33).

Finally, IVF is less successful in women with a septate uterus compared with women who have undergone metroplasty (43). For this reason, hysteroscopic metroplasty should be considered in women before undergoing IVF, an emotionally and financially expensive procedure.

Unicornuate Uterus

Failure of the Mullerian ducts to completely or partially develop results in a unicornuate uterus. There are four types of unicorunate uteri: unicornuate uterus with a communicating rudimentary horn, with a noncommunicating rudimentary horn, with or without a cavity and an isolated unicornuate uterus. Further, approximately 40% of patients with a unicornuate uterus will have an associated urinary tract anomaly (35). Two patients have been reported with ipsilateral ovarian agenesis, suggesting that in some instances unicornuate uterus may result from complete agenesis of all the organs derived from one urogenital ridge (44, 45).

The unicornuate uterus is an uncommon anomaly, representing only 4.4% of uterine anomalies (46). Collectively, unicornuate uteri are associated with relatively poor reproductive outcome. In a review of 151 women with an untreated unicornuate uterus who had a total of 260 pregnancies the mean abortion rate was 37.1%, the mean preterm delivery rate was 16.4%, the mean term delivery rate was 45.3%, and the mean live birth rate was 55.1% (47). However, different types of unicornuate uterus are associated with different reproductive success rates. The success rate is dependent on numerous factors that include: variations in the vascular contribution from the uterine artery and utero-ovarian artery of the contralateral side, extent of the reduction of muscular mass of a unicornuate uterus, degree of cervical competence, and presence and extent of coexistent pelvic disease such as endometriosis. In the largest series of women with a unicornuate uterus who were infertile or had recurrent pregnancy loss, the live birth rate in those with a communicating rudimentary horn was 15%, with a noncommunicating rudimentary horn was 28%, and with a rudimentary horn without a cavity 35%. Only one woman had a unicornuate uterus without a rudimentary horn and did not have a live birth (48). The highest live birth rates are observed in women with a rudimentary horn, with or without a cavity (49).

The rudimentary horn can be removed by laparotomy or laparoscopy. Laparoscopic removal by an experienced surgeon confers benefits over laparotomy in reduced postoperative pain and shorter hospitalization. Nevertheless, the surgical technique is similar. First, the ipsilateral round ligament is ligated and the ipsilateral tube is removed, being sure to avoid disruption of the ovarian blood supply as the ovary is left in situ. The utero-ovarian ligament and uterine artery are then ligated. Laparoscopically this can be achieved using bipolar diathermy, staples, and scissors. The rudimentary horn is then removed, being careful to avoid deep dissection into the myometrium of the remaining unicornuate uterus. The surgical bed is made hemostatic using cautery and sutures. If the procedure is performed laparoscopically the rudimentary horn can be removed through a trocar port after morcellation or through a colpotomy incision.

This laparoscopic technique of a rudimentary uterine horn removal was first reported in 1990 (50). Since then, 32 additional cases have been reported in small case series. Complex unicornuate anomalies may benefit from a combined laparoscopic and hysteroscopic approach (51) or from interventional radiology (52). Interventional radiology may facilitate minimally invasive surgery of unusual or complex uterine anomalies. The use of intraoperative needles and guide wires, under ultrasound control, facilitates the creation of communication between a functional and obstructed uterine horn, creation of communication between the vagina and

uterine cavity in the case of an obstructed cervix, and so forth, thus avoiding laparoscopy or laparotomy to correct the anomaly in select cases (52).

Reasons for removing rudimentary horns include reduction in dysmenorrhea, preventing or reducing endometriosis caused by retrograde menstrual effluent, and avoiding a horn or tubal gestation. For these reasons it is generally accepted that the noncommunicating rudimentary horn with functional endometrium be removed, particularly in symptomatic women. There is no consensus whether to remove communicating rudimentary horns or horns without functional endometrium. Further, there is no evidence that removal of such rudimentary horns improves reproductive outcome.

Bicornuate Uterus

A bicornuate uterus results from failure of the Müllerian ducts to completely fuse. The central myometrium may extend to the level of the internal cervical os (bicornuate unicollis) or external cervical os (bicornuate bicollis). The latter is distinguished from uterus didelphys because it demonstrates some degree of fusion between the two horns, whereas in classic uterus didelphys the two horns and cervices are separated completely.

The bicornuate uterus is a common anomaly representing 46.3% (46) of uterine anomalies. Although 25% of women with recurrent pregnancy loss or infertility will have a bicornuate uterus, most women with this anomaly have no difficulty conceiving (47). After conception, however, women with a bicornuate uterus are at an increased risk of mid-trimester pregnancy loss and preterm birth. In a review of 260 women with an untreated bicornuate uterus who had a total of 627 pregnancies, the mean abortion rate was 36%, the mean preterm delivery rate was 23%, the mean term delivery rate was 40.6%, and the mean live birth rate was 55.2% (47).

Bicornuate uterus rarely requires surgical treatment. Metroplasty is reserved for women who have experienced recurrent spontaneous abortion, mid-trimester loss, premature birth, and in whom no other cause has been identified. Transabdominal metroplasty has been reported to significantly improve the reproductive outcome in women with bicornuate uteri who experience recurrent spontaneous abortions or premature deliveries before surgery. Term pregnancy rates after uterine unification procedures have approached 90% (53). The recent report of laparoscopic metroplasty with a subsequent ongoing pregnancy suggests that minimally invasive approach may be feasible (54).

Uterus Didelphys

Complete failure of fusion of the paired Mullerian ducts results in duplication of the uterine corpus and cervix called uterus didelphys, and represents 11.1% of uterine anomalies (46). A longitudinal vaginal septum is present in most women with a didelphys uterus, and may facilitate the early diagnosis when identified on routine speculum examination (55). The urinary tract should be evaluated because anomalies are present in 23% of these women (56).

Compared with other uterine anomalies uterus didelphys has a relatively good prognosis for achieving pregnancy. Heinonen (56) followed 49 women with uterus didelphys for a mean follow-up of 9 years and found an infertility rate of 13%. There is, however, still some increase in adverse pregnancy outcomes. A review of 114 patients with an untreated didelphys uterus who had a total of 152 pregnancies demonstrated mean miscarriage, preterm delivery, and term delivery rates of 32.9%, 28.9%, and 36.2%, respectively. The mean live birth rate was 56.6% (47).

Historically, Strassman reunification, hemihysterectomy were performed on the didelphyus uterus; however, such procedures are technically difficult and are unlikely to improve the reproductive outcome. Further, they can result in cervical incompetence or cervical stenosis.

Resection of a vaginal septum, if present, is appropriate if it is associated with obstruction, dyspareunia, or infertility, if intercourse occurs on the part of the vagina contralateral to the ovulation side or if the septum blocks sperm from reaching the cervix.

ENDOMETRIAL POLYPS

Endometrial polyps are benign, localized overgrowths of endometrium. They are commonly identified during the investigation for abnormal uterine bleeding and infertility. Little is know about the association between endometrial polyps and fertility. The mechanism by which polyps may adversely affect fertility is also poorly understood but may be related to mechanical interference with sperm transport, embryo implantation, or through increased production of inhibitory factors such as glycodelin that can inhibit natural killer cell function (57).

Endometrial polyps are identified by hysteroscopy in 16.5% (58) to 26.5% (59) of women with otherwise unexplained infertility. The rate is much higher (46.7%) in infertile women with endometriosis (58) and lower (0.6% [60] to 5% [61]) in women with recurrent pregnancy loss.

Hysterosalpingography has a sensitivity of between 50% (62) and 98% (63) for intrauterine lesions, and it is unable to reliably distinguish between submucosal myomas and endometrial polyps, which may partly reflect operator technique. Sonohysterography and HSG have similar diagnostic accuracies (52% vs. 60%) (64). The gold standard for diagnosis is hysteroscopy. Hysteroscopy permits polypectomy to be undertaken, under direct vision, concurrently.

The only randomized trial examining the effect of polypectomy on pregnancy rate after IUI demonstrated a statistically significant improvement in pregnancy rate in women who underwent hysteroscopic polypectomy (mean polyp size = 9 mm) compared with those who did not undergo polypectomy (63.4% vs. 28.2%) (65). Three nonrandomized studies also

found an association between polypectomy and improved spontaneous pregnancy rates. Varasteh et al. (66) studied infertile women with and without endometrial polyps and found a pregnancy rate of 78.3% after polypectomy compared with 42.1% in those with a normal uterine cavity. Spiewankiewicz et al. (67) reported a pregnancy rate of 76% in infertile patients after polypectomy, whereas Shokeir et al. (68) reported a 50% pregnancy rate after polypectomy in such patients. These studies suggest women with otherwise unexplained infertility may benefit from polypectomy.

The effect of endometrial polyps on IVF remains unclear. In the first study to examine the effect, 83 women with ultrasonographically identified endometrial polyps <2 cm in diameter were divided into two groups before oocyte retrieval during IVF. Forty-nine women completed the standard lVF-ET treatment and 34 women underwent hysteroscopic polypectomy immediately after oocyte retrieval. In the latter group, the embryos were cryopreserved and transferred in a subsequent cycle. No statistically significant difference was observed in pregnancy rates between the two groups and compared with the overall pregnancy rate for their clinic during the same period of time (69). Although they concluded that endometrial polyps <2 cm have no deleterious effect on conception following IVF treatment, the effect of embryo cryopreservation on pregnancy rate after IVF treatment outcome may have negated any positive effect of polypectomy before IVF on the outcome of a fresh cycle.

Another study also found no effect of ultrasonographically identified endometrial polyps on IVF success rate. Thirty-three women with an endometrial polyp (mean size = 8.3 mm; range 5–12 mm) were compared with 54 without an endometrial polyp undergoing IVF. No difference was found between the groups with respect to implantation and miscarriage rates after IVF treatment (70).

Similarly, endometrial polyps <1.5 cm in size had no effect on IVF outcome in a study that divided patients undergoing IVF with intracytoplasmic sperm injection (ICSI) into three groups: women with ultrasonographically identified endometrial polyps discovered during ovarian stimulation (n = 15), women who underwent hysteroscopic polyp resection before their ICSI cycle (n = 40) and women without polyps (n = 956). There was no statistical difference between the three groups: the pregnancy rates were 53.3%, 45.0%, and 40.1%, respectively (71).

These studies suggest that endometrial polyps <2 cm in size appear to have no impact on IVF outcome. Further studies are required to examine the effect of larger polyps, polyp location, and number of polyps on IVF outcome.

If an endometrial polyp is identified during an IVF cycle management options include continuation of the cycle cancellation, embryo cryopreservation, or polypectomy and continuation of the IVF cycle. The latter option was examined in a case series of six patients who underwent hysteroscopic polypectomy with a wire-loop without use of electric current during an IVF cycle (72). A 50% pregnancy rate (3/6) was observed, suggesting hysteroscopic polypectomy may not be detrimental to IVF cycle outcome.

Although endometrial polyps have been observed more frequently in women with recurrent pregnancy loss, the effect of treatment has not been studied. If other causes of recurrent pregnancy loss have been excluded, hysteroscopic polypectomy is reasonable to perform.

Polpectomy can be performed blindly using a transcervical sharp curette; however, hysteroscopy-directed polypectomy using scissors, a loop electrode, electric probe, or a morcellator is preferred to minimize damage to the surrounding endometrium and to ensure the polyp has been removed in its entirety. Operative resectoscopy with a loop electrode appears to be the technique of choice for endometrial polyps >2 cm or with a fundal implant, whereas division of the polyp stalk using a bipolar electrode appears to be preferable for smaller, nonfundal polyps (73). The recently introduced intrauterine morcellator has been used for excision of polyps (and myoma); this approach has been demonstrated to reduce the operative time compared with loop electrode excision (8.7 minutes, 95% confidence interval [CI]: 7.3–10.1 versus 30.9 minutes, CI: 27.0 –34.8) (74).

FIGURE 3

American Fertility Society classification of intrauterine adhesions. Disease severity is staged from I to III based on cumulative score: stage I (mild) 1–4, stage II (moderate) 5–8, stage III (severe) 9–12.

Extent of Cavity Involved	<1/3	1/3 - 2/3	>2/3
	1	2	4
Type of Adhesions	Filmy	Filmy & Dense	Dense
	1	2	4
Menstrual Pattern	Normal	Hypomenorrhea	Amenorrhea
	0	2	4

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INTRAUTERINE ADHESIONS

In 1894, Heinrich first described intrauterine adhesions causing amenorrhea after curettage for postpartum hemorrhage. Joseph Asherman (75) detailed such adhesions in 1948 in a report of 29 women with amenorrhea because of stenosis of the internal cervical os. Shortly thereafter he described obliteration of the uterine cavity secondary to trauma to the uterine body and the term Asherman's syndrome (76) was ascribed. In 1989, the American Fertility Society classified intrauterine adhesions (Fig. 3) from stage I to III based on the extent and type of adhesions and the menstrual pattern.

Intrauterine adhesions are caused by an insult to the endometrium that engenders adhesion of the myometrium to the opposing uterine wall. The most common antecedent event is uterine curettage to the vulnerable gravid uterus. Adhesion formation is noted in 7% to 30% of patients undergoing hysteroscopic examination after D&C for spontaneous abortion (77–79). Uterine infection can also cause intrauterine adhesions, particularly genital tuberculosis, which is associated with uterine cavity obliteration in over half of cases (80).

The prevalence rate of intrauterine adhesions (IUA) in the general population is estimated to be 1.5% (81). The prevalence rate varies with the population studied and the diagnostic modality used. Intrauterine adhesions are identified by saline sonohysterography during the investigation of infertility in 0.3% of women (82). Transvaginal ultrasonography identified IUA in 13.5% of a group of women, some of whom were investigated for primary or secondary infertility and some after three failed IVF attempts. If IUAs are identified by transvaginal ultrasonography the positive and negative predictive values for identifying the IUAs on hysteroscopy are 97% and 71%, suggesting a high correlation between these modalities (83). Hysteroscopy, the gold standard for the diagnosis of IUA, will identify IUA in 3% to 16% of women undergoing hysteroscopy before their first IVF attempt (59, 84). Hysteroscopy identified IUA in 7% to 21.8% of women with recurrent pregnancy loss (85, 86). The use of diagnostic hysteroscopy permits concurrent treatment of IUA in many cases.

The reproductive outcomes of women with IUAs are generally poor. Schenker and Margalioth (87) reported pregnancies in 45% of 292 women with IUA who did not receive treatment before attempting to conceive. Of these pregnancies, 40% ended in spontaneous abortion and another 23% in preterm deliveries.

Intrauterine adhesions have been treated by blind lysis with a curette or other instruments introduced through the cervix. As blind lysis of adhesions can cause trauma to the basal layer of endometrium and may promote adhesion reformation, the current practice is hysteroscopic adhesiolysis. Hysteroscopic adhesiolysis can be performed using the tip of hysteroscopic forceps for blunt dissection, sharp dissection with hysteroscopic scissors, or the use of a knife electrode. Fluoroscopy may enhance the procedure (88), and pressure lavage under ultrasound guidance has also been reported (89).

Although the success of different techniques is uncertain, and many studies fail to present their results according to the severity of the adhesions, it appears that the treatment of IUA improves fertility and reduces subsequent pregnancy loss. The mean term live birth rate of the six published series of hysteroscopic adhesiolysis in infertile women using various techniques is 33%. The rates of first and second trimester pregnancy loss in these series were 11% and 14%, respectively (90). A correlation between the extent of uterine adhesions and subsequent pregnancy outcome following therapy has been observed in the largest study that classified IUAs (91). This study reported a term pregnancy rate of 81.3% among women with mild disease, 66.0% among women with moderate disease, and 31.9% of those with severe disease.

To reduce the chance of recurrent IUA, the use of hormone therapy (estrogen with or without a progestin), intrauterine stents, IUDs, and antibiotics have been advocated. There is no evidence to support the use of these adjuvant measures. Properly designed studies are required to assess the influence of these interventions on recurrent IUAs.

MYOMAS

Uterine myomas or fibroids are a common, benign disease of the uterus. Myomas arise from a single uterine smooth muscle cell, and may grow in any part of the uterus under the influence of local growth factors, cytokines, and sex hormones, including estrogen and progesterone (92, 93).

Most commonly, myomas are asymptomatic masses detected on clinical examination or diagnostic imaging. In a study examining the prevalence of myomas observed at the time of laparoscopic tubal ligation, only one-third of the women who had myomas diagnosed during the procedure had previously been given a diagnosis of myomas, indicating that myomas had either not been detected on previous examinations or that the patients had not reported sufficient symptoms to have been diagnosed (94). This emphasizes the largely asymptomatic nature of uterine myomas.

The prevalence of uterine myomas varies with age, race, and diagnostic modality. In a random sample of US women, aged 35 to 49 years, the cumulative incidence of myomas by the age of 50 was >80% for Black women and approached 70% for White women as diagnosed by review of surgical specimens and/or ultrasonography. Further, African American women are more likely to have multiple myomas and larger myomas (95). The prevalence of myomas observed at the time of laparoscopic tubal ligation was 9% in Caucasian women and 16% in African American women (94).

Three European cohort studies found a lower prevalence of myomas than those examining US populations. A German cohort study found 10.7% of women of mean 40 years of age reported having one or more myomas (96). An Italian cohort study reported a rate of 21.4% among women aged 30 to 60 examined ultrasonographically (97), whereas a Swedish

study found only 7.8% of women between 33 and 40 years of age had ultrasonographically detectable myomas (98).

Although frequently asymptomatic, myomas may be associated with menorrhagia, pelvic pain, bladder and bowel dysfunction from pressure, infertility, and recurrent pregnancy loss. Approximately 5% to 10% of infertile women have at least one myoma, and myomas are the sole etiologic factor in 1% to 2.4% of infertile women (99). There are various potential mechanisms by which myomas could cause infertility. These include chronic endometrial inflammation, abnormal vascularisation, increased uterine contractility, and abnormal local endocrine patterns, all of which may interfere with sperm transport or embryo implantation (99–101).

Myomas may be solitary lesions or multiple lesions peppering the uterus; they may grow in any part of the uterus. Although recognizing that myomas are of variable shape and size, they are loosely classified as submucosal if they distort the uterine cavity, intramural if they reside predominantly within the uterine myometrial wall, and subserosal if they they protrude out of the uterine surface. The number and location of myomas correlates with symptomatology and effect on fertility. There have been no randomized, appropriately powered studies examining the effect of myomas on fertility. Retrospective and case control studies demonstrated that submucosal and intramural myomas that protrude into the endometrial cavity are associated with decreased pregnancy rate (PR) and implantation rate (IR) in patients who attempt to conceive spontaneously or who are undergoing IVF (66, 102–104) and the PR improves after their removal (105–107). It is generally accepted that submucosal myomas decrease fertility, and their removal improves pregnancy rates. The influence of myomas that do not distort the endometrial cavity on spontaneous conception and assisted reproductive technology outcomes remains controversial. Several studies suggest an adverse effect on clinical PR and IR in women undergoing IVF, particularly with large myomas (e.g., >4 cm) (108–114), whereas others fail to show such an association (115–120). It must be noted that only one study was adequately powered to detect a difference in pregnancy rates (120). Given such conflicting results from retrospective, nonrandomized studies it is difficult to determine the effect of myomas that do not distort the uterine cavity on spontaneous pregnancy and IVF treatment associated pregnancy rates.

Nonsurgical measures used to treat symptomatic myomas or used preoperatively to restore normal hemoglobin levels or decrease the size of the tumors are infrequently used in the patient with infertility. GnRH agonist therapy, mifepristone, and uterine artery embolization play a role in decreasing symptoms associated with myomas; however, they are of limited value in the treatment of infertile women, as detailed below.

GnRH agonists induce a hypoestrogenic state, and therefore can reduce myoma volume up to 40% with improvement in symptoms in most women (121–123). Unfortunately, GnRH agonist use is limited by side effects and a decrease in bone density. It is estimated that up to 6% of bone mineral density might be lost in the first 6 months of GnRH therapy. However, the bone loss is restored almost completely 2 years after stopping treatment (124). On the other hand, irreversible loss of bone with pathologic consequences may occur with prolonged (>6 months) treatment (125). The use of estrogen and progestin or raloxifene add-back may mitigate the negative effect of GnRH agonists on bone density (126, 127). GnRH agonists have no role in the management of the infertile patient with myomas, as GnRH agonists suppress ovarian function and myomas regrow after cessation of GnRH-agonist therapy (128).

Mifepristone, a progesterone receptor modulator with primarily antagonistic properties, has been shown to decrease myoma size in several trials (129–131). Mifepristone has been shown to reduce myoma volume from 26% to 74% after 3 or more months of therapy (129). The only randomized, placebo-control trial reported a 47% reduction in uterine volume after 6 months of mifepristone group compared with a 10% increase in the placebo group (131). In the longest reported follow-up of myoma size after mifepristone therapy discontinuation, 18% of women experience myoma regrowth 6 months after discontinuation of therapy (132). Although most women tolerate mifepristone well, adverse effects may include amenorrhea, hot flushes, elevated hepatic enzymes, and endometrial hyperplasia. Amenorrhea occurs in over 90% of women who take mifepristone (129); this is because of disruption of follicular development and inhibition of ovulation (133). For this reason mifepristone has no role in the management of the infertile patient with myomas.

Uterine artery embolization (UAE) involves injection of a sclerosing substance into one or both uterine arteries to embolize the myomas blood supply. Without a proper blood supply it has been shown that myomas decrease in size and the associated symptoms are reduced (134). This procedure is unfortunately not without complication. The acute degenerative process can be painful, and pelvic infection can occur in 1% to 2% of cases. Hysterectomy is necessary after UAE in 1% of women for haemorrhage or severe tissue necrosis (135). Future fertility is uncertain, and up to 5% of women undergoing UAE develop ovarian failure because of inadvertent interference with the ovarian blood supply (134). For these reasons, UAE is not currently recommended for the treatment of myomas in women wishing to preserve or enhance their fertility.

A new technique of myolysis has been reported. Myolysis refers to the technique where an attempt is made to disrupt or abolish the blood supply to the myoma and cause shrinkage using radiofrequency electricity, supercooled cryoprobes, or focused ultrasound (136). At present, the procedure is rarely performed, and is not recommended for women who wish to get pregnant, because there is a significant risk of uterine rupture (137, 138).

MYOMECTOMY

The current management of myomas for fertility preservation or enhancement is surgical removal either by laparotomy,

laparoscopy, or hysteroscopy. The goals of myomectomy include: restoration of uterine morphology, return of normal menstrual function, and enhancement of fertility.

Abdominal Myomectomy

Myomectomy by laparotomy or minilaparotomy incision (abdominal myomectomy) is the technique of choice for women with multiple myomas or a significantly enlarged uterus (i.e., >14 week size or myomas >8 cm) (139, 140). After access to the peritoneal cavity is achieved, the surgeon should evaluate the size, location, and number of myomas present. Conservation of uterine blood supply and minimization of blood loss are priorities. Methods to minimize blood loss are discussed below, but cannot replace good surgical technique. The aim should be to reduce the number of uterine incisions and place them as to enable removal of multiple adjacent myomas. With solitary and large myomas it is best to locate the incision where the overlying myometrium is thinnest.

The uterine incision is carried down through the overlying myometrium into the myoma. The myoma is grasped and traction applied. Using a combination of sharp and blunt dissection the myoma is enucleated from its myometrial bed remaining in the plane of the pseudocapsule. Morcellation of myomas during their removal may help reduce the size of both the uterine and skin incisions required. Major blood vessels should be secured during the dissection process. Closure of the defect left by the myoma is performed in multiple layers, as necessary, to achieve a good closure. Particular care must be taken near the endometrium to prevent entry into the cavity and ensure no suture material is placed within the endometrial cavity that may impede healing of the endometrium in the event the cavity is broached. The serosal edge is carefully approximated, preferably using a continuous subserosal suturing technique.

Complications of abdominal myomectomy can occur intraoperatively or postoperatively. Intraoperative complications include injury to the bowel or urinary tract and blood loss. The volume of blood lost during abdominal myomectomy varies with the size and location of the myomas. Myomas are often surrounded by large, supporting blood vessels that originate in the surrounding myometrium. These vessels should be secured before myoma enucleation as blood loss from these vessels can be significant and may necessitate conversion to hysterectomy. An average blood loss of 540 cc was reported in a review of abdominal myomectomy for uterine sizes exceeding 14 weeks (141). A number of methods have been used to minimize blood loss during surgery. Mechanical techniques including tourniquets and clamps to occlude the uterine and ovarian arteries have been shown to be effective. A randomized trial of 28 women evaluated the use of triple tourniquets applied to both the ovarian and uterine arteries during abdominal myomectomy found significantly less blood loss in the tourniquet group compared with the control group with no tourniquets (difference of 1,870 mL, 95% CI 1,159–2,580, $P<.0001$ (142). The pressure exerted by such tourniquets can damage the uterine artery or its branches and mask inadequate hemostasis that becomes apparent once the tourniquets are removed. Laparoscopic uterine artery occlusion before myomectomy has also been associated with a reduction in intraoperative blood loss; however, the effect on fertility is unknown (143).

Nonmechanical techniques to reduce blood loss during abdominal myomectomy were the subject of a recent Cochrane Library review (144). The review highlights the paucity of randomized data on the use of such techniques. Eight randomized control trials were included: one each on intramyometrial vasopressin, intramyometrial ornipressin, vaginal misoprostol (a prostaglandin E_1 analogue) 400 μg given 1 hour preoperatively, oxytocin 15 units IV over 30 minutes at the start of the uterine incision, pericervical tourniquet, chemical dissection with sodium-2-mercaptoethanesulfonate (mesna), intramyometrial bupivacaine plus epinephrine, and the enucleation of the myoma by morcellation while it is attached to the uterus. A significant reduction in blood loss was observed with misoprostol (−149.00 mL, 95% CI −229.24 to −68.76), vasopressin and analogues (−298.72 mL, 95% CI −593.10 to −4.34), bupivacaine plus epinephrine (−68.60 mL, 95% CI −93.69 to −43.51), and pericervical tourniquet (−1,870.00 mL, 95% CI −2,547.16 to −1,192.84). There was no evidence of effect on blood loss with myoma enucleation by morcellation and oxytocin.

GnRH agonists have been used to minimize blood loss by reducing uterine volume preoperatively. A number of controlled and uncontrolled studies of women with uterine myomas have documented a reduction in uterine volume after treatment with a GnRH agonist. The reported reduction in volume varied between 35 and 65% (145). A Cochrane Library review evaluated the role of pretreatment with GnRH agonists before hysterectomy or myomectomy for uterine myomas (146). The review included 20 randomized, controlled trials that compared GnRH agonists to no pretreatment or placebo. Pre- and postoperative hemoglobin and hematocrit were significantly improved by GnRH analogue therapy before surgery. Uterine volume, myoma volume, intraoperative blood loss, and the need to use a vertical abdominal incision versus a suprapubic transverse incision were all reduced, suggesting that pretreatment with a GnRH agonist (duration of treatment ranged from 2 to 4 months in included studies) before myomectomy is beneficial. There was no statistical difference in operative time. Despite use of one or more of these techniques, 31% of UK gynecologists report the regular need for blood transfusions (147).

A meta-analysis was published in 1998 of pregnancy outcomes following abdominal myomectomy performed for infertility. Of the 23 included trials, only nine were prospective and none were randomized. In 10 of the trials myomas were the only infertility factor identified. Overall, there was a 57% pregnancy rate following abdominal myomectomy (148). Since that time, several others have documented a similar improvement in pregnancy rate after abdominal myomectomy (149–151).

Laparoscopic Myomectomy

Laparoscopic myomectomy requires the same thoughtful approach and principles as abdominal myomectomy as detailed above. The surgical mode of access does not change the technique of myomectomy itself. Following the introduction of the principal trocar and the laparoscope, ancillary ports are placed under direct vision avoiding the epigastric vessels. Pedunculated myomas are excised using bipolar forceps and scissors, or newer coagulating and cutting instruments such as EnSeal® or LigaSure®. Intramural myomas are removed by first incising the uterine serosa with scissors or a monopolar needle. The incision is extended into the myoma. The technique of excising the myoma is similar to the open procedure. The myoma is grasped and traction applied. The myoma is dissected from the surrounding myometrium, taking care to secure hemostasis along the way. Once the myoma has been extracted additional hemostasis is obtained, usually by electrodessication, with minimizing damage to adjacent myometrium. Myomas, especially large ones, may be subdivided to facilitate the enucleation process and reduce the size of the uterine incision. Laparoscopic closure of the myoma cavity uses sutures, in a matter similar to abdominal myomectomy, with the use of laparoscopic instruments. Removal of the myoma from the abdominal cavity may be by a transabdominal or transvaginal route. Transabdominal removal is achieved either by using a laparoscopic morcellator or by extending a port site to accommodate a small myoma or portions of the subdivided larger myoma. Transvaginal removal through a colpotomy avoids the need for port site extension; however, the longer operative time, risk of infection, bowel or ureteral injury, and the need to maintain two surgical sites must be considered (152).

Some have used a combined laparoscopy and laparotomy approach (laparoscopic-assisted myomectomy) in the presence of large intramural myoma. A minilaparotomy incision is performed after the laparoscopic excision of the myoma. The minilaparotomy permits prompt removal of the myoma(s) and effective closure of the uterine defect (153).

In all reported studies fertility is improved after laparoscopic myomectomy. The pregnancy rate appears to vary widely between 20% and 81% (150, 154–157), results that are comparable to those observed after abdominal myomectomy.

Abdominal versus Laparoscopic Myomectomy

The first randomized controlled trial comparing abdominal and laparoscopic myomectomy was published in 1996 (158) found less pain, shorter hospitalization, and shorter recovery with laparoscopic surgery. Two case–control studies also found laparoscopic myomectomy to be associated with less pain and shorter hospitalization; however, operative time was significantly longer in the laparoscopic myomectomy groups, and in one report was associated with greater blood loss (159, 160).

The only randomized comparison of abdominal versus laparoscopic myomectomy for fertility (161) found no significant difference in reproductive outcomes between groups. One hundred thirty-one women were randomized and followed for an average of 32.4 months. Both groups had similar rates of pregnancy, abortion, preterm delivery, and Cesarean section (Table 1). Nonrandomized comparisons have also reported similar pregnancy rates following laparotomy compared with laparoscopic myomectomy (150, 157).

Although the recurrence rate of myomas is difficult to assess precisely, it is estimated that 10% of women will have a clinically significant recurrence 10 years after abdominal myomectomy (162). There appears to be no difference in the rate of recurrent myomas observed by ultrasound at 40 months after laparoscopic or laparotomic myomectomy (163).

The advantages of laparoscopic myomectomy over abdominal myomectomy are: less postoperative pain and analgesic requirements, shorter hospitalization and recovery period, and cosmetically smaller abdominal scars. These are well-recognized advantages of laparoscopic access. Laparoscopic myomectomy is associated with fewer postoperative adhesions peripheral to the site of surgery. Postoperative adhesions, as documented by second-look laparoscopy, are present in 51.1% of patients after laparoscopic myomectomy and 89.6% after laparotomy (140), but the impact of such adhesions on pregnancy rates is unknown. However, laparoscopic myomectomy is not without limitation. Laparoscopic myomectomy is associated with a longer operative time and requires advanced endoscopic skills. Further, laparoscopic removal of large myomas (>8 cm) increases the risk of hemorrhage, the risk of conversion to laparotomy, and operative time and as such is not recommended.

TABLE 1

Pregnancy outcome following laparoscopic and abdominal myomectomy.

	Abdominal myomectomy	Laparoscopic myomectomy
Pregnancy rate (n, %)	33/59 (55.9)	30/56 (53.6)
Abortion rate (%)	12.1	20
Preterm delivery rate (%)	7.4	5
Cesarean section rate (%)	77.8	65
Uterine rupture	0	0

Note: Taken from reference [161].

Taylor. The uterus and fertility. Fertil Steril 2008.

The difficulty associated with the removal of large myomas from the abdomen and concern over the quality of laparoscopic uterine closure has led some to advocate laparoscopy-assisted myomectomy where the dissection is performed by laparoscopy and a small suprapubic incision is made to remove the myoma and close the uterus (153). The use of an isobaric lifting device may obviate the need for laparoscopic guidance and may overcome many of the limitations of the laparoscopic approach.

Isobaric laparoscopy (gasless laparoscopy) was introduced to simplify laparoscopic procedures, but the initial abdominal wall lifting apparatus did not offer adequate exposure of the pelvis (164). A new lifting device, the Laparo Tenser System (Lucini Surgical Concept, Milan, Italy) achieves an intraperitoneal view that is comparable to that obtained with pneumoperitoneum. Access is achieved by insertion of a trocar through an intraumbilical incision after lifting the abdominal wall. Under direct visualization, two lower incisions lateral to the rectus muscles are performed without using trocars. Conventional laparotomy instruments are employed, and the procedure can be performed under regional anaesthesia. Since the first case of gasless laparoscopic myomectomy with abdominal wall lifting was reported in 1996, over 200 such procedures have been reported (164–167). Isobaric laparoscopy combines the advantages of laparoscopy with the ease of abdominal surgery. As more cases are reported its use may expand.

A legitimate concern exists regarding the integrity of the myometrium after myomectomy and particularly the effectiveness of laparoscopic suturing and the subsequent risk of uterine rupture. Fortunately, uterine rupture in associaton with pregnancy is a rare event. Several large prospective studies have observed no cases of uterine rupture (168, 169) or few (170). The risk of uterine rupture hightlights the importance of obtaining proper hemostasis while minimizing damage to the myometrium and obtaining good closure of the myoma cavity.

Vaginal Myomectomy

Vaginal myomectomy was first reported in 1994 to avoid an abdominal incision (171). To perform myomectomy through the vaginal route via colpotomy, women must have adequate vaginal access, good uterine mobility, and a maximum myoma dimension of 11 cm (172). Depending on the location of the myoma, an anterior or posterior colpotomy is made to reach it, the myoma is enucleated, and the uterine wall sutured similar to the technique of laparoscopic or abdominal myomectomy. Myomas that are situated predominantly posteriorly are easier to access, as it is technically simpler to make a posterior colpotomy than an anterior one and because there is more space for uterine manipulation in the posterior pelvic compartment.

As only a few small series have been published, the safety and utility of vaginal myomectomy has not been determined.

Hysteroscopic Myomectomy

Hysteroscopic access has revolutionized and significantly facilitated myomectomy for totally submucous myomas or those with an intramural component.

Submucous myomas are frequently symptomatic and associated with uterine bleeding. Preoperative administration of a GnRH agonist has been shown to reduce preoperative anemia and decrease the size of submucous myomas (146, 173, 174). This type of preoperative treatment may also reduce the surgical time, bleeding, and the volume of distension fluid required, although conflicting results have been reported (175, 176). Preoperative intravaginal misoprostol (a prostaglandin E_1 analogue), in doses from 100 μg to 400 μg per vagina or orally given from 2 to 12 hours preoperatively, improves cervical dilation and reduces the risk of cervical laceration (177).

Hysteroscopic myomectomy is typically performed under general or spinal anaesthesia. The cervix is dilated (e.g., Pratt 29 to 33) and the hysteroresectoscope is advanced transcervically. Pitressin has been shown to decrease intraoperative blood loss, decrease distension fluid absorption, and facilitates cervical dilatation (178). The uterus is distended by the use of an electrolyte free, low viscosity solution such as 1.5% glycine, 3% D-sorbitol, 5% mannitol, and cystosol. However, the recent development of a bipolar hysteroscopic system (VersaPoint®), and bipolar scissors, and the use of a special morcellator to excise submucous myoma allows surgery to be performed in an electrolyte-rich media such as normal saline in selected cases (74). Pressure should be kept below the patient's mean arterial pressure to limit fluid intravasation. Close measurement of inflow and outflow during the operation is imperative. The resection is performed using a wire monopolar or bipolar cutting loop. The loop electrode is passed superior to the myoma to be resected and withdrawn back toward the insulated sheath of the hysteroresectoscope. The myoma is progressively shaved down to the level of the endometrium, until the uterine cavity is normalized or the myoma has been debulked satisfactorily.

Complication rate increases with increasing size and number of myomas. Up to 6.6% of women will experience a complication of hysteroscopic myomectomy that includes hemorrhage, cervical laceration, infection, uterine perforation, or fluid overload. Standard electrosurgical operative hysteroscopy mandates the use of an electrolyte-free, low viscosity solution. These solutions, if absorbed in excessive amounts, lead to dilutional hyponatremia. Long-term morbidity and even death have been reported, making prevention of dilutional hyponatremia critical. Fluid intravasation increases as the intrauterine pressure increases; therefore, the minimum pressure needed to maintain safe visualization should be maintained. The pressure should not exceed the patient's mean arterial blood pressure. Deep resection into the myometrium should also be avoided, as this could lead to opening up large calibre vessels with rapid intravasation. Finally, an automated fluid management system should be used and the procedure terminated if the fluid deficit is $>$1,000 mL to minimize the risk of dilutional hyponatremia.

The treatment of submucous myomas with deep intramural extension is more difficult, and multiple procedures may be necessary for complete resection. As many as 22% will

require a second procedure for incomplete resection or symptom recurrence (179). Myomas recur, as seen by ultrasound, 24 months postoperatively, in 6% of these women (176).

There are no randomized control trials examining fertility after hysteroscopic myomectomy. An observational study of 26 women, 11 with primary infertility and 15 with recurrent pregnancy loss, with a submucous myoma as the only explanation for their diagnosis, reported improved reproductive outcomes after hysteroscopic myomectomy. After a mean postoperative follow-up period of 40 months 81% of women with primary infertility conceived and 63% of those with recurrent pregnancy loss achieved a live birth (180). A similar improvement was observed in an observational study of 59 infertile women with a solitary submucous myoma who underwent hysteroscopic myomectomy (105). This same study also reported the pregnancy rate from all previous studies of hysteroscopic myomectomy, which was 48%. It has been observed that pregnancy rate after hysteroscopic myomectomy increases in direct proportion with increasing myoma size (66, 105). Uterine rupture during pregnancy or labor has never been reported after hysteroscopic myomectomy.

CONCLUSION

In conclusion, successful human reproduction depends upon the complex process of embryo implantation. During implantation the embryo comes into intimate contact with the hormonally primed endometrium. There are numerous prerequisites for successful implantation, one of which is an anatomically normal uterine cavity. Congenital anomalies and acquired diseases of the uterus may interfere with normal implantation and placentation that may lead to infertility and pregnancy loss.

Septate uterus is the most common congenital uterine anomaly. It is usually associated with spontaneous pregnancy loss, but may also impair fertility. The reported rates of pregnancy loss, before and after septum resection in women with otherwise unexplained infertility or recurrent pregnancy loss, provide the current evidence of the benefit of this procedure.

The unicornuate uterus is an uncommon congenital anomaly. Rudimentary horns with functional endometrium may be removed to reduce dysmenorrhea, prevent or reduce endometriosis caused by retrograde menstrual effluent, and avoid a horn or tubal gestation. There is no consensus whether to remove communicating rudimentary horns or horns without functional endometrium. There is no evidence that removal of such rudimentary horns improves fertility outcome.

The bicornuate uterus is a common congenital anomaly and is associated with good reproductive outcomes. Compared with other uterine anomalies uterus didelphys has a relatively good prognosis for achieving pregnancy. Uterine unification procedures are not recommended routinely. Vaginal septa may interfere with fertility and removal should be considered.

A causal relationship between endometrial polyps and infertility is not certain. Their removal prior to embarking on assisted reproductive techniques may be justified, though limited evidence supports this practice.

Evidence from numerous observational studies suggests that intrauterine adhesions may cause infertility. The pregnancy rate after hysteroscopic resection correlates with the severity of adhesions.

A conclusive cause–effect relationship between uterine myomas and fertility and recurrent pregnancy loss requires further investigation. Myomas that distort the uterine cavity, irrespective whether they are submucous or intramural, adversely affect fertility both spontaneous and during IVF treatment. It is essential to use a precise surgical technique when performing a myomectomy not to adversely affect future fertility.

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