MASTER CLASS
Intrauterine Adhesions

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Intrauterine adhesions continue to plague gynecologists and reproductive endocrinologists. Approximately 70 years ago, Asherman and Toaff came out with their landmark paper on patients who present with intrauterine synechiae and amenorrhea: Asherman's syndrome. The scarring can affect not only menstrual flow, but implantation as well, even in the environment of apparently normal menstruation.

When these adhesions are removed, proper care must be taken to minimize damage to the normal intrauterine cavity. Moreover, strategies must be considered to reduce subsequent postoperative adhesions. This is especially problematic because the intrauterine cavity is a pseudospace. The removal of intrauterine synechiae places traumatized tissue against traumatized tissue. This situation would appear to enable subsequent postoperative adhesion formation.

For this Master Class in gynecologic surgery, I have elicited the help of Dr. Charles March. Dr. March spent 30 years in the department of obstetrics and gynecology at the University of Southern California, Los Angeles, where he became professor in 1987. During his tenure there, Dr. March was a prolific writer, especially in the area of operative hysteroscopy, and was the recipient of numerous awards including many resident-teaching awards. In 2000, Dr. March was given a Pioneer in Hysteroscopy award from the American Association of Gynecologic Laparoscopists.

Since 2003, Dr. March has been in private practice, where he specializes in infertility treatment and sees patients from across the country for operative hysteroscopy secondary to intrauterine synechiae. Even so, Dr. March continues to win teaching awards, now as a voluntary faculty member.

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Hysteroscopic Lysis of Intrauterine Adhesions

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Many clinicians view intrauterine adhesions (Asherman's syndrome) as a problem that occurs rarely, and only after a D&C. In fact, Asherman's syndrome is far from being a rare condition, and the types of antecedent factors and their significance are quite different today from what they were only a decade or so ago.

Asherman's syndrome can occur after any type of gynecologic surgery, and we must shift our thinking and heighten our index of suspicion to accommodate the growing body of data that supports this claim.

A literature review published in Fertility and Sterility 15 years ago reported that approximately 90% of all cases of Asherman's syndrome occurred after curettage, mainly after D&C for a spontaneous abortion or one performed to control a postpartum hemorrhage. Although these two antecedent factors remain the most common causes, there has been a significant increase in the number of patients who develop endometrial scarring after gynecologic surgery, particularly following abdominal and hysteroscopic myomectomy.

Women who have had myomectomy or other types of uterine surgery make up an increasing proportion of all patients with adhesion formation and a variant of Asherman's syndrome known as endometrial sclerosis.

Endometrial sclerosis, commonly called an "unstuck Asherman's," is an end-stage disease in which the basalis layer of the endometrium has been severely damaged or even removed. In these women, the hysterosalpingography (HSG) may demonstrate a normal cavity or one of slightly reduced size, but with little or no scarring.

This change presents new challenges because the damage that follows gynecologic surgery other than curettage is a much less curable condition.

Our Index of Suspicion
Key to our role as gynecologists is suspecting the problem. Any change in menstrual flow and pattern—from amenorrhea to any decrease in the duration or amount of bleeding—that follows any type of uterine surgery, irrespective of how minimal that surgery might have been, must prompt us to suspect that this patient may have scarring in her uterus. All patients with a history of intrauterine trauma must be considered at risk.

In addition to endometrial trauma, pregnancy (or recent pregnancy) and hypoestrogenism are important keys. The pregnant or recently pregnant uterus appears to be more vulnerable to scar formation.

Concomitantly, breast-feeding increases the risk of adhesion formation because women who breast-feed remain estrogen deficient. Estrogen has a tremendous effect in promoting the healing of the uterus and regeneration of the endometrium. Women who breastfeed don't have that stimulus.

To a lesser extent, infection also can play a role. Decades ago, infection was viewed as critical, in that it was the "infected abortion" that was thought to cause Asherman's syndrome. Today, infections are an uncommon cause of the problem. I have treated more than 1,000 patients with Asherman's, and fewer than 5 had any clinical evidence of infection around the time of their original surgery. Still, the possibility of Asherman's resulting from infections still exists.

Pelvic tuberculosis by itself, without any surgical trauma, causes scarring in the uterus. Considering the diversity of our society and the rise in antibiotic-resistant TB, we ought to keep it in mind.

It is also important to appreciate the fact that the presence of normal menstrual flow does not rule out the presence of intrauterine adhesions. Approximately three-quarters of women with Asherman's syndrome have amenorrhea or hypomenorrhea, but the remainder have menses of normal flow and duration. Other symptoms of intrauterine adhesions include infertility, recurrent miscarriage, and placenta accreta or its more severe variants.

Methods of Diagnosis
The diagnosis will most frequently be made by either HSG or a saline-infusion sonogram. However, these methods provide us with only a presumptive diagnosis. Both will demonstrate irregular, lacunalike defects spaced throughout the cavity. Access to the oviducts may or may not be blocked. A definitive diagnosis comes only with hysteroscopy.

We should individualize our diagnostic methods depending on the patient's history and symptoms and our own index of suspicion. For instance, a patient who presents with amenorrhea and monthly cramping following a D&C would benefit from a pelvic ultrasound. This study is likely to demonstrate fluid in the uterus. Her hematometra is secondary to outflow tract obstruction. There is no reason in this case to do a saline-infusion sonogram or an HSG. The next appropriate step is hysteroscopy, which will allow the diagnosis to be made with certainty so that treatment can commence.

Consider another patient with postcurettage amenorrhea. She has little or no fluid in the uterus and her endometrium is thin and/or irregular. A pregnancy test is negative and a uterine sound cannot be passed into the cavity. In this case, it is wise to proceed to hysteroscopy because it would not be possible to pass the contrast material for HSG—or the saline for a saline-infusion sonogram—beyond the site that blocked passage of the sound.

Hysteroscopy provides us with absolute proof of intrauterine adhesions. It allows us to directly inspect the uterine cavity and assess the extent, nature, and location of the adhesions. This also allows us to classify the disease, which is critical because classification enables us to make meaningful comparisons among different types of treatment regimens or adjunctive therapies. Finally, adhesiolysis under hysteroscopic guidance is more efficacious and less traumatic to the adjacent normal tissue.

Scissors vs. Heat
Since the introduction of hysteroscopy to treat intrauterine adhesions, the prognosis has gone from dismal to excellent. Hysteroscopic management not only enables us to cut all the scar tissue, but it ensures that we will not damage adjacent normal endometrium. There is no justification today for treating Asherman's syndrome by a technique other than hysteroscopy.

Although comparative studies are not available, we advocate that only scissors be used to cut adhesions, and we use them in our own practice.

Adhesiolysis methods that use a resectoscope, an Nd:YAG laser, or a monopolar or bipolar electrode have their proponents. However, all of these modalities deliver energy to the endometrial surface and can cause further damage to the endometrium. Remember that these same instruments are used to cause endometrial ablation.

Years ago, it was demonstrated that—in contrast to what occurs after a scalpel has been used to make an incision—tissue damage is observed far from the operative site when electrodes or an Nd:YAG laser is used for the same purpose. These energy sources offer no advantage—neither speed nor improved hemostasis (intrauterine scars do not bleed, but myometrium does)—over scissor dissection. In a patient with a damaged endometrium, it is prudent to limit the risk of further injury.

Although I have performed surgery that was not successful, it was not because of the inability of the flexible or semirigid scissors to cut through dense scars.

For women with extensive scarring, we should use simultaneous laparoscopy to reduce the risk of uterine perforation. This group of patients is increasing in relative frequency. The main antecedent factors for severe disease are the postpartum curettage performed 2-4 weeks after delivery, and scarring after myomectomy or metroplasty.

After the cutting of all adhesions under direct vision using hysteroscopy, I advise the placement of a splint into

The Cook balloon uterine stent's triangular shape conforms to the normal uterus.

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the uterus to help reduce adhesion reformation, and the prescription of 1-2 months of high-dose estrogen treatment to promote healing of the tissue and overgrowth of the endometrium.

We use the Cook balloon uterine stent, which has a triangular shape and therefore conforms to the shape of the normal uterus. (See photo, page 36.) This configuration allows it to reduce the risk of reformation of adhesions that had been along the margins of the cavity.

If the adhesions are limited to the endocervical canal and lower uterine segment, a Foley catheter is used as a stent instead of the Cook device because the former has a much wider diameter.

If a Foley catheter is used, the portion distal to the balloon is removed prior to insertion. After insertion of the Foley and inflation of its balloon, ligatures of No. 1 silk are placed around the catheter close to the cervix. This step keeps the balloon inflated and allows the trailing edge to be removed, thereby reducing patient discomfort.

The stent remains in place for 5 days to 3 weeks, depending on the type of stent used and the location and density of the adhesions. During the time that the stent is in situ, a broad-spectrum antibiotic is prescribed.

Following surgery, high-dose estrogen therapy (usually 3-4 mg of micronized oral estradiol) is prescribed for 30-60 days in order to maximally stimulate the endometrium, especially those areas under and adjacent to the adhesions. On the last 5 days of estrogen treatment, 10 mg of medroxyprogesterone acetate is added.

After the menstrual period that follows cessation of the estrogen-progestin treatment, we must perform HSG, hysteroscopy, or a saline-infusion sonogram to assess thoroughly the structure and configuration of the uterus. The last step in postoperative surveillance is a midcycle ultrasound to check endometrial growth and development.

The importance of verifying the normalcy of the uterine cavity and the complete resolution of adhesions before permitting conception cannot be overemphasized. The prognosis for the patient whose problem has been only partially solved is not good.

Variable Success, Mitigating Risks

The rates of cure of Asherman's syndrome vary dramatically according to the antecedent factors involved. In women with Asherman's syndrome that occurs after a D&C for a first-trimester abortion, whether spontaneous or induced, we can achieve a 98% structural success rate (normal follow-up HSG and ultrasound). This rate drops to 50% for Asherman's that occurs after a D&C for postpartum hemorrhage that is performed 2-4 weeks after delivery. The success rate drops further—to 20%—for treatment of scarring that follows myomectomy.

The low success rate of treatment for Asherman's af-ter myomectomy is especially disconcerting because these cases make up an increasing proportion of all those with intrauterine adhesions that we see today. As women delay childbearing, there are more who will develop myomas prior to seeking their first pregnancy at an age older than 35 years.

If one or more myomas were removed because of symptoms, or to improve the likelihood of a successful pregnancy, then attempts to achieve a successful implantation may be stymied by the resultant scarring.

The key to increasing the cure rates for postmyomectomy Asherman's syndrome—and to reducing the incidence and severity of postmyomectomy scarring—could lie in the approach to fibroid removal.

The best approach for a woman who may want to become pregnant in the future, and who has a myoma that occupies a fair amount of the endometrial surface, may be to extract it abdominally. This approach provides a better chance of sparing the endometrium because the fibroid can often be "peeled" away from the endometrial surface, thereby maintaining the basalis layer within the outer layer of the myoma's capsule.

If the hysteroscopic approach is used, all of the endometrium over the surface of the myoma will be removed in order to extract the tumor.

The European Society of Hysteroscopy's classification of myomas is a helpful guide to plan the ideal route of surgery based on the extent of the intracavitary component. I have found this system—coupled with the size and location of the tumor (or tumors) and the patient's desire for future fertility—to be very useful in planning the ideal surgical approach.

We also should be extremely selective in our use of GnRH agonists. These agents allow anemia to be reversed, cause endometrial atrophy, and can make myomectomy easier to perform. However, the atrophic, estrogen-depleted endometrium may be more prone to adhesion formation.

To prevent intrauterine scarring following a D&C performed for postpartum hemorrhage 2-4 weeks after delivery, when the uterus is most vulnerable to scarring, I would propose to the patient that she not breast-feed, that a splint be placed in her uterus, and that she receive estrogen therapy. Although there are no studies on the efficacy of this prophylactic approach, these measures may help prevent the development of intrauterine adhesions, which are quite difficult to cure.

Administering prophylactic antibiotics at the time of D&C is a common practice and may help prevent subclinical infection. For the pregnancy loss that occurs very early in gestation, medical rather than surgical termination may be considered as a method of reducing the risk of scar formation. If curettage is necessary, it is advisable to perform surgery shortly after the fetal demise has been diagnosed. Curettage performed long after fetal demise is associated with a higher risk of scar formation, probably because some degree of fibrosis has begun.

Subsequent Pregnancy

The overall pregnancy rate after successful treatment for intrauterine adhesions is approximately 75%. (Other causes of infertility prevent us from reaching 100%.) In patients who conceive, approximately 85% of the pregnancies are successful. During pregnancy, there are several potential complications that must be anticipated in patients who have been treated for Asherman's syndrome. One is an incompetent cervix. These patients often have had many cervical dilatations because of curettages and hysteroscopies before becoming pregnant. An ultrasound can be used to assess the shortening of the cervix and any funneling of the membranes.

We must also consider the possibility of placenta accreta, which can be easily diagnosed with either high-resolution ultrasound or MRI in late pregnancy.

The advantages of suspecting the problem are several. For example, a patient can bank her own blood because placenta accreta can be associated with significant blood loss at delivery, and she can plan the timing and/or site of her delivery to optimize hospital resources and ensure access to a large amount of blood products and consultants from various specialties.

Even if the placenta appears to have been delivered complete and intact, uterine exploration is advised to verify that there are no retained fragments. Placenta accreta occurs significantly more often in patients who become pregnant with only partially treated Asherman's syndrome than in patients whose uterine cavity is normal. The successful-pregnancy rate in patients with incompletely resolved intrauterine adhesions is only 20%, and 18%-28% of these patients will have placental complications.

This means that once a diagnosis of intrauterine adhesions has been made, the patient should be offered therapy if she wishes to conceive. The recommendation to "try to conceive and see how it works" is a recipe for a bad outcome.

About 20% of my patients have needed more than one procedure in order to restore the cavity to normalcy. The second—or, rarely, even a fifth—procedure may be considered extreme if the postoperative HSG and ultrasound that followed a prior hysteroscopic adhesiolysis were "pretty normal." However, the poor outcome in those with partially treated disease speaks volumes, especially in women who are older and are less fertile than in the past.

An important resource for patients with this condition is Asherman's Syndrome International, which is accessible at http://groups.yahoo.com/group/Ashermans. ∎

Ovarian Endometriomas May Predict More, Deeper Lesions

L A S V E G A S — The presence of ovarian endometriomas indicates severe disease in endometriosis patients with lesions of the ureter, intestine, or vagina, based on data from 500 women presented at the annual meeting of the American Association of Gynecologic Laparoscopists.

Although previous research suggests that endometriosis in general is exacerbated by estrogen, the relationship between ovarian endometriomas in particular and the number and location of endometrial lesions has not been widely studied.

To evaluate the association between ovarian endometriomas and disease severity, Dr. Charles Chapron of Université René Descartes, Paris, and his colleagues conducted a retrospective study of women who had surgery for deep infiltrating endometriosis between 1992 and 2000 and a prospective study of patients who had surgery for deep infiltrating endometriosis between 2001 and 2005.

Overall, 924 lesions were histologically confirmed, and they included 463 (50%) uterosacral lesions, 219 (24%) intestinal lesions, 167 (18%) vaginal lesions, 56 bladder lesions (6%), and 19 (2%) ureter lesions.

Patients who had ovarian endometriomas were nearly four times as likely to have more lesions and deeper lesions in the intestine and ureter and nearly twice as likely to have more lesions and deeper lesions in the vagina, compared with patients without ovarian endometriomas, Dr. Chapron reported.

But the presence of uterosacral lesions, which accounted for half of the total number of lesions found, did not appear to be associated with the presence of an ovarian endometrioma, he noted.

—Heidi Splete

Gynecologic Surgeons Urged to Seek Cystoscopy Privileges for Final Check

S A N F R A N C I S C O — Gynecologic surgeons should seek cystoscopy privileges so that they can conclude operations with a routine check for iatrogenic injuries to the ureter, according to speakers at a conference sponsored by the Society of Gynecologic Surgeons.

Dr. Michael P. Aronson said studies comparing gynecologic operations completed with cystoscopy to similar operations completed without cystoscopy have shown that universal cystoscopy can reduce bladder injuries by a 6:1 ratio. "We have probably always been creating these injuries and not been aware of them," said Dr. Aronson, director of Women's Health Services at the University of Massachusetts Medical Center in Worcester, Mass.

Ureter injuries are usually easy to repair while the patient is still in the oper-ating room, he added, but they can cause loss of renal function if not detected.

At one time or another most experienced surgeons have accidentally injured a ureter during a gynecologic procedure, agreed Dr. John O. L. De Lancey, director of pelvic floor research at the University of Michigan in Ann Arbor. "If you looked and checked, at least you have done everything you can do," he said.

Sometimes urologists will object to the granting of cystoscopy privileges to gynecologic surgeons, warned Dr. Kris Strohbehn, director of the division of urogynecology/reconstruction at Dartmouth Medical School, Hanover, N.H. "Emphasize to them that this is for everybody's benefit," he said; they will not want to be called repeatedly to the operating room.

—Jane Salodof MacNeil