

Progesterone for Miscarriage Prevention

Analysis by Dr. Joseph Mercola



STORY AT-A-GLANCE

- > The National Institute for Health and Care Excellence (NICE) has recommended women who experience bleeding early in pregnancy and have had a miscarriage be offered progesterone to reduce the risk of losing another pregnancy
- > The guidance is based on research evidence that shows progesterone may prevent 8,450 miscarriages each year. There are different types of progesterone, including vaginal suppositories, gel, insert, oral capsule or injection
- > Women may experience some side effects, including abnormal vaginal bleeding, chest pain, flu-like symptoms, unusual fatigue, and fluid retention
- > Pregnant women have added challenges during the pandemic including exposure to people who asymptomatically carry COVID-19. Take care to wash your hands, steer clear of drugs that have a negative effect on the growing baby, maintain healthy levels of vitamin D and seek to eat foods high in vitamin C

When a woman is pregnant, she is truly eating for two. Every food, medication, supplement and drug affects her growing baby. Her body also produces different levels of hormones to support the pregnancy. Each month, a woman's body cycles through a variety of hormones that regulate the buildup of blood in the uterus to support a pregnancy, the maturation of an egg and the withdrawal of hormones that lead to menstruation.¹

Progesterone is one of those hormones and the one that is often called the "pregnancy hormone" because of the important role it plays, from implantation of the embryo to delivery of the baby. After the egg is released from the ovary, the corpus luteum produces progesterone to maintain the early stages of pregnancy.³

The corpus luteum is a group of cells that form just after the egg leaves the ovary. The progesterone makes the uterus a healthy environment for a fertilized egg to implant and begin to grow.⁴ As the fertilized embryo implants, progesterone stimulates the further growth of blood vessels and triggers the endometrium to secrete nutrients to support growth.

During these early weeks, progesterone is essential to establish the placenta. As the placenta is established, it takes over producing progesterone at around Week 12. During the remaining two trimesters, progesterone levels continue to rise and play a role in strengthening the pelvic wall muscles, preventing lactation and growing of the mother's breast tissue.

Scientists have not identified serious medical consequences of producing too much progesterone,⁵ yet supplementing with progesterone when you aren't pregnant has been associated with a small risk of developing breast cancer.⁶ However, without enough progesterone women can experience irregular and heavy menstrual periods and a drop in progesterone levels can lead to miscarriage.

Progesterone May Help Prevent Early Miscarriage

The National Institute for Health and Care Excellence (NICE) has recommended that women who experience bleeding early in pregnancy and have had at least one miscarriage be offered progesterone supplementation to reduce the risk of losing another pregnancy. The guidance was based on research evidence that showed women with more miscarriages had better results with progesterone supplementation.

According to the article in the BBC, 1 in 5 pregnant women experience spotting in the first 12 weeks of pregnancy. This is light bleeding that occurs intermittently. If bleeding

occurs alongside the pregnancy, this is called a threatened miscarriage. Today, most women with bleeding are sent home and asked to wait to see what happens.

However, new guidance from NICE recommends using a progesterone pessary in the vagina twice a day to deliver progesterone supplementation that supports the pregnancy. One trial carried out at Tommy's National Center for Miscarriage Research showed those who had bleeding and no previous miscarriages didn't experience benefits from progesterone supplementation.

Past research has evaluated the use of progesterone to support pregnancy. One study¹¹ published in 2005 looked at randomized controlled trials of women who received progesterone supplementation before 34 weeks gestation. The data indicated it reduced the incidence of preterm birth in high-risk women.

A second paper¹² published in 2013 found the results of 17 trials showed no evidence to support the use of progestagens for the treatment of threatened miscarriage. A third animal study¹³ published in 2020, analyzed the use of progesterone during early pregnancy on fetal development.

They found administration could alter the pituitary and testicular function in male children. The results suggested progesterone had a sex-specific effect in early pregnancy and should be used only "when there's clear evidence of efficacy and for as limited time as necessary."¹⁴

Progesterone May Prevent 8,450 Miscarriages Each Year

The NICE guidance was based on studies published in 2020, which found progesterone given to women with bleeding in early pregnancy could prevent 8,450 miscarriages each year. Both studies were published January 30, 2020. The study published in the American Journal of Obstetrics and Gynecology¹⁵ examined the results of two major clinical trials that were led by Tommy's National Center for Miscarriage Research and the University of Birmingham.

The clinical trials were the Progesterone in Recurrent Miscarriage trial (PROMISE)¹⁶ and Progesterone in Spontaneous Miscarriage trial (PRISM).^{17,18} The PROMISE trial studied 836 women at 45 hospitals in the Netherlands and U.K.¹⁹ The data revealed that those with recurrent miscarriages had a 2.5% higher live birth rate when supplemented with progesterone.²⁰

In the PRISM trial,²¹ 4,153 women from 48 hospitals in the U.K. were given progesterone with early pregnancy bleeding. The data revealed there was a 5% increase in live birth compared to those given a placebo. In women with three or more miscarriages, the data showed a 15% increase in the number of babies born to those given progesterone.²²

The second study on which the NICE guidance was based was published in BJOG: An International Journal of Obstetrics & Gynaecology.²³ This paper looked at the economics of the PRISM trial and concluded the average cost of treatment was £204 (\$272.19) per pregnancy. They concluded that:²⁴

"The results suggest that progesterone is associated with a small positive impact and a small additional cost. Given available evidence, progesterone is likely to be a cost-effective intervention, particularly for women with previous miscarriage(s)."

Women who are not pregnant may have symptoms of low progesterone that include irregular menstrual cycles, vaginal dryness, mood changes, headaches or migraines. Progesterone helps to complement estrogen during a normal menstrual cycle.²⁵ Without the effect of progesterone, estrogen may increase the risk of weight gain, breast tenderness, fibroids and gallbladder problems.

Different Types of Administration of Progesterone

Not all forms and types of progesterone are created equally. Doctors prescribe progesterone to regulate the menstrual cycle, treat hyperplastic precursor lesions in the endometrium and as a contraceptive.²⁶ Synthetic progesterone²⁷ may be associated with birth defects, so it is important to be sure you are using a natural source and always

consult with your health care provider when using progesterone, whether you are pregnant or not.

Progesterone can come as a vaginal gel, suppository, insert, oral capsule or injection.²⁸ Vaginal gels are used once a day and are the only FDA-approved product for assisted reproduction, such as in vitro fertilization. Thus far there have been over 40 million doses prescribed in the past decade.

Vaginal suppositories are wax-based and inserted two to three times a day. However, leaking can be messy and although they are widely used, they are not FDA-approved. Vaginal inserts are approved for supplementation but not progesterone replacement.

While they are not formulated or FDA-approved for vaginal use, progesterone oral capsules have been used vaginally, up to three times a day, as they have fewer side effects when used vaginally, than when taken orally.

Finally, progesterone can be given as an oil-based injection. It's the oldest method of delivery and is injected into the buttocks once daily. Because it's oil-based, the injections can be painful and skin reactions are common.

Women who use progesterone supplementation in early pregnancy may experience some side effects. These side effects should be reported to their health care professional as soon as possible.^{29,30,31}

Abnormal vaginal bleeding	Breast changes or discharge	Vision changes
Allergic reactions	Chest pain	Problems talking and walking
Confusion	Severe headaches	Dark urine
Flu-like symptoms	Sudden numbness or weakness	Pain, swelling, warmth in the leg

Shortness of breath	Nausea and vomiting	Light-colored stools
Loss of appetite	Right upper belly pain	Unusual fatigue
Yellowing of the eyes or skin	Stomach cramps	Bloating
Back pain	Depressed mood	Mood swings
Increased appetite	Fluid retention	

Added Challenges if You Are Pregnant During the Pandemic

Women who are pregnant during the pandemic have a few added challenges to stay healthy and protect the health of their child. Pregnancy places a higher demand on pulmonary functions. Thus, women with underlying medical conditions such as heart disease, diabetes, high blood pressure or lung problems may have a higher risk of infection and severe disease.

It is important to communicate any changes with your doctor, such as decreased fetal movement, or if you believe you're having signs of preterm labor. Researchers believe up to 80% of those with COVID-19 will have mild symptoms or be asymptomatic.³² This is similar to studies done with flu in England, which found the majority of those were asymptomatic.³³

This means you need to take care even with individuals who appear to be healthy. A vital step in prevention is excellent handwashing for at least 20 seconds and avoiding touching your face.

You also need to be aware that taking supplements or medications during pregnancy can have affects on your growing baby that are not always well understood or documented. Even commonly accepted over-the-counter medications and supplements may have long-term consequences.

For example, there is evidence to suggest that acetaminophen, commonly sold as Tylenol, may double the risk of autism³⁴ and increase the risk of attention deficit disorders in children.³⁵

It is also crucial to maintain healthy levels of vitamin D during your pregnancy. In one Cochrane systematic review,³⁶ the authors found evidence that vitamin D could reduce the risk of preeclampsia, low birth weight and preterm birth. It also plays a functional role in reducing the risk of upper respiratory infections,³⁷ which includes flu and COVID-19.

Vitamin C plays a role in the treatment of COVID-19, but large doses should not be used preventively. To protect your health, seek out foods that are high in vitamin C,³⁸ such as bell peppers, kiwi fruit, strawberries, broccoli, tomatoes and snow peas.

Sources and References

- 1 Merck Manual, Menstrual Cycle
- 2, 27, 29 Fertility Center, What Does Progesterone Do in Pregnancy?
- ³ My Cleveland Clinic, Corpus Luteum
- 4, 5, 6 You and Your Hormones, Progesterone
- ⁷ The BMJ, 2021;375:e2896
- ^{8, 9} BBC, November 24, 2021
- ¹⁰ BBC, November 24, 2021, para 5 & 7 under subhead 1
- 11 Current Opinions in Obstetrics and Gynecology, 2005;17(6)
- 12, 30 Facts, Views & Vision Obstetrics and Gynecology, 2013;5(1)
- 13, 14 Scientific Reports, 2020;10:21920
- 15 American Journal of Obstetrics and Gynecology, 2020;223(2)
- 16, 20 Health Technology Assessment, 2016;20(41)
- ¹⁷ Miscarriage Association, The PRISM Trial
- ¹⁸ New England Journal of Medicine, 2019;380
- 19, 21 Royal College of Obstetricians and Gynecologists, January 31, 2020
- ²² Royal College of Obstetricians and Gynecologists, January 31, 2020 para 6
- ²³ BJOG: An International Journal of Obstetrics and Gynaecology, January 30, 2020
- ²⁴ BJOG: An International Journal of Obstetrics and Gynaecology, January 30, 2020, Line 3, para 2 under Table
 2
- ²⁵ Healthy Women, Low Progesterone Symptoms
- ²⁶ American Family Physician, 2000;62(8)
- ²⁸ Resolve, Progesterone and Pregnancy
- 31 RxList, Progesterone Injection

- ullet World Health Organization, Coronavirus Disease 2019 Situation Report 46 Page 2
- 33 The Lancet Respiratory Medicine, 2014; doi.org/10.1016/S2213-2600(14)70034-7 Summary/Findings line 7
- 34 JAMA Pediatrics 2016;170(10):964-970
- ³⁵ JAMA Psychiatry, 2020;77(2):180
- ³⁶ Cochrane Database of Systematic Reviews, January 14, 2016 doi.org/10.1002/14651858.CD008873.pub3 Author conclusions
- ³⁷ Journal of Infection in Developing Countries, 2015;9(4) Abstract
- ³⁸ My Food Data, April 3, 2020