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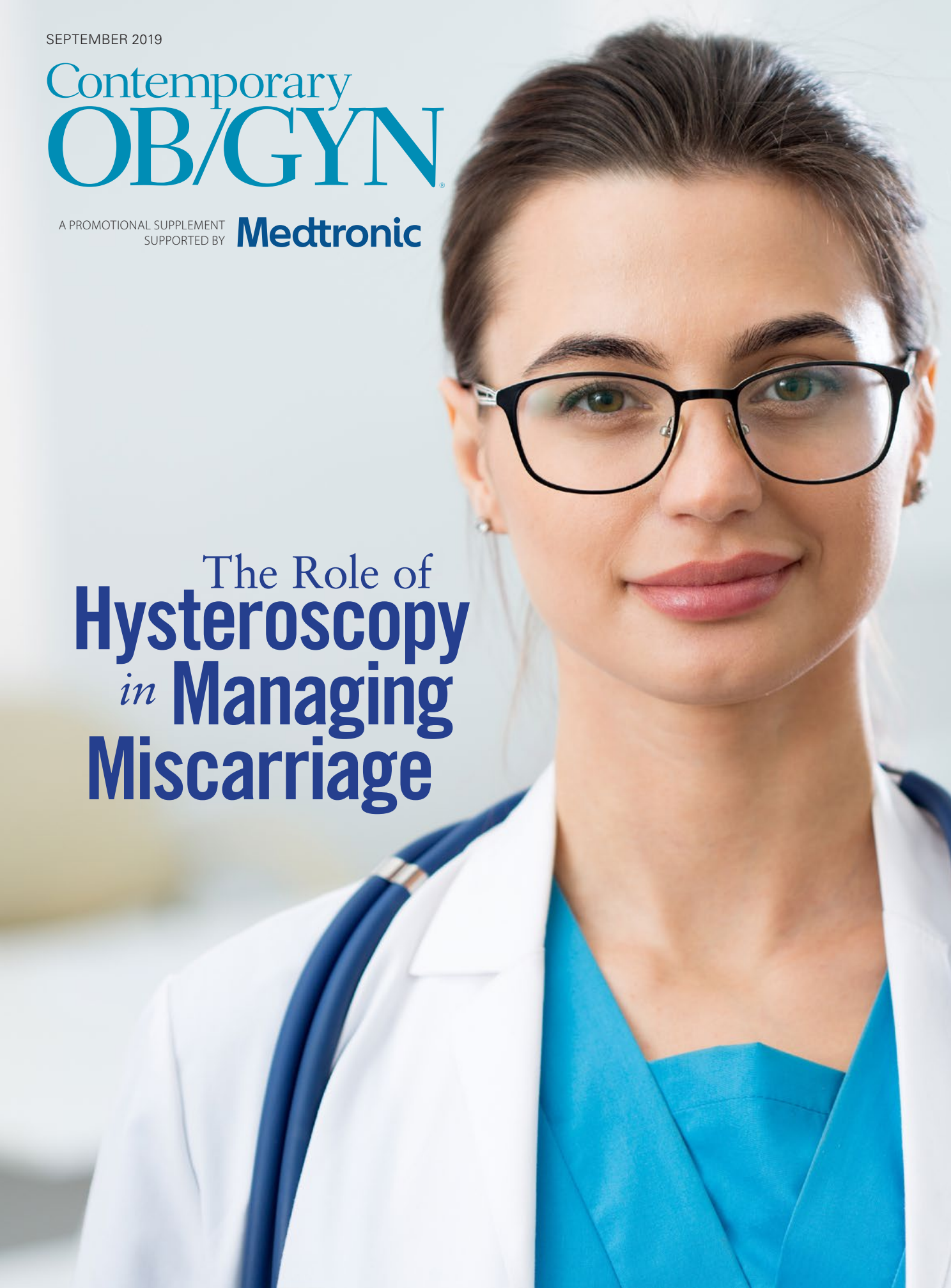
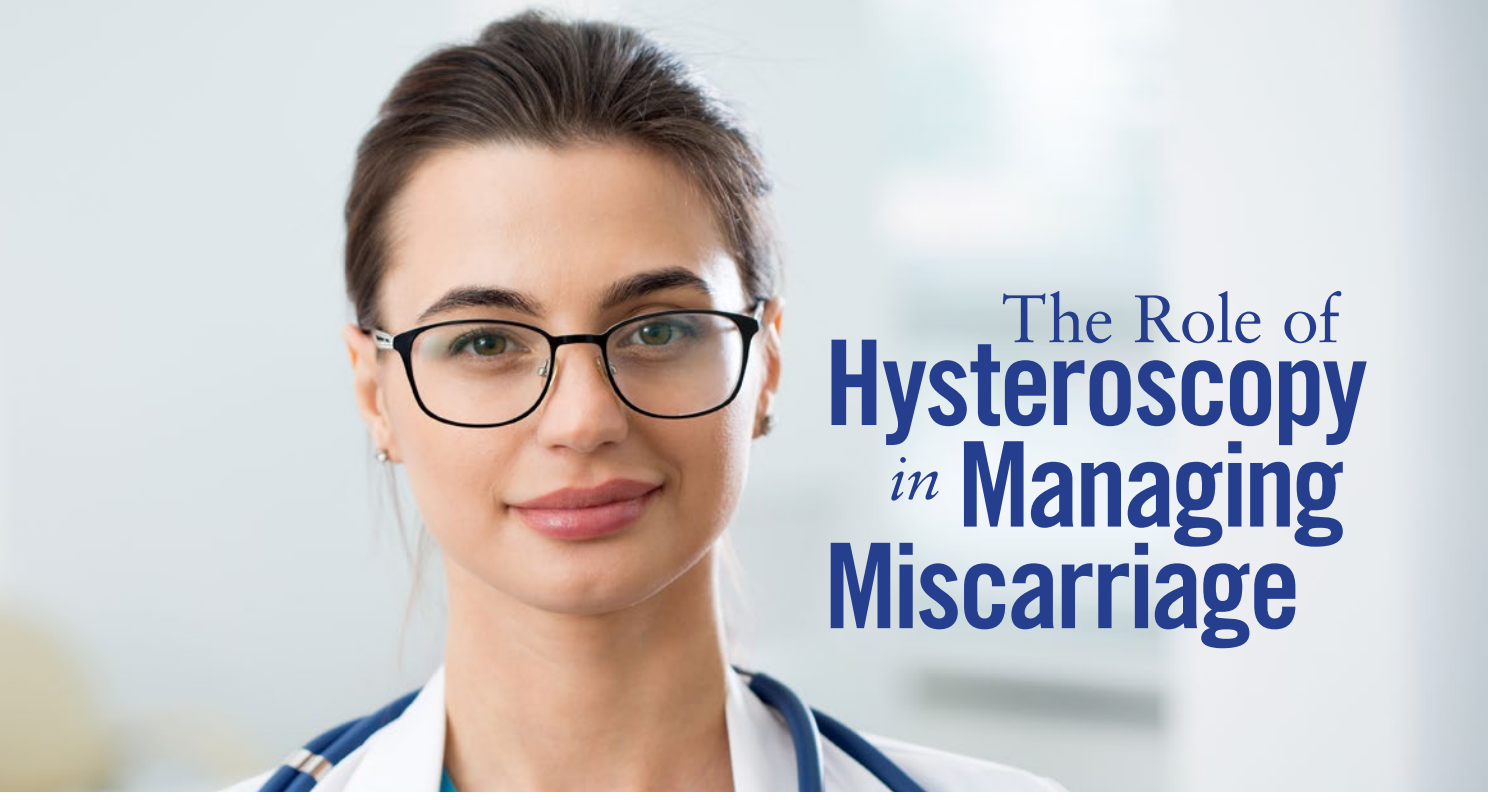


The Role of Hysteroscopy *in* Managing Miscarriage

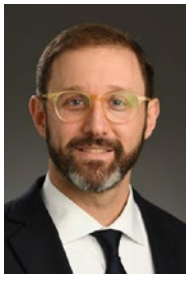


The Role of Hysteroscopy *in* Managing Miscarriage

Panelists

Aaron K. Styer, MD, is a board-certified reproductive endocrinologist, founding partner, and medical director of CCRM Boston in Chestnut Hill, MA. He is also a staff physician at Beth Israel Deaconess Medical Center and is an associate professor of obstetrics, gynecology, and reproductive biology at Harvard Medical School. Dr. Styer is nationally recognized for his expertise in elective single embryo transfer, predictors of IVF success, LGBTQ family building, egg donation, and fertility outcomes in women with uterine fibroids and endometriosis. Dr. Styer is active in patient outcomes research and education. He serves on several national committees in reproductive medicine, including the Society for Assisted Reproductive Technology Clinical Online Reporting System research committee, and is an active member of the Patient Education Committee of the American Society for Reproductive Medicine.

Zev Williams, MD, PhD, is chief of the Division of Reproductive Endocrinology and Infertility and the Wendy D. Havens Associate Professor of Women's Health at Columbia University Irving Medical Center in New York, NY. A nationally recognized clinician and researcher in the area of recurrent pregnancy loss and infertility, Dr. Williams leads the Columbia University Fertility Center. While at Albert Einstein College of Medicine in New York, Dr. Williams established the Program for Early and Recurrent Pregnancy Loss (PEARL), which involves a clinical care site focused on a multidisciplinary approach to preventing recurrent miscarriage as well as a basic/translational research program. The PEARL program focuses on public education surrounding pregnancy loss, including webinars, public lectures, online informational videos, and online blogs.



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AARON STYER, MD, has a financial affiliation with Medtronic (consultant).

ZEV WILLIAMS, MD, PHD, has a financial affiliation with Medtronic (consultant).

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IN TODAY'S SOCIETY, approximately 15% to 25% of pregnancies will end in miscarriage.[1] Miscarriages can occur for a variety of reasons, including genetic abnormalities, medical conditions, and lifestyle choices (Table). Recurrent pregnancy loss, meaning miscarriages in two or more pregnancies, is less common, but still represents approximately 5% of all miscarriages.[1]

While determining the cause of any miscarriage is important, it is especially vital in women with recurrent pregnancy loss who remain interested in future conception. In this supplement, two experts in the management of miscarriage discuss the steps they take to uncover the underlying cause of recurrent pregnancy loss and the importance of hysteroscopy in finding the answers physicians and patients need.

TABLE Common Causes of Recurrent Pregnancy Loss[1]

Cytogenetic	Male factors
Antiphospholipid syndrome	Psychologic
Hormonal or metabolic	Alloimmune
Environmental, occupational, or personal habits	Anatomic
	Infectious

Miscarriage in today's society

***Moderator:* How do the majority of women end up in your practice following miscarriage?**

Aaron Styer, MD: The most common means by which women come to my practice after miscarriage include referral from their ob/gyn or through an Internet search of fertility specialists who have expertise in managing recurrent pregnancy loss. Many patients are referred by word of mouth from the community as well. These women are typically referred to me by former or current patients.

Zev Williams, MD, PhD: The patients I see are typically those who have had a fair number of pregnancy losses for which the underlying etiology is unknown. The work that we do here focuses on trying to understand these really challenging cases of unexplained pregnancy loss, to figure out why they've been happening, and then put together a plan to help prevent them in the future.

***Moderator:* At what point do you recommend to your colleagues that they send challenging cases to a specialist like yourself?**

Dr. Williams: There are high-quality standard protocols that both the American Society for Reproductive Medicine and the American College of Obstetricians and Gynecologists have put out for the basic evaluation of a pregnancy loss.[1,2] When that basic approach fails to identify the cause, that's typically when it's helpful to look at a deeper level for possible underlying causes.

I have seen patients for the first time who have had more than six miscarriages, although I would typically recommend referring patients with approximately three losses to a specialist when the initial workup fails to identify a cause.

Dr. Styer: Most frequently, colleagues will wait to refer their patients to me until two or more miscarriages have occurred. Some providers will refer earlier due to a specific patient request, if a patient has suffered a miscarriage in later stages of the first or second trimester of pregnancy, or if the patient is older than age 40 years and has diminished ovarian reserve.

Managing missed miscarriage

***Moderator:* When you have a woman who arrives in your office after a missed miscarriage, or multiple missed miscarriages, what does your initial workup look like? What is included within the evaluation?**

Dr. Styer: Prior to diagnostic testing, the initial step is to ensure that the miscarriage has resolved and that all products of conception (POC) have been passed. This is usually confirmed by the patient's referring ob/gyn or provider. During initial consultation, I also review the typical causes of miscarriage, discuss our approach for testing, and review the possible limitations of testing.

Initial testing will determine the karyotype of the patient and her partner (if she has a male partner) and will evaluate autoimmune and clotting factors. An essential step is to evaluate the endometrial cavity with hysteroscopy to ensure that the uterine cavity has healed appropriately and that there are no retained products of conception (RPOC). Concurrently, an endometrial biopsy is performed to exclude chronic endometritis.

Dr. Williams: In order for a pregnancy to succeed, a remarkable number of processes have to happen correctly. Perturbation or an abnormality during any of these processes can result in pregnancy loss and perhaps recurrent pregnancy loss.

When a new patient comes to our practice, our approach is to very systematically look at all the different steps that have to go right, to try to identify where the problem lies, and then to target the intervention to correct that problem. With the advances we've seen in terms of understanding the causes of pregnancy loss and the tools we have available to help identify those causes, we are currently able to determine the cause of pregnancy loss in approximately 90% of all cases. That's a big improvement from a decade or so ago, when close to half of all cases of pregnancy loss were unexplained.

***Moderator:* What are the primary treatment options available to women with a missed miscarriage?**

Dr. Williams: In women with a missed miscarriage, frequently called a missed abortion, they are typically offered the initial choice of expectant versus medical versus surgical management in my practice. Surgical management can involve either manual vacuum aspiration, which does not require anesthesia, or a traditional suction dilation and curettage (D&C), which does. In cases in which there is a concern for the presence of adhesions, a hysteroscopically targeted removal of the gestational sac may be warranted.

One of the key factors when evaluating pregnancy loss is to determine if the loss is due to genetic factors or something else. If there is a clear genetic anomaly that is the overriding determinant, it's critically important to obtain a sample from the pregnancy loss POC. While it is possible to obtain POC from miscarriage tissue that passes spontaneously or after medical intervention, there is a much higher likelihood of successfully obtaining POC through a surgical intervention. That is a key consideration when discussing treatment options.

Dr. Styer: From my perspective, the medical management of miscarriages with misoprostol and/or mifepristone is utilized more commonly than in prior years. However, I have seen similar rates of RPOC among patients undergoing medical treatment versus surgical treatment with D&C. As a result, I use the same approach of diagnostic office hysteroscopy for referred patients treated with either option.

Hysteroscopy in miscarriage

***Moderator:* When is hysteroscopy indicated following miscarriage?**

Dr. Williams: Hysteroscopy is a tool that can give us additional useful information. For example, if there's a concern that a patient has a uterine septum that may not have been resected, hysteroscopy allows you to determine exactly where the embryo implanted. There is also a role for hysteroscopy to help identify gross morphologic abnormalities that may point to a genetic basis for the miscarriage that can't be readily detected with traditional approaches. Finally, in cases in which a patient has a history of RPOC or adhesion development, removing the gestational sac under direct visualization may offer benefit.

Dr. Styer: Routine pelvic ultrasound or sonohysterogram does not provide the same level of optimal detection of RPOC compared to direct visualization that is standard with office hysteroscopy. In my fertility practice, the clinical goal is always to optimize the chance of implantation prior to beginning fertility treatment. To this end, initial hysteroscopy as part of the evaluation of the uterine cavity following pregnancy loss is ideal to ensure that we exclude all barriers to future pregnancy success.

***Moderator:* Specifically, in women with RPOC, why is a hysteroscopically-guided procedure potentially a better treatment option than a blind or ultrasound-guided D&C?**

Dr. Williams: The concern with suction D&C is that, when it's done without direct visualization, there can be either too much tissue removed that results in adhesions or too little tissue left behind that does not pass spontaneously and leaves a woman at higher risk of subsequent pregnancy loss.

The advantage of a hysteroscopically-guided procedure is that it allows you to remove tissue under direct visualization so you can be more confident that you have removed all of the RPOC. Suction D&C can result in incomplete resection of the tissue and uterine adhesions.[5]

***Moderator:* How commonly will women who have had a previous D&C following one or more miscarriages be referred to your practice?**

Dr. Styer: I would estimate that about 50% of the women referred to my practice have had a D&C, while the remainder have been treated by medical management. That treatment choice can be driven by a variety of factors, including patient characteristics and preferences, patient history, as well as the experience and preference of the treating ob/gyn.

***Moderator:* Are there any potential advantages of a suction D&C compared to a hysteroscopically-guided procedure in women with RPOC after miscarriage?**

Dr. Styer: In my opinion, there are no obvious advantages of suction D&C compared to hysteroscopic removal of RPOC. The risks of damage to the uterine lining following a D&C are increased compared to a hysteroscopic approach.[3] Especially for women who wish to conceive in the future, minimizing inadvertent damage to the endometrium is a primary goal.

Genetic testing following miscarriage

***Moderator:* When is genetic testing indicated following miscarriage?**

Dr. Styer: Genetic testing assists in determining if a patient and couple have a normal complement of chromosomes. In approximately 70% of cases, sporadic pregnancy loss is due to an abnormal chromosomal makeup of the embryo/fetus.[4] Consequently, it is essential during the initial workup to first determine if the parents have any karyotypic abnormalities. If this testing is normal, genetic testing of the POC may detect genetic abnormalities.

Tissue samples are typically obtained by sampling POC after a D&C or hysteroscopically-guided procedure. Once tissue is removed, it can be sent for cytogenetic/karyotyping evaluation or gene array analysis. Gene array analysis has been recently implemented in clinical practice and most accurately detects genetic abnormalities in POC.

Dr. Williams: One of the great advances that has happened in recent years is the ability to do direct testing on DNA from POC. That avoids the need to have to culture fetal cells. Culturing fetal cells was often a problem because the cells that were collected would sometimes turn out to be maternal cells instead of fetal cells, or the tissue would not be of sufficient quality to culture any fetal cells. Now that we can extract DNA directly from POC, we have a much higher likelihood of getting genetic information and answers following a pregnancy loss.

***Moderator:* Do you typically order genetic testing in all of the women who come into your practice following a miscarriage?**

Dr. Williams: Yes, but remember that the majority of my patients are women who have had multiple cases of pregnancy loss. Nonetheless, my personal feeling is that genetic testing may be helpful even after a first or second loss. There is often a tremendous sense of self-blame and guilt among women who suffer a pregnancy loss, even though we know that most cases are due to genetic anomalies and have nothing to do with anything the woman did wrong. It's quite common that the couple will blame themselves for the loss. Being able to present them with genetic information showing that the fetus was abnormal at the moment of fertilization and was never destined to become a healthy delivery can bring a sense of closure and relief to the couple.

Choosing a hysteroscope for your practice

***Moderator:* What is your hysteroscopic resection device of choice, and why is that your preference?**

Dr. Williams: I use the TruClear™ system by Medtronic. It allows me to get excellent visualization of the uterine cavity while simultaneously removing and extracting tissue. That allows me to avoid having to enter and exit the uterine cavity multiple times to remove the full tissue, which not only keeps operating time down but also reduces the risk of introducing an infection into the uterus. For smaller uterine lesions and polyps, I'll often go in hysteroscopically and use the TruClearTM system as a resection device to manually remove tissue.

Dr. Styer: I also use the TruClear™ system for multiple clinical indications. I prefer to use this system due to the ease of setup, in either the office or the operating room, for our staff. From the patient perspective, the size of the hysteroscope is small enough that there is minimal need to dilate the cervix.

The ability to directly visualize and quickly resect tissue/pathology with the TruClear™ system is excellent, especially compared to typical procedures in which scissors or a grasper are used, making it difficult to efficiently remove tissue/pathology in its entirety. Most importantly, the design of the resection blade allows for removal of only the necessary pathology or abnormal tissue and minimizes unnecessary trauma to surrounding normal endometrial tissue.

***Moderator:* Are there any other unique features of the TruClearTM system that you find to be particularly useful?**

Dr. Styer: First, the coupled fluid management system and resection device allow for removal of pathology with concurrent suction of pathology and blood/debris. This provides excellent visualization in the field of resection. Also, the overall efficiency of the TruClear™ system as a resection device facilitates the removal of tissue/pathology quickly and in an atraumatic fashion. The TruClear™ system allows the surgeon to remove pathology without damaging or inadvertently resecting the normal endometrium that is adjacent to the pathology of interest.

Dr. Williams: One other thing I particularly appreciate about the TruClear™ system is that it allows me to enter the uterus without the need for electrocautery.

Key Takeaways

- Following miscarriage, clinicians should ensure that there is complete passage of POC from the intrauterine cavity. Just because a patient's human chorionic gonadotropin levels fall below zero does not necessarily mean that there are not RPOC.
- Particularly in cases of unexplained miscarriage, collecting as much information as possible in terms of the location and appearance of the gestational sac and uterus can be very informative.
- In women with RPOC following suction D&C, a repeat D&C may be a harmful option compared to direct hysteroscopic resection because of the increased risk of intrauterine adhesions.[5]

***Moderator:* For those providers who have little or no experience with a hysteroscope, how would you recommend they go about learning more about the technical aspects of its use?**

Dr. Williams: The evidence is accumulating that in cases of RPOC among women who have had a miscarriage, especially those who have had a previous D&C, there are advantages to being able to directly visualize the tissue at the time of removal. For clinicians interested in learning more about the technical aspects of hysteroscopy, there are videos online that are very good. I'd also encourage them to speak to their colleagues and perhaps observe live cases so that there is a greater comfort level when they are doing procedures on their own. It may even be helpful having an experienced colleague at their side for the first few cases.

Dr. Styer: For the reproductive surgeon committed to operative hysteroscopy, the TruClear™ system is the ideal device for several reasons. The entry into the uterus is very straightforward. And as I mentioned previously, the TruClear™ system allows the surgeon to remove pathology quickly with optimal direct visualization of the uterine cavity.

As with any device clinicians use for the first time, there is a learning curve with the TruClear™ system. The learning curve is not steep, however, and the clinical use of the device is intuitive for either the attending physician or the trainee.

***Moderator:* This has been a terrific discussion. We want to thank both of you for your insights. I hope that our audience is able to take away some helpful information from our discussion to inform their practice's approach to the use of hysteroscopy in the management of miscarriage.**

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