**SOME DISEASE MODIFYING THERAPIES ARE SAFE DURING PREGNANCY AND BREASTFEEDING (NO)**

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A significant proportion of MS mothers are exposed to disease modifying therapies (DMT) during pregnancy. The information on pregnancy outcomes for babies exposed to DMT is increasing, but the study samples are still small. Thus, the safety of these medications has not been fully established and discontinuation of DMT prior to pregnancy must still be the recommended way. Even though these drugs do not appear to cause any major fetal malformations in animal studies they have been shown to cause miscarriages in animals, and this has been seen also in humans. Moreover, the natural course of MS during pregnancy, i.e. the pregnancy-associated low relapse rate makes the necessity of DMT questionable during pregnancy. Despite discontinuation of the DMT before pregnancy, the mothers rarely experience disabling relapses during the course of pregnancy.

Breast-feeding among MS mothers is common. It is considered beneficial for the mother-infant relationship and it reduces the incidence of infections and allergies experienced by the infant. The postpartum period is, however, a challenging time regarding controlling the disease activity, as after the delivery relapses are frequent, but DMT are not recommended during breastfeeding. Breastfeeding mothers have been noted to have a lower postpartum relapse rate than MS-patients who did not breast-feed, but this is likely due to a selection bias; mothers with stable disease choose breastfeeding, whereas mothers with active disease choose DMT and are less likely to breastfeed. They are likely to experience more frequent relapses postpartum, before the DMT will have time to affect the relapse rate.

The American Food and Drug Administration's (FDA) pregnancy risk classification scheme gives information on the risk whether a given medication could cause a fetal loss, a major malformation, low birth weight or infant death. This classification is mostly based on animal data or short-term human studies, and conclusions are drawn rather from lack of safety data in humans than from evidence of safety in human trials.

When a drug is first marketed there are usually no human data on the effects of in utero drug exposure. The only data on fetal effects initially available in the product labeling usually comes from animal reproductive toxicology studies. Because little is known before marketing about a drug's teratogenic potential, postmarketing surveillance of drug use in pregnancy is critical to the detection of drug-induced fetal effects. With current postmarketing surveillance methods this process can take considerable time. The tables below show the current FDA risk classification in terms of MS drug safety during pregnancy and lactation.

**Table 1. Safety of MS therapies during pregnancy according to FDA pregnancy risk classification**

| Medication | FDA category | Adverse events following in utero exposure |
|---|---|---|
| Glatiramer acetate | B | None known in humans or animals |
| Interferon-beta | C | Spontaneous abortions in animals |
| Methylprednisolone | C | Fetal deformities in humans, do not use in first trimester<br>Neonatal immunosuppression in humans |
| Mitoxantrone | D | Low birth weight, preterm delivery, kidney anomalies |
| Natalizumab | C | Spontaneous abortions, thymic atrophy, decreased hepatic hematopoiesis, increased splenic hematopoiesis |
| Gilenya | C | Spontaneous abortions in animals<br>Cardiac and vascular malformations in animals |

**Table 2. Safety of MS therapies during lactation according to FDA pregnancy risk classification**

| Medication | FDA category | Safety during lactation |
|---|---|---|
| Glatiramer acetate | B | Unknown so avoid |
| Interferon-beta | C | Unknown so avoid |
| Methylprednisolone | C | Pump and discard 8-24 h after each infusion |

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|---|---|---|
| Mitoxantrone | D | Probably hazardous |
| Natalizumab | C | Unknown so avoid |
| Gilenya | C | Possibly hazardous, so avoid |

**Table 3. The FDA pregnancy risk classification scheme.**

| CATEGORY | INTERPRETATION |
|---|---|
| **A** | Adequate, well-controlled studies in pregnant women have not shown an increased risk of fetal abnormalities to the fetus in any trimester of pregnancy. |
| **B** | Animal studies have revealed no evidence of harm to the fetus, however, there are no adequate and well-controlled studies in pregnant women.<br>**OR**<br>Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester. |
| **C** | Animal studies have shown an adverse effect and there are no adequate and well-controlled studies in pregnant women.<br>**OR**<br>No animal studies have been conducted and there are no adequate and well-controlled studies in pregnant women. |
| **D** | Adequate well-controlled or observational studies in pregnant women have demonstrated a risk to the fetus. However, the benefits of therapy may outweigh the potential risk. For example, the drug may be acceptable if needed in a life-threatening situation or serious disease for which safer drugs cannot be used or are ineffective. |
| **X** | Adequate well-controlled or observational studies in animals or pregnant women have demonstrated positive evidence of fetal abnormalities or risks. The use of the product is contraindicated in women who are or may become pregnant. |