

a pre-filled dose of a bio-adhesive gel—meaning the gel coats and adheres to the vaginal walls. The vaginal gel is the only once daily progesterone that is FDA approved for ART and through weeks 10-12 of pregnancy. The efficacy of this method is well established through many clinical trials. Patients sometimes complain, after multiple days of use, of a waxy build up which is harmless but annoying, and can be cleared by the patient. Progesterone levels reached in the blood with vaginal progesterone can be lower than levels achieved with intramuscular preparations. However, vaginal preparations deliver higher levels of progesterone to the endometrium which is desirable and the pregnancy outcomes are the same.

VAGINAL TABLETS

The newest method for progesterone delivery is a vaginal applicator that delivers an oval tablet to be inserted 2 or 3 times daily. This formulation was recently FDA approved and fertility centers are now gaining experience with this new option. The hope was to deliver progesterone in a patient friendly manner without the vaginal discharge or residue complaint of the other methods. Unfortunately all vaginal methods of progesterone delivery result in some vaginal discharge including this newest formulation.

hCG INJECTIONS

In the past, injections every few days of human Chorionic Gonadotropin (hCG), the same hCG that is used to trigger ovulation, were used to stimulate the body's own progesterone production to support the endometrium in lieu of medicinal progesterone. Since hCG can increase the likelihood of ovarian hyperstimulation in a small subset of patients, it is used less often.

DECIDING WHICH PREPARATION TO USE

The method of administration is usually determined by physician preference as well as availability, patient convenience and price. Absorption and duration of action will vary by the form of progesterone used. Patients can and should discuss the various delivery methods with their physician, any concerns they may have with a particular delivery method, as well their preference for one method over another.

COMMON SIDE EFFECTS

While progesterone is an extremely safe medication and necessary for IVF completion and success, there are several potential side effects such as headaches, constipation, nausea or diarrhea, joint pain, perineal pain, depression, nervousness, sleepiness, decreased libido, breast discomfort or enlargement and excessive urination at night. These side effects discontinue when the medication is stopped.

RESOLVE: The National Infertility Association is the community for women and men diagnosed with infertility. RESOLVE provides a host of resources that empowers the millions of Americans facing infertility to take control of their family-building journey and find resolution.

The mission of RESOLVE is to provide timely, compassionate support and information to people who are experiencing infertility and to increase awareness of infertility issues through public education and advocacy.

RESOLVE is a non-profit, 501(c) (3).

For more information visit the RESOLVE website at resolve.org.

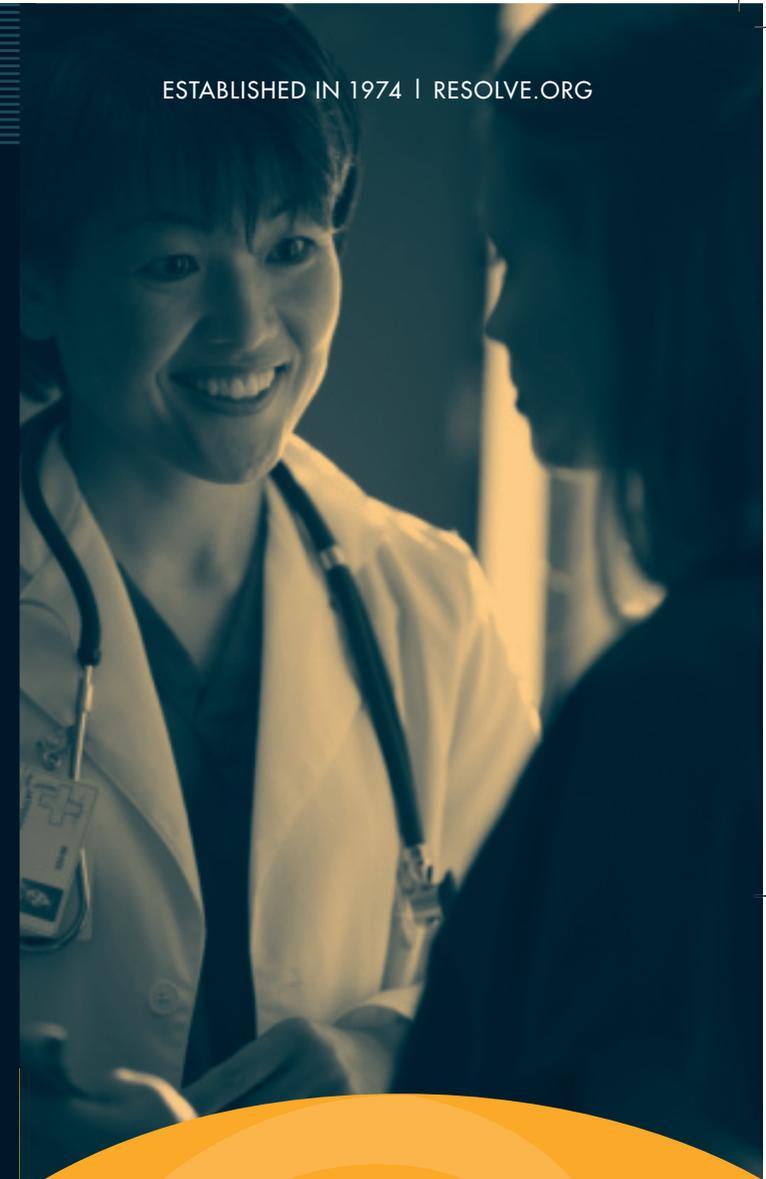
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Progesterone
support in assisted
reproductive
technology



What is Progesterone?

Progesterone, which is naturally produced in the body, is often called the pregnancy hormone. Progesterone is also available as a medication and is universally prescribed with in vitro fertilization (IVF) and other assisted reproductive technology (ART) treatments as it is necessary to achieve and maintain pregnancy. Progesterone thickens the uterine lining (endometrium) and prepares it for implantation of the fertilized egg (embryo). Throughout the first trimester, progesterone supports pregnancy.

THE NORMAL MENSTRUAL CYCLE AND THE ROLE OF PROGESTERONE

A normal menstrual cycle is approximately 28 days. The hormone estrogen plays a primary role during the first half of the cycle—the follicular phase—during which time follicle maturation takes place. The follicle houses the egg and produces estrogen, which is responsible for building up the uterine lining, preparing it to receive the embryo.

The second half of the cycle is known as the luteal phase. During ovulation (at mid cycle) the egg is released from the follicle. After releasing the egg, the follicle transforms into the corpus luteum, and progesterone is released, which maintains the uterine lining necessary for implantation and pregnancy. If implantation and pregnancy occur, the corpus luteum is responsible for producing sufficient progesterone until approximately weeks 8-10 of pregnancy. (At this point the placenta takes over this function.)

MEASURING AND INTERPRETING PROGESTERONE LEVELS

Progesterone levels can be measured by a blood test. A serum or blood progesterone level is expected to rise after a woman ovulates and fall if pregnancy does not occur, triggering the next menstrual cycle.

A serum progesterone level is sometimes ordered to confirm whether ovulation has or has not occurred, however not all reproductive endocrinologists regularly check progesterone levels during ART treatment. In order to correctly interpret serum progesterone levels the physician must know where a woman is in her menstrual cycle. While progesterone levels can detect that ovulation has already occurred, they cannot determine whether a pregnancy will go to term.

WHY PROGESTERONE IS NEEDED IN IVF

Reproductive endocrinologists agree that patients undergoing IVF require luteal phase progesterone support to maximize successful IVF outcome but there are no standards regarding

dose, type of progesterone or length of treatment. There is more than one correct way to use progesterone, therefore some patients undergoing IVF use progesterone only during their luteal phase, to support the endometrium, but discontinue use with their positive pregnancy test. (If pregnancy does not occur, progesterone is stopped automatically.) More commonly, a pregnant IVF patient will usually be prescribed progesterone through weeks 6-12 of pregnancy depending on the physician—there is wide variation in recommended dose and duration. Most often the approach is to add progesterone after egg retrieval and prior to embryo transfer in case the normal production of progesterone was interfered with by the IVF medications or egg retrieval procedure.

Since progesterone is considered safe in pregnancy and because it is difficult to determine who may have an absolute need for progesterone support, most IVF patients are given some form of progesterone support as described below. It should be stressed that the formulations commonly used are “natural progesterone,” meaning they are exactly like the progesterone produced in the body, and should not be confused with synthetic progesterone (called progestin), which is chemically different from natural progesterone.

PROGESTERONE FORMULATIONS

The current prescription progesterone choices deliver progesterone either intramuscularly (via injection), orally or vaginally. The following explains the available options and advantages and disadvantages of each delivery method. There are currently seven ways of prescribing progesterone. From the patient’s perspective, the vaginal route is generally preferred to the injection method. In addition, pharmacies can dispense progesterone formulations from FDA approved manufacturers or they can make their own progesterone drugs for dispensing which are not FDA reviewed, inspected, or approved.

INTRAMUSCULAR

The oldest method for progesterone delivery is intramuscular. This requires that the patient receives daily injections of an oil formulation directly into the muscle. The efficacy of this method is well established and all oil-based preparations deliver progesterone equally well. The chief complaint with this method is pain at the injection site. Occasionally patients display an allergic reaction at the site which in the past was most often due to the use of peanut oil; this is less common today, as non-peanut oils are used more often. Additionally, these injections are difficult to self administer and usually require the assistance of someone else.

ORAL CAPSULES

Reproductive endocrinologists have long been aware of patient complaints regarding intramuscular progesterone injections and have been searching for alternatives for many years. Micronized progesterone, administered through oral capsules, is used for other gynecologic reasons, and has been tried in IVF with mixed results. While very patient friendly, absorption rates are unpredictable, therefore this is an unreliable way to deliver progesterone for IVF cycles. Additionally, the progesterone is processed through the liver which destroys 95% of the progesterone and can cause side effects such as drowsiness and irritability. Although some reproductive endocrinologists prefer this system, it is not as commonly used as other delivery methods.

ORAL CAPSULES DELIVERED VAGINALLY

To overcome the issue of unpredictable absorption, a popular method of administering progesterone is via oral capsules inserted vaginally. It should be noted that the FDA has not approved this use nor have the capsules been formulated for vaginal delivery. Patients are instructed to insert the capsule vaginally up to three times a day. Although inconvenient, patients generally accept this method and the main common complaint is vaginal discharge that contains residue from the capsule. As with all progesterone preparations, it is possible that the patient will develop a vaginal yeast infection. While not serious, this can be annoying. It is possible to use antifungal vaginal cream as long as its use is timed to not coincide with the insertion of the progesterone.

VAGINAL SUPPOSITORIES

Fertility specialty pharmacies have been making vaginal progesterone suppositories in specific doses (compounding) for many years. Because this method of compounding is not regulated by the FDA, the quality of this delivery system cannot be guaranteed. Inserting suppositories vaginally is generally accepted by patients and the only complaint is similar to the complaints associated with the oral capsules, e.g. vaginal discharge mixed with the suppository residue. Again, this is annoying but not harmful, and patients are encouraged to clear the residue periodically to improve their tolerance of this method.

VAGINAL GEL

A popular method of delivery that has been available for over 10 years is a vaginal applicator method that delivers