



MotherToBaby

Medications & More During Pregnancy & Breastfeeding
Ask The Experts

Fact Sheet

by the **Organization of Teratology Information Specialists (OTIS)**

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Methotrexate

In every pregnancy, a woman starts out with a 3-5% chance of having a baby with a birth defect. This is called her background risk. This sheet talks about whether exposure to methotrexate may increase the risk for birth defects over that background risk. This information should not take the place of medical care and advice from your health care provider.

What is methotrexate?

Methotrexate is a medication that can stop the growth of cells and can interfere with the immune system. Methotrexate is prescribed to treat many conditions, including cancers and autoimmune conditions like rheumatoid arthritis and psoriasis. Methotrexate is also used to treat ectopic pregnancies (ones that grow outside the uterus). It can be taken by mouth, intravenous injection, or intramuscular injection. Methotrexate is prescribed in a range of doses including low doses for rheumatoid arthritis to high doses for cancer. Methotrexate is sold under the brand names Otrexup®, Trexall®, and Rasuvo®.

Methotrexate decreases the body's ability to break down and use folic acid. During pregnancy, folic acid is important for normal development of the baby. If you have recently stopped taking methotrexate and are planning to get pregnant, talk with your health care provider about taking folic acid and what dose you should take.

How long does methotrexate stay in the body?

Every person's ability to break down medication is different. The time for methotrexate to leave the body also varies with dose. However, methotrexate is mostly cleared from the body of a non-pregnant adult within one week after the last dose is taken. Certain medications may slow down the clearance of methotrexate. Individuals who have reduced kidney function or a condition that leads to extra body fluid may clear methotrexate more slowly.

I am currently taking methotrexate, but would like to become pregnant. How long do I need to wait to become pregnant after I stop taking methotrexate?

Some health care providers suggest waiting 1 to 3 months after stopping methotrexate to ensure the medication has been cleared from the body. However, there are no reports of babies being born with methotrexate-related birth defects when mom stops taking this medication before conception.

I have recently been treated with methotrexate for an ectopic pregnancy and I want to try to become pregnant again. What do I need to know?

Before you try to become pregnant again, you should confirm with your health care provider that the ectopic pregnancy has been treated and you are no longer pregnant. Your health care provider may want to monitor your levels of hCG (a hormone produced during pregnancy) in order to confirm you are not pregnant.

If I get pregnant while taking methotrexate, what should I do?

Contact your health care provider right away so they can discuss your specific risks, as well as suggest prenatal testing. Prenatal testing may involve a blood or amniotic fluid test that can assess for neural tube defects (such as spina bifida, a defect involving the baby's spinal cord) and a detailed ultrasound to look at the growth and development of the baby. Ultrasounds done in the second or third trimester can show some birth defects associated with methotrexate, but are not able to detect all potential problems caused by a methotrexate exposure.

Will my past methotrexate use make it harder for me to get pregnant?

Probably not. One study on infertility patients treated with methotrexate for ectopic pregnancy suggested a

decreased number of eggs available for fertilization, however this was temporary. Other studies have not shown risks to fertility with use of methotrexate. Because methotrexate is known to increase the risk for birth defects when taken in the first trimester, women who are actively trying to become pregnant should not be taking methotrexate.

Does exposure to methotrexate cause an increased risk for miscarriage?

Since methotrexate can be used to abort pregnancies or treat ectopic pregnancies, it seems likely that methotrexate use in early pregnancy would increase the risk of a miscarriage. Small studies have reported an increased risk for miscarriage, however more studies are needed to determine the chance a woman might have of a miscarriage after exposure to methotrexate during pregnancy.

Can taking methotrexate in pregnancy cause birth defects?

Yes. The use of methotrexate in the first trimester has been associated with a specific pattern of birth defects. This pattern of birth defects includes malformations of the infant's head, face, limbs, and bones. Poor growth, developmental delay, and intellectual disability have also been described. For other birth defects, like heart defects and oral clefts, the evidence is currently not strong enough to show that methotrexate is the cause.

Limited evidence suggests that a pregnant woman will be at risk for having a baby with methotrexate-related birth defects if she takes 10 mg or more of methotrexate per week between 6 and 8 weeks after conception (8 to 10 weeks after the first day of her last menstrual period). More research is needed on the risks related to specific timing and dose of methotrexate to draw firm conclusions.

One 2009 review paper reported no increase in miscarriage or birth defect rates in 101 women with rheumatoid arthritis who were exposed to 5-25mg/week of methotrexate in the first trimester. While reassuring, this paper does not mean there is no risk for low dose methotrexate exposure in the first trimester.

Is it OK to restart methotrexate after the first trimester?

No. Methotrexate should continue to be avoided after the first trimester. During the second and third trimesters of pregnancy, the baby is still growing and the brain is still developing. Poor growth and learning problems have been associated with methotrexate, so use after the first trimester is a potential concern.

Can I take methotrexate while breastfeeding?

There are no studies looking at the effects of methotrexate in the breastfed infant. Methotrexate passes into breast milk in small amounts. Because of its toxic properties and possible buildup of the drug in an infant's body, some providers do not recommend methotrexate in breastfeeding.

However, some breastfeeding experts believe that weekly low-dose methotrexate, such as the dose used for the treatment of rheumatoid arthritis, is a low risk to the breastfed infant. If a woman and her health care provider decide to continue low-dose methotrexate treatment while breastfeeding, monitoring of the baby's blood count is suggested. Be sure to talk to your health care provider about all your breastfeeding questions.

If a man uses methotrexate, will it cause infertility or birth defects in the baby?

Methotrexate may cause an increased risk for infertility, not birth defects. Low sperm count has been seen in some men using methotrexate. Most of these men were using high doses of the medication, as well as other medications used to treat cancer. Sperm levels returned to normal after the men stopped taking methotrexate. Men who need to take methotrexate as part of cancer treatment may want to consider banking sperm prior to treatment.

There are no reports suggesting that men who use methotrexate at the time of conception are more likely to father a baby with a birth defect. Four studies noted no increase in birth defects in the children of 65 men who had taken methotrexate around the time of conception. However, due to general concern rather than actual risks, some health care providers recommend that men wait at least 3 months after stopping methotrexate before trying to conceive. For more information, please see the MotherToBaby fact sheet Paternal Exposures and Pregnancy at <https://mothertobaby.org/fact-sheets/paternal-exposures-pregnancy/pdf/>.

MotherToBaby is currently conducting a study looking at autoimmune conditions and the medications used to treat these conditions in pregnancy. If you are interested in taking part in this study, please call 1-877-311-8972 or sign up at <https://mothertobaby.org/join-study/>.

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