

Why do certain diseases go into remission during pregnancy?

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During pregnancy, many women experience remission of autoimmune diseases like multiple sclerosis and uveitis. Now, scientists have described a biological mechanism responsible for changes in the immune system that helps to explain the remission.

The expression of an enzyme known as pyruvate kinase is reduced in [immune cells](#) in pregnant women compared to non-pregnant women, according to Howard R. Petty, Ph.D., biophysicist at the University of Michigan Kellogg Eye Center and Roberto Romero, M.D., of the National Institutes for Health. The study, which appears online ahead of print in the August issue of the *American Journal of Reproductive Immunology*, also reports that expression of the enzyme is lower in pregnant women compared to those with pre-eclampsia, a condition with inflammatory components.

The study is significant because the newly discovered mechanism points to a pathway that could be targeted for treatment. "It may be possible to design drugs that mildly suppress pyruvate kinase activity as a means of replicating the immune status of normal pregnancy," says Petty. In addition to pre-eclampsia, he believes that [rheumatoid arthritis](#), [type 1 diabetes](#), and uveitis may eventually yield to similarly designed drugs.

In his search to explain the phenomenon, Petty knew to look for a metabolic pathway or mechanism with two characteristics. It had to "dial down" the intensity of the normal [immune response](#), an action needed so that a pregnant woman does not reject the fetus, which has proteins from

the father that are "foreign" to the mother. At the same time, such a mechanism must support cell growth needed by the developing fetus.

The activity of the enzyme pyruvate kinase—and its product, pyruvate—fills both roles: promoting cell growth while modifying the immune response. Because pyruvate kinase activity is depressed during pregnancy, [cell metabolism](#) supports an increased production of lipids, carbohydrates, [amino acids](#), and other substances that support cell growth.

Petty explains that our normal robust immune response depends upon pyruvate to promote calcium signaling, which, in turn, stimulates the production of messenger molecules called cytokines. When pyruvate is decreased during pregnancy, calcium signaling is also reduced, and the immune response is different than that in non-pregnant individuals.

Says Petty, "Modification of signaling along this pathway allows the pregnant woman to maintain an immune response, but at a level that will not harm the fetus."

The study included 21 women in their third trimester of a normal pregnancy, 25 women with pre-eclampsia, and a control group of non-pregnant women. Petty and colleagues used a variety of methods to confirm their findings, including fluorescence microscopy and flow cytometry, which are used to study cell signaling.

The higher levels of the enzyme seen in women with pre-eclampsia bolster the study's findings, says Petty.

"Pre-eclampsia has features of inflammatory disease. If you don't reduce these pyruvate levels, you heighten inflammatory disease," he adds. Petty wonders whether one day enzyme levels could be tested early in pregnancy to predict the likelihood of developing pre-eclampsia or other

complications.

It is possible, says Petty, that the general mechanisms described in the current study may apply to more than one complication of pregnancy. This possibility—and that of designing drugs to suppress pyruvate kinase activity—is the focus of future research. "I have a long list of things I'd like to see developed for the clinic in the next five years," adds Petty.

More information: Leukocyte Pyruvate Kinase Expression Is Reduced in Normal Human Pregnancy but Not in Pre-eclampsia. Amer J Reprod Immunol, online 6.15.10 at [www3.interscience.wiley.com/cgi.../123525215/HTMLSTART](http://www3.interscience.wiley.com/cgi-bin/jpages/123525215/HTMLSTART)

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