NORTHWEST CENTER for Reproductive Sciences
The Art and Science of Reproductive Technologies

12333 NE 130th Lane, Suite 220
Kirkland, WA 98034
425-284-4400 phone
425-899-9803 fax

1730 Minor Ave., Suite 150
Seattle, WA 98101
206-262-1101 phone
206-262-1151 fax

www.nwreprosci.com

PROGESTERONE SUPPLEMENTATION PATIENT INFORMATION

Progesterone is an important hormone that is produced by the ovary during the female menstrual cycle. During the first half of a normal cycle, the follicle produces estrogen that causes the uterine lining (endometrium) to proliferate and thicken. Progesterone levels are low during this phase. Just before ovulation occurs, the follicle begins to produce progesterone and the level rises quickly after the egg is released. The follicle, now called a "corpus luteum", will produce progesterone for only two weeks unless stimulated to continue by the early developing embryo. This progesterone prepares the uterine lining (endometrium) for implantation of the embryo. Once implantation has occurred, appropriate levels of progesterone are vital to maintain the pregnancy. During early pregnancy the corpus luteum will continue to release progesterone until the placenta takes over that function, usually at approximately 8-10 weeks gestation. When pregnancy is not achieved, the corpus luteum regresses at the end of the luteal phase (normally around 14 days after ovulation) and menses begins.

Abnormalities of progesterone production can occur either due to inadequate follicle function or to incomplete luteinization of the follicle. In the case of IVF, we suction many of the cells that produce progesterone when we retrieve the eggs. All these situations can cause short menstrual cycles, poor implantation rates during fertility treatments and an increased risk of a miscarriage during the first trimester. Careful evaluation of the follicle before and the corpus luteum after ovulation can be helpful. The luteal progesterone level can be measured in the blood but this can be misleading because progesterone is released in pulses. Indirect evaluation of luteal progesterone production can be performed by obtaining a sample of the endometrial lining (endometrial biopsy) for evaluation by a pathologist but this can also be misleading. Unfortunately, no reliable method of evaluating the progesterone production currently exists. Consequently, we liberally use progesterone supplements because we know that adequate levels are important and there is no harm from the additional progesterone.

If production of progesterone is suboptimal, progesterone supplementation is usually given. In some instances the ovaries do not make progesterone and complete replacement of progesterone is necessary. An example would be a woman who has premature ovarian failure. To achieve a successful pregnancy with donor eggs, hormonal therapy consisting of first estrogen and then subsequently estrogen and progesterone is necessary. This therapy may also be used for preparation of the uterus before the transfer of previously frozen embryos.

There are two types of progesterone generally available for therapy. "Progestins" are synthetic derivatives of the progesterone molecule that have strong progesterone like action and can be taken orally. They are not used during pregnancy because of concerns regarding a slight increased risk of birth defects. Natural progesterone, on the other hand, is the same hormone that is produced by a woman's ovaries. Scientific data suggest that this type of progesterone is safe in pregnancy and is used exclusively in our infertility program.

Natural progesterone does not absorb well when taken orally. In the past, supplemental progesterone was given in the form of vaginal suppositories but these are messy and cause vaginal irritation. Special oral preparations of micronized progesterone are available but absorption is poor and the molecule is metabolized into other forms when it is taken orally. With the advent of assisted reproductive techniques such as IVF, we utilize more aggressive replacement consisting of intramuscular injections once or twice a day or vaginal administration. While intramuscular administration is effective and has been used very successfully, the injection can be painful. More recently, vaginal administration of progesterone in gel form or in micronized capsule form has been shown to be as effective as the injections in maintaining pregnancy in IVF cycles. These preparations are less messy but can still produce some vaginal irritation.

At NCRS, we begin progesterone supplementation for IVF on the day of egg retrieval. Initially, we utilize intramuscular progesterone to avoid having the gel or capsules in the vaginal canal at the time of embryo transfer. After transfer, we allow patients to switch to the vaginal route if they prefer.

Prometrium 200 mg Capsules

Prometrium 200 mg capsules contain micronized progesterone suspended in peanut oil. Prometrium capsules are inserted into the vagina three times daily, approximately every eight hours. Insertion should be high within the vagina (like a tampon). We recommend that you remain lying down for 15-30 minutes following insertion to allow time for the body to absorb the medication and to decrease vaginal leaking. Some pink tinged vaginal discharge can be expected and a mini pad is helpful to protect the undergarments.

CAUTION: PATIENTS WHO ARE ALLERGIC TO PEANUTS SHOULD NOT USE PROMETRIUM.

Crinone Gel 8%

This preparation may have advantages for certain patients. Crinone contains natural progesterone in a specially formulated vaginal gel. The gel coats the vaginal lining to provide long-lasting absorption of progesterone. The gel is contained in a small applicator that is inserted into the vagina and the gel expelled. One applicator twice a day is the usual dose but may vary depending on your situation. Be sure to follow the recommendations of your physician.

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Progesterone levels measured in the blood are lower when the gel is used rather than injections. However, since progesterone is being absorbed through the vagina, a high level of progesterone reaches the lining of the uterus. Normal endometrial development with good pregnancy rates can be achieved with this preparation.

MISCELLANEOUS ISSUES

Be aware that most of the package inserts for progesterone contain warnings about use during pregnancy. These warnings are confusing to patients because the FDA requires that all progestins be labelled according to "class labelling". Thus because synthetic progesterone derivatives should not be taken during pregnancy such as the progestin in oral contraceptives, every progesterone carries the same warnings. The only exception is Crinone gel which was tested and passed the FDA tests for safety in pregnancy. Nevertheless, the other progesterone supplements that we suggest have been used world-wide in tens of thousands of pregnancies without increased risks of birth defects.

If you have any questions regarding progesterone supplementation and the available options, our physicians and nurses would be happy to discuss them with you.