

Performing IUI In The Office Setting

Intrauterine insemination is at the forefront of many Ob/Gyns' efforts to move beyond evaluating infertility to treating the condition. In this article, the authors detail patient selection, procedural protocols, success rates, and more for this increasingly common component of gynecologists' office-based care.

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Several factors have converged in recent years to encourage Ob/Gyns to extend their fertility care beyond the basic workup to provision of first-line therapies.

Those factors include many physicians' desire to reduce their obstetric caseloads in favor of office-based services, and managed care contracts that effectively discourage referrals. Further, many fertility patients would rather receive care from their long-time Ob/Gyn than from a reproductive endocrinologist at a referral center, and the development of new, straightforward fertility technologies has made it relatively easy for gynecologists to accommodate those patient preferences.

Perhaps the most striking manifestation of this trend is that many Ob/Gyns now perform intrauterine insemination (IUI) in the office setting. Should you join their ranks? Let's look at what's entailed in providing IUI and examine the benefits and drawbacks of adding this procedure to the care an Ob/Gyn provides.

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The appeal of IUI

For properly selected patients, IUI offers pregnancy rates comparable to those achieved by in vitro fertilization (IVF) and other assisted reproductive technologies (ARTs) that are far more costly and involved.¹ Meanwhile, fees for IUI range from \$250 to \$1,000 per cycle, compared to IVF fees ranging between \$10,000 and \$12,000. Further, we've found that third-party payers generally will cover IUI (which is reported with CPT code 58322), while securing reimbursement for IVF can be difficult, or impossible, in certain states and with particular insurers and managed care plans.

IUI carries essentially the same risks of antenatal and perinatal complications as pregnancies resulting from normal sexual intercourse. In a 1999 study of perinatal outcomes, the incidence of preterm delivery, low birth weight, low Apgar scores, and need for neonatal care among IUI-induced pregnancies was similar to that of pregnancies resulting from regular intercourse and from IVF.² Also, the risk of spontaneous abortion is no greater after IUI than it is after normal intercourse if the insemination is performed properly.

In terms of the appeal the procedure holds for clinicians, no specific laboratory certification is required to offer IUI in the office setting. Also, many of the sperm-preparation devices used to facilitate insemination are exempt from CLIA and other governmental regulations, although some

third-party payers might require inspection certification.

Still, the decision to offer IUI should not be made lightly. Ob/Gyns must commit themselves to staying current with the rapidly changing field of fertility medicine and, in our view, must be willing to perform inseminations on weekends or holidays in order to provide their patients with the optimal chance of conceiving. Most Ob/Gyns already have much of the equipment needed for this type of treatment; a minimal investment might be necessary to purchase semen processing kits, IUI catheters, ovulation prediction kits, and, possibly, a vaginal ultrasound probe for proper ovulation detection.

Most importantly, the physician must be willing to organize his or her practice and staff in a way that allows for proper execution of each step in the IUI protocol. More than most procedures an Ob/Gyn will perform in the office, the success of IUI is very strongly tied to precise adherence to proven methods for everything from preparing the sperm to inseminating the patient. In fact, in a 1997 study of pregnancy rates after IUIs performed at infertility centers, we found that unsuccessful outcomes often were attributable to physician error and a lack of familiarity with the procedure.³

Identifying IUI candidates

IUI is indicated for patients with a cervical factor (cervicitis, cervical stenosis, a severely thickened cervical wall), vaginal anomalies, anti-sperm antibodies in the cervix or uterus, male-factor infertility (which accounts for the inability to conceive in approximately 40% of cases), sexual dysfunction in either partner, immunologically mediated infertility, and unexplained infertility. Roughly 10% of all infertility cases are idiopathic.

In the above-cited cases, IUI may be administered before other ARTs are attempted. IUI is not appropriate for patients with ovarian failure, pelvic disease, or tubal occlusion. Patients

with these complications require other therapies and, in most cases, should be referred to a reproductive endocrinologist.

As with any infertility treatment, a full evaluation of both partners is a prerequisite to therapy. In the case of IUI, it is important to determine that, in addition to the condition that would make a woman a candidate for IUI, she does not have a concomitant condition that would preclude successful insemination.

The IUI protocol

Timing is of the essence when performing IUI. The procedure must be done on the anticipated day of ovulation, or as close to it as possible. For that reason, ovulation management—either through pharmacological intervention or simply by monitoring the patient's menstrual cycle—is crucial to successful insemination.

Detection of the luteinizing hormone (LH) surge via urine analysis remains a standard for gauging the onset of ovulation. (Normal and pre-ovulatory hormone levels are listed on page 82.) Numerous over-the-counter ovulation predictor kits are designed for urinary LH detection at home or in the practice setting. While these kits have an overall accuracy rate of 98%, patients anxious to conceive often misinterpret the results, mistaking a false positive as a sign that ovulation is occurring. For that reason, the Ob/Gyn should double-check the results by running the test in the office.

Effective ultrasound use also is integral to predicting ovulation and to identifying the optimal timing of IUI. We feel strongly that Ob/Gyns should receive additional training in transvaginal ultrasound before offering fertility treatment.

An ultrasound scan is performed to evaluate the number and size of the follicles. The identification of a dominant follicle (which will be approximately 22 mm in diameter) indicates that ovulation is imminent. If a second ultrasound scan the next day reveals that the same follicle has returned to a smaller size, ovulation has occurred.

Sonography also is used to gauge the thickness of the endometrium. A thickness of 8 mm is required for proper implantation. An overly thick (between 12 mm and 14 mm) or thin (less than 8 mm) endometrium can be corrected with hormone therapy. An inadequate endometrium often



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indicates the existence of other reproductive problems that must be corrected before IUI is attempted.

If thickened cervical mucus is detected, use of the expectorant guaifenesin may be advised to stimulate the production of thinner, more abundant mucus.

We have found that use of an ovulation induction agent-clomiphene citrate, human chorionic gonadotropin (hCG), or human menopausal gonadotropin (hMG)-increases the success rate for IUI by 10%. We must stress, however, that these agents should never be prescribed when the cause of infertility is unknown; they should be reserved for clearly identified cases of ovulatory problems.

Clomiphene citrate usually is the first-line ovulation-induction agent. We typically start patients on 50 mg b.i.d. and increase the dosage to 100 mg b.i.d. if basal body temperature charts and other means of assessment, such as sonography, fail to demonstrate a response to the medication. It also is important to assess the cervical mucus of patients receiving clomiphene therapy. Clomiphene has been shown to bring about a thickening of that mucus and so has the paradoxical effect of making insemination more difficult.

If the patient does not respond to clomiphene, use of injectables (follitropin beta, menotropins, or others) may be necessary to initiate ovulation for the next cycle. This might necessitate referring the patient to a reproductive endocrinologist for administration and hormonal (estradiol) monitoring of ovulation.

If administered correctly, superovulation agents carry only the normal risk of multiple gestation. Twin, triplet, or higher-order gestations resulting from ovulation induction invariably can be attributed to hyperstimulation due to improper use of these agents, either through physician error or the patient's disregard for instructions on how to use the medication. So in addition to monitoring the patient for negative effects, it is important to impress upon her and her partner the need to follow directions exactly when taking fertility agents.

Proper sperm processing is crucial to successful insemination, as well. Processing separates the sperm from the seminal fluid so that only fully motile, morphologically valid sperm are placed beyond the cervical mucus. A processed 0.5 mL

specimen should contain between 20 million and 30 million sperm/cc.

Semen processing also is necessary to purify the sperm. With coitus, only "good" sperm can enter the uterus through the cervix. Since the cervix is bypassed during IUI, this process must be replaced by clinical means. Otherwise, introducing sperm along with its seminal agents and factors into the uterus via IUI will trigger contractions of the uterine wall and will result in failed conception or other complications.

Semen samples should be monitored carefully at each insemination for the presence of adequate numbers and quality of sperm. This can be done by viewing the processed specimen under a microscope.

Processing can offset abnormalities identified in the sperm and maximize the chances of a successful outcome. In a 1995 study addressing how sperm morphology affects the efficacy of an IUI-ovulation induction regimen, pregnancy rates were significantly higher among couples with more than 14% normal sperm morphology than among those whose sperm morphology was less than 14% normal.⁴

Once the exclusive function of andrology labs, semen processing also has become more common in the Ob/Gyn's office. Newer, "office-friendly" processing techniques allow the physician to prepare semen without special licensing, equipment, or overhead. In-office semen processing takes anywhere from 30 minutes to 2 hours, depending on which device or method is used.

Because no 2 semen specimens are the same, no single technology will effectively process all specimens. For example, a normal specimen can be processed via "swim-up" or other conventional separation techniques, while a more deficient specimen (e.g., one with 15 million sperm cells/cc with 40% motility) might require processing via centrifugation or other techniques. It therefore makes sense to invest in and utilize several sperm processing technologies, each averaging between \$25 and \$70 in price.

The procedure

Once the sperm sample is processed and the Ob/Gyn has ascertained that ovulation is about to occur, insemination is performed.

Because ovulation occurs between 24 hours and

Normal levels of key reproductive hormones

Hormone evaluation is crucial to successful insemination. The following chart lists key reproductive hormones and the ideal level for each.

HORMONE	NORMAL LEVEL
Luteinizing hormone (LH)	
Follicular phase (day 2 or 3)	<7 mIU/mL
Day of LH surge	>15 mIU/mL
Follicle stimulating hormone (FSH)	
Follicular phase	<13 mIU/mL
Day of LH surge	>15 mIU/mL
Estradiol	
Day of LH surge	>100 pg/mL
Mid-luteal phase (7 days after 0)	>60 pg/mL
Progesterone	
Day of LH surge	<1.5 ng/mL
Mid-luteal phase	>15 ng/mL
Prolactin	
	<25 ng/mL
Free Triiodothyronine (FT₃)	
	1.4-4.4 pg/mL
Free Thyroxine (FT₄)	
	0.8-2.0 ng/dL
Total Testosterone	
	6.0-89 ng/dL
Free Testosterone	
	0.7-3.6 pg/mL
DHEA-S	
	35-430 µg/dL
Androstenedione	
	0.7-3.1 ng/mL

35 hours after the LH surge, the procedure must be performed within that period,⁵ even if that means opening your office and calling the patient in on a Sunday or other inconvenient time.

Some researchers argue that if ovulation occurs on a Sunday, IUI can be performed on a Saturday or Monday without reducing the chance of pregnancy.⁶ We feel strongly, however, that reproductive medicine is an around-the-clock proposition, and that an Ob/Gyn must be available at all times if he or she is serious about helping couples conceive.

Ideally, semen is obtained within an hour of the procedure. Because sperm can lose potency within 24 hours, a fresh specimen must be obtained. The initially viscous semen is allowed to stand for between 15 and 30 minutes to liquefy before processing.

The patient assumes the standard position for a pelvic exam, lying straight and flat on the examination table. To avoid unwanted body curvature, pillows cannot be placed beneath the patient except under her head. If desired, stirrups

can be used to stabilize her feet.

A speculum is used to facilitate introduction of the IUI catheter intracervically and to ensure proper placement of the specimen. The physician should be able to see clearly through the vagina and isolate the exocervix.

Neither a local anesthetic nor antibiotic prophylaxis is needed. The exocervix is cleansed with a sterile pad that has been soaked with saline, Ringer's lactate, or a similar solution. Overall, patient preparation takes about 5 minutes.

A 0.5-cc specimen of sperm processed from the partner's ejaculate is aspirated into the reservoir of an 18-cm polyethylene catheter. The device's outer shaft, roughly 1 mm in diameter, is flexible so as not to traumatize the uterus and to facilitate placement despite an anteflexed or retroflexed uterus.

The catheter is slowly inserted through the vagina and cervix to the fundus. The catheter should extend 5.5 cm into the uterus. (The outer shaft is marked in 1-cm increments.) Insertion should take between 60 and 90 seconds, and must be accomplished in a slow, steady manner to prevent trauma.

The sperm then are injected slowly into the uterine fundus. It is imperative that the injection be very deliberate-taking about 2 minutes to deliver the 0.5-cc specimen. Injecting too briskly and striking the uterine wall will distend the endometrial muscles, leading to cramping or myometrial contractions.

Once the sperm are injected, the catheter is gently removed (this should take about 60 seconds) and the patient instructed to remain lying flat and still for 15 minutes. While theories vary greatly among Ob/Gyns and reproductive endocrinologists, we see no need to elevate the patient's legs to keep the sperm within the uterus. Nor is there risk of sperm discharge after the 15-minute rest period.

If the procedure is performed correctly, the patient should feel no discomfort and should be able to resume her normal activities upon leaving the office. Subsequent sexual intercourse has not been shown to impede fertilization, but we suggest abstinence for 24 hours after insemination just to be safe.

If the dominant follicle is fully ruptured on the day of the insemination and tests show that there

are no sperm deficiencies, we do only 1 insemination per cycle. In all other cases, however, we perform a second insemination between 12 and 24 hours after the first one. Some researchers report no significant difference in pregnancy rates between patients who were inseminated twice within a cycle and those who received only 1 IUI treatment per cycle.^{7,8} However, because sperm loses its fecundity within 24 hours after ejaculation, we opt for a second insemination in about 80% of cases. We have seen an increase of approximately 6% in the procedure's success rate when a second insemination is performed.

Testing for pregnancy is performed 2 weeks after IUI. Testing procedures are no different for an IUI-induced pregnancy than for one that occurs after normal intercourse (an at-home OTC pregnancy test, followed by a confirmatory in-office urine or blood analysis).

We feel that IUI should be administered for a minimum of 3 cycles in order to be effective. Our overall pregnancy rate with the procedure is approximately 25% without superovulation and 35% when superovulation is employed. Those rates reflect a composite of higher and lower etiology-specific rates. If pregnancy has not been induced after the sixth cycle, consider referring the patient to a reproductive endocrinologist for a more aggressive infertility workup and, possibly, IVF or other ARTs.

Finally, Ob/Gyns must understand that time is a factor when treating infertility. Because the patient's "biological clock" ticks with every failed attempt at conception, the physician must develop a clear sense of when to refer her to an infertility specialist to more comprehensively address reproductive difficulties.

Offering IUI requires a commitment of both practice and personal time, but we believe that it also enables the Ob/Gyn to perform an invaluable service while adding a valuable dimension to his or her practice.

Editor's Note: Dr. P.M. Zavos also serves as president of ZDL, Inc., a Lexington-based company that markets sperm-processing kits and other infertility treatment devices.

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