# Managing Rheumatologic Diseases in Pregnancy

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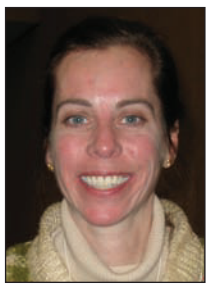
FROM A SYMPOSIUM SPONSORED BY THE AMERICAN COLLEGE OF RHEUMATOLOGY

SNOWMASS, COLO. – Corticosteroids can be thought of as the 'go-to' drugs for the management of rheumatologic disorders in pregnancy.

"Corticosteroids have been my ace in the hole in treating many patients during pregnancy. They're potent immunosuppressives that can get you out of a lot of trouble. And although they can have side effects, if used judiciously they are a reasonable treatment choice," Dr. Bonnie L. Bermas stressed at the symposium.

Reassuringly, transplant registries comprising many tens of thousands of organ recipients have shown no increased rate of congenital anomalies with the use of corticosteroids in pregnancy.

However, an influential University of Toronto meta-analysis has concluded that "although prednisone does not represent a major teratogenic risk in humans at therapeutic doses, it does increase by an order of 3.4-fold the risk of oral cleft" (Teratology 2000;62:385-92).



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DR. BERMAS

"What this translates to in your practice is, the cleft palate incidence increases from 1 in 1,000 in the general population to about 1 in 300 live births exposed to steroids in utero. That's how I counsel my patients who need to be on corticosteroids in the first trimester," said Dr. Bermas, clinical director of the lupus center at Brigham and Women's Hospital in Boston.

After 12-14 weeks' gestation, however, the palate is formed. And although steroids are no longer associated with an increased risk for cleft palate after that point in gestation, other risks remain. These include gestational diabetes, gestational hypertension, osteoporosis in the mother, premature rupture of the membranes, and small-for-gestational-age infants.

Prednisone and methylprednisolone—the steroids rheumatologists utilize most often—don't cross the placenta efficiently, and hence are much less likely to cause fetal adverse effects than are dexamethasone or betamethasone.

Steroids that are administered to the mother make their way into breast milk only in low concentrations. If she's on less than 20 mg/day of prednisone, she can breastfeed normally. For women on higher doses, Dr. Bermas advises pumping and discarding the breast milk for the first 4 hours after a dose is taken.

Dr. Bermas emphasized that the key to successful treatment of rheumatologic disorders during pregnancy is a clear-eyed assessment of and accommodation to the patient's tolerance for risk—and the physician's, as well.

"There are some women who do not drink caffeinated beverages or take any medications, not even a Tylenol, and who will eat only organic foods while pregnant. There are others who are willing to tolerate some risk during pregnancy. And as clinicians, we have our own risk tolerances, too. For example, azathioprine is a medication that I feel comfortable using during pregnancy, but I have colleagues who won't because they wouldn't be able to sleep at night," she explained.

The reason she prescribes azathioprine during pregnancy—despite its category D rating from the Food and Drug Administration, indicating "positive evidence of risk"—is that there's an enormous transplant literature showing no increase in congenital anomalies with in utero exposure to this drug.

Mycophenolate mofetil (CellCept) also has a category D rating. But unlike azathioprine, mycophenolate mofetil has no extensive and reassuring transplant literature. As a result, Dr. Bermas said that she avoids it in pregnancy and nursing.

Other rheumatologic medications to avoid in pregnancy are methotrexate, penicillamine, 6-mercaptopurine, and

chlorambucil, she continued.

The use of tumor necrosis factor inhibitors during pregnancy is an extremely challenging question. Although at present the FDA rates them as category B ("no evidence of risk in humans"), that could very well change as a result of a reported association (J. Rheumatol. 2009;36:635-41) with VACTERL anomalies, which include vertebral anomalies, anal atresia, cardiac defects, tracheoesophageal fistula, renal anomalies, and limb abnormalities. On the other hand, several editorials and review articles have expressed the view that the risk of VACTERL anomaly after in utero exposure is overstated.

When lupus patients on antimalarials become pregnant, Dr. Bermas said she generally keeps them on the medication. She also allows patients to remain on antimalarials while nursing, which is consistent with the position of the American Academy of Pediatrics.

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For mild cases of rheumatologic disease in pregnancy, Dr. Bermas reported that she relies on NSAIDs and/or prednisone at 5-10 mg/day. She halts the NSAID after the second trimester in order to avoid premature closure of a patent ductus arteriosus. For an inflammatory mild arthritis, she considers adding sulfasalazine.

She said she manages moderate disease with higher-dose steroids, azathioprine, or cyclosporine. For severe disease, Dr. Bermas reported that she turns to pulse steroids, azathioprine, cyclosporine, or intravenous immunoglobulin. In life-or-death situations, there are many case reports of cyclophosphamide being used successfully in the third trimester, a time by which most organogenesis is completed.

Dr. Bermas reported having no financial conflicts of interest. ■