Pregnancy and Rheumatic Disease

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

- Often rheumatic diseases affect women during their childbearing years, when pregnancy is an expected event.
- With careful medical and obstetric management, many women with rheumatic disease can have successful pregnancies if they and their physicians are prepared to handle the possible complications.
- Rheumatic diseases with the potential to affect the kidney and especially antiphospholipid syndrome (APS) are more likely to affect pregnancy outcome than others.

Effects of pregnancy on rheumatic disease

The effects of pregnancy on rheumatic diseases vary by condition. Rheumatoid arthritis (RA), lupus and APS typically are modified by pregnancy. For instance, symptoms of RA almost invariably improve in pregnant patients, frequently resulting in a reduced need for medications, but usually flare up postpartum.

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. A prolonged period of clinical remission before conception decreases the chance of a flare during pregnancy.
APS, a prothrombotic condition, offers an increased risk of venous and arterial clots as well as obstetric complications such as miscarriage or hypertension during pregnancy. When combined with urinary loss of proteins and edema, the possibility exists for pre-eclampsia, a very serious condition. This is further intensified by a pregnant woman’s natural tendency to thrombosis which the body develops to avoid massive bleeding during delivery. Thus, for women with APS, pregnancy, especially the time around delivery, is a particularly dangerous period and dictates special surveillance.

Pulmonary hypertension complicates some rheumatic diseases (LUPUS, APS, Sjögren’s and particularly scleroderma), but can exist unrelated to any other illness. Because this severe disease frequently is aggravated by pregnancy, resulting in high mortality, pregnancy must be considered inadvisable.

Other diseases such as scleroderma (in the absence of pulmonary hypertension or lung fibrosis), polymyositis, dermatomyositis and vasculitis do not seem to be particularly influenced by pregnancy. However, it is still recommended that pregnancy be pursued only when these diseases are under control.

**Effects of rheumatic disease on pregnancy**
During pregnancy, the effects of inflammation when rheumatic disease becomes active as well as the then necessary anti-inflammatory and/or immunosuppressive drugs can cause problems. Those diseases with the potential to affect the kidney and, especially, APS are more likely to affect pregnancy outcome than others.

Patients who have or have had kidney disease, due to vasculitis, scleroderma or, more frequently, lupus, in general are at increased risk of severe hypertension and pre-eclampsia. If renal 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. Conversely, women with severely impaired renal function, uncontrolled hypertension and/or active kidney involvement usually are advised against getting pregnant.

APS probably has the greatest impact on pregnancy. It is related to both early and late miscarriage, prematurity and low-weight babies, as well as thrombosis and pre-eclampsia. Thus, pregnancy in
women with APS should always be considered as high risk, and be the subject of close medical and obstetric monitoring. Therapy is based on low-dose aspirin and heparin.

Finally, a rare condition named congenital heart block can occur in 2% of children born to mothers with anti-Ro antibodies (most frequently seen in patients with LUPUS and Sjögren’s syndrome). Anti-Ro antibodies can gain access to the fetal circulation and produce disturbances in the baby’s heart, which result in a slow heart rate. These babies may need a permanent pacemaker. Thus, women with anti-Ro antibodies also should be closely monitored including fetal heart scans during pregnancy.

**Use of medication during pregnancy and lactation**

Information regarding the safety of many drugs in pregnant women is incomplete and difficult to obtain. Recently, however, a group of obstetricians, rheumatologists and internists with experience in the management of pregnancy in women with rheumatic diseases reached consensus on the use of antirheumatic drugs during pregnancy and lactation. A summary of these conclusions is shown in Table 1.

<table>
<thead>
<tr>
<th>Table 1: Acceptable medications during pregnancy and lactation</th>
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<tr>
<td><strong>NSAID</strong></td>
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<tr>
<td>Sulfasalazine</td>
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<td>Antimalarials</td>
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<td>Corticosteroids</td>
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<td>Cyclosporine A</td>
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<tr>
<td>Azathioprine</td>
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<tr>
<td>Mycophenolate</td>
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<tr>
<td>Methotrexate</td>
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<tr>
<td>Cyclophosphamide</td>
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<tr>
<td>Anti-tumor necrosis factor (TNF)</td>
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<tr>
<td>Rituximab</td>
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<tr>
<td>Warfarin</td>
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<td>(could be prescribed with caution, only after first trimester)</td>
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<td>Heparin</td>
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Ideally, women should take no medications until pregnancy and nursing are completed. However, the consequences of withdrawing medication necessary for keeping the mother’s disease under control often are more serious than the risk of fetal malformations.

**Management of pregnancy in women with rheumatic diseases**

All women with rheumatic disease should undergo counseling before conception for their specific risk profile and subsequent design of a management plan. At that time, the several clinical features that substantially can increase the risk of pregnancy complications (Table 2) should be reviewed.

Table 2: What makes a pregnancy “high risk”?

- Previous poor obstetric history
- Renal impairment
- Cardiac involvement
- Pulmonary hypertension
- Restrictive lung disease
- Active disease
- Antiphospholipid antibodies
- Antibodies against extractable nuclear antigens (Ro, La)
- In vitro fertilization (IVF)/multiple pregnancy

Each woman’s disease should be well under control for a period of at least 3-6 months before attempting pregnancy. In the case of medications that are not contraindicated, usual treatment should not be altered, due to the risk of a disease flare. Corticosteroids should be used at doses below 10 mg/d whenever possible, due to the risk of associated complications such as hypertension, diabetes, excessive weight gain, susceptibility to infections and premature rupture of membranes. Hydroxychloroquine, frequently discontinued during pregnancy for fear of fetal toxicity, especially in the U.S., is an extremely safe drug for both the mother and the fetus, and should not be stopped before, during or after pregnancy.

Women with APS must receive low-dose aspirin, with or without heparin depending on the previous obstetric and thrombotic history. In all women with antiphospholipid antibodies, prevention of thrombosis using heparin following delivery is mandatory for 6 weeks. Those with previous thrombosis should re-start 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 dipstick also must be frequently performed to assure the early detection and treatment of pre-eclampsia.
Points to remember

- All women should undergo counseling before conception for their specific risk profile and subsequent design of a management plan.
- Ideally, women should take no medications until pregnancy and nursing are completed. However, the consequences of withdrawing medication necessary for keeping the mother's disease under control are often more serious than the risk of fetal malformations.
- 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 a combined medical and obstetric team with experience in high risk pregnancies.

To find a rheumatologist

For a listing of rheumatologists in your area, click here.

Learn more about rheumatologists and rheumatology health professionals.

For more information

The American College of Rheumatology has compiled this list to give you a starting point for your own additional research. The ACR does not endorse or maintain these Web sites, and is not responsible for any information or claims provided on them. It is always best to talk with your rheumatologist for more information and before making any decisions about your care.

Arthritis Foundation
www.arthritis.org

National Institutes of Health
www.nih.gov

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