

Pregnancy & Rheumatic Disease



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Rheumatic diseases often affect women during their childbearing years, when pregnancy is an expected event. For years, women with potentially serious systemic autoimmune diseases have been advised against getting pregnant. We now know that, with careful medical and obstetric management, most of these women can have successful pregnancies. Successful, however, does not mean uneventful. Doctors and patients must be ready to deal with possible complications for both mother and child. Further, women should not consider getting pregnant until their rheumatic disease is under control.

Fast Facts

- Diseases with the potential to affect the kidneys, especially lupus and antiphospholipid syndrome (APS), are more likely to affect pregnancy outcome than others.
 - Each woman's rheumatic disease should be well under control for a period of at least 3–6 months before attempting pregnancy. As long as your medicines are not harmful to the fetus, you should remain on your medicines to prevent risk of a disease flare. Any changes should be discussed in advance with your rheumatologist.
 - Women with a low-risk profile can be managed with usual visits to the rheumatologist as a precaution. Those with a high-risk profile should be managed by both the rheumatologist and obstetric team with experience in high-risk pregnancies
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What are the effects of pregnancy on rheumatic disease?

The effects of pregnancy on rheumatic diseases vary by condition. **Rheumatoid arthritis (RA)**, **systemic lupus erythematosus (SLE)** and **antiphospholipid syndrome (APS)** typically are modified by pregnancy. For example, RA symptoms often improve in pregnant patients, frequently resulting in a reduced need for medication, but they may flare up after delivery.

The relationship between lupus activity and pregnancy is more debated. In general, there is a tendency for mild to moderate flares, especially during the second half of pregnancy and the post-partum period. However, most of these flares do not endanger the mother's or the baby's life, nor do they substantially alter the long-term prognosis of lupus. Being in clinical remission for 3–6 months prior to getting pregnant decreases the chance that a flare will occur during the pregnancy.

Antiphospholipid syndrome (APS) increases the risk of clots in veins and arteries as well as complications such as miscarriage, premature birth or hypertension (high blood pressure) during pregnancy. Patients with kidney disease have a risk of developing pre-eclampsia as well. Pre-eclampsia and eclampsia are conditions that may damage the mother's kidneys and liver. They also increase the risk of premature birth or death of the fetus. So, pregnancy – especially the time close to delivery – is a particularly dangerous period for women with APS, and special care is needed.

Pulmonary hypertension is a type of high blood pressure that affects arteries in the lungs and heart. It sometimes causes complications in rheumatic diseases like lupus, APS, Sjögren's syndrome and scleroderma. Because pulmonary hypertension frequently worsens during pregnancy – especially in the post-partum period – it is not advised for women with this condition to become pregnant.

Other diseases such as polymyositis, dermatomyositis and vasculitis do not seem to be affected by pregnancy. As long as a patient does not have pulmonary hypertension or lung fibrosis, scleroderma does not appear to be affected by pregnancy either. However, it is still recommended that patients consider pregnancy only when these diseases are under control and with the care of your rheumatologist.

What are the effects of rheumatic disease on pregnancy?

During pregnancy, the effects of inflammation when a rheumatic disease becomes active and the necessary medications to control the inflammation can cause problems. Diseases with the potential to affect the kidneys (especially APS) are more likely to affect pregnancy outcome than those that do not.

Patients who have or have had kidney disease, due to vasculitis, scleroderma or lupus, generally have an increased risk of severe hypertension and pre-eclampsia. If kidney function and blood pressure prior to pregnancy are normal and the disease is inactive at the time of conception for a period of at least six months, the outcome is likely to be good. Women with severely impaired kidney function, uncontrolled hypertension (high blood pressure) and/or active rheumatic disease flares are advised not to get pregnant.

APS probably has the greatest impact on pregnancy. It is related to both early and late miscarriage, premature birth and low-weight babies, as well as thrombosis (condition where blood clots form in the blood vessels) and pre-eclampsia. Thus, pregnancy in women with APS should always be considered as high risk and require close medical and obstetric monitoring. Treatment is based on low-dose aspirin and heparin.

Finally, a rare condition named congenital heart block can occur in 2 percent of children born to mothers with anti-Ro antibodies (most frequently seen in patients with lupus and Sjögren's syndrome). Anti-Ro antibodies can get into the circulatory system of a fetus and interfere with the baby's heart, which can cause a slow heart rate. These babies may need a permanent pacemaker. So, women with anti-Ro antibodies also should be closely monitored and have scans of the baby's heart done during pregnancy.

Use of rheumatic drugs during pregnancy and lactation

During pregnancy, the effects of inflammation when rheumatic disease becomes active and medications used to treat rheumatic disease can cause problems. Information on the safety of many drugs in pregnant women is incomplete and difficult to obtain. Based on the information available, most rheumatologists generally recommend the following:

| | Pregnancy | Lactation |
|----------------------------------|-------------------------------|------------------|
| NSAID | Yes (avoid after 32 weeks) | Yes |
| Sulfasalazine | Yes | Yes |
| Antimalarials | Yes | Yes |
| Corticosteroids | Yes | Yes |
| Cyclosporine | Yes | Probably Yes |
| Azathioprine | Yes | Probably Yes |
| Mycophenolate | No | No |
| Methotrexate | No | No |
| Cyclophosphamide | Yes | No |
| Anti-tumor necrosis factor (TNF) | Yes | Yes |

Table 1: Acceptable medications during pregnancy and lactation

| | Pregnancy | Lactation |
|-----------|--|------------------|
| Rituximab | No | No |
| Warfarin | No (with caution, only after first trimester) | Yes |
| Heparin | Yes | Yes |

This list should only be considered a general guide and may not apply in all situations. Women who are pregnant or considering pregnancy should discuss their medications with both their rheumatologist and their obstetrician. Many women would prefer to take no medication during pregnancy and nursing. However, the consequences of not being on medicine and the risk of their rheumatic disease flaring are important considerations that should be discussed with both the rheumatologist and obstetrician.

Several drugs (particularly **methotrexate** and **cyclophosphamide** have effects on sperm cells in men. It is recommended that these medications be stopped for 3 months before a man fathers a child.

Management of pregnancy in women with rheumatic diseases

All women with rheumatic disease should undergo counseling about their specific risks if they are thinking about having a baby. During that discussion with your doctor, you can review specific concerns of pregnancy and learn what pregnancy complications can occur.

Here are a few things that make a pregnancy “high risk.”

- Previous pregnancy with complications
- Underlying kidney disease
- Underlying heart disease
- Underlying lung disease (including pulmonary hypertension)
- Flare of rheumatic illness
- A history of previous blood clot

- The presence of SSA and SSB antibodies
- IVF (in vitro fertilization)
- Pregnancy with twins, triplets, etc.
- Mother being over 40

Each woman's rheumatic disease should be well under control for a period of at least 3–6 months before attempting pregnancy. As long as your medicines are not harmful to the fetus, you should remain on your medicines to prevent risk of a disease flare. Prednisone should be used at doses below 10 mg/day whenever possible, due to the risk of associated complications such as high blood pressure, diabetes, excessive weight gain, risk of infections and premature rupture of membranes. **Hydroxychloroquine** is an extremely safe drug for both the mother and the fetus and should not be stopped before, during or after pregnancy. High blood pressure should be managed using medicines that are safe during pregnancy. Captopril and enalapril are safe drugs during breastfeeding.

Women with antiphospholipid antibody syndrome (APS) must receive low-dose aspirin, with or without heparin, depending on their medical history. In some women with APS or a previous history of blood clots, heparin usage is recommended for 4–6 weeks after delivery to help prevent blood clots. Those with previous blood clot should restart warfarin as soon as possible after delivery, since this drug is safe during lactation (Table 1).

Women with a low-risk profile should include in their usual treatment plan regular three-monthly visits to the rheumatologist, as a precaution. However, those with a high-risk profile should be managed by a combined medical and obstetric team with experience in high-risk pregnancies. Visits should be more frequent as pregnancy advances (weekly during the late third trimester), and include monitoring of fetal and maternal well-being. Blood pressure measurements and urine testing should be frequently performed to assure the early detection and treatment of pre-eclampsia.

Reviewed March 2014. Written by Guillermo Ruiz-Irastorza, MD, PhD, and Munther A. Khamashta, MD, FRCP, PhD, and reviewed by the American College of Rheumatology Communications and Marketing Committee. This information is provided for general education only. Individuals should consult a qualified health care provider for professional medical advice, diagnosis and treatment of a medical or health condition.

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