

Important cause of preeclampsia discovered

21 January 2021, by Anne Sliper Midling



The results of many years of research have been a long time coming. Gabriela Silva (in a white coat) used tissue samples from a biobank, including placenta samples from 90 women with preeclampsia obtained immediately after birth. The samples were examined using advanced microscopes. Credit: NTNU

Despite being the subject of increasing interest for a whole century, how preeclampsia develops has been unclear—until now.

Researchers believe that they have now found a primary cause of [preeclampsia](#).

"We've found a missing piece to the puzzle. Cholesterol crystals are the key and we're the first to bring this to light," says researcher Gabriela Silva.

Silva works at NTNU's Centre of Molecular Inflammation Research (CEMIR), a Centre of Excellence, where she is part of a research group for [inflammation](#) in pregnancy led by Professor Ann-Charlotte Iversen.

More effective treatment possible

The findings are good news for the approximately three percent of [pregnant women](#) in Norway who

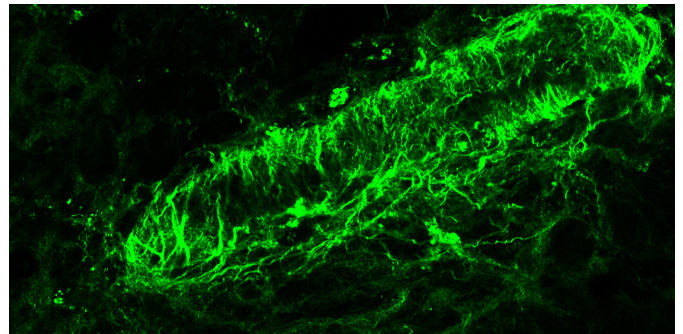
get this disease. Worldwide, preeclampsia is a leading cause of illness and death in both mother and fetus.

In a [preeclamptic pregnancy](#), the placenta does not develop properly, and the baby sometimes also receives too little nutrition.

The symptoms of preeclampsia are often mild, but in some cases the condition becomes so severe that the baby needs to be delivered prematurely.

Preeclampsia does not disappear until the baby is born. Since no one has understood why the condition occurs, the current treatment is to monitor and alleviate the symptoms.

Silva believes that future treatment will now become more effective.



Through advanced microscopes, the researchers were able to detect the cholesterol crystals. Here is a vein from the uterine wall. The green is both cells and a fiber-forming protein. Credit: NTNU

Cholesterol checked in uterine wall and placenta

"A pregnancy is actually a kind of natural inflammatory condition, and in the case of preeclampsia, the inflammation has become too strong and leads to disease," Silva says.

Women who have had preeclampsia have an [increased risk](#) of developing cardiovascular disease later in life.

It was precisely this connection that led the researchers to choose to examine cholesterol in pregnant [women](#) with preeclampsia. Cholesterol is a major cause of cardiovascular disease.

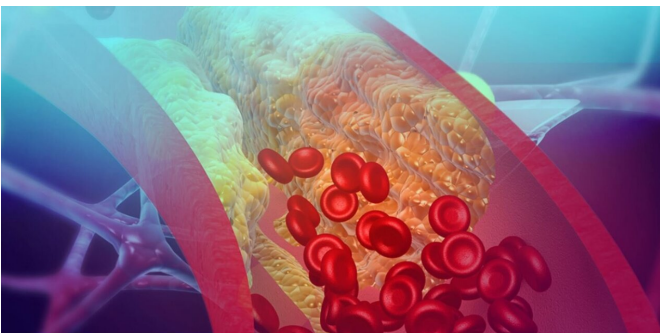
Cholesterol crystals are found in plaque that clogs blood vessels. The crystals are formed when bad cholesterol accumulates in the blood vessel walls. Studies have shown that [cholesterol crystals](#) are a particularly powerful initiator of inflammation in the body and can cause the blood to clot.

When the immune response runs wild

Cholesterol crystals are identified as harmful substances in the body that need to be cleared out. But the defense cells that come in to do the job aren't able to break them down. They call for reinforcements, and more immune cells come in, to no avail. The [immune response](#) runs wild, and the inflammatory process escalates.

Silva found that the inflammation was at its highest in the region called the maternal-fetal interface, where the mother's cells come into direct contact with fetal cells. This happens in the placenta and uterine wall.

"This direct contact means that the inflammation directly affects the communication between mother and fetus and contributes to even greater inflammation in the mother," says Silva.



The heart pumps about five litres of blood through the

body every minute. The blood vessels that carry blood from the heart become clogged with something called plaque. Cholesterol crystals are found in plaque. Credit: NTB scanpix

All pregnant women have high cholesterol levels

Cholesterol levels are high in all pregnant women, because both the fetus and the placenta need cholesterol. But levels were even higher in women with preeclampsia. They also had much more of the bad cholesterol, which is the type of cholesterol found in people who are at high risk for cardiovascular disease.

Silva went to great lengths to solve the riddle. She used tissue samples from a biobank that the research group at CEMIR has built up, and included placenta samples from 90 women with preeclampsia obtained immediately after birth. The researchers therefore had [tissue samples](#) from both the uterine wall and the placenta. The samples were examined using advanced microscopes.

It has taken years of research to arrive at the result.

Women at risk should have their cholesterol checked

Future treatment for preeclampsia may simply include cholesterol-lowering medications, such as statins, but further research is needed to clarify their effects.

"Some women have an increased risk of preeclampsia right from the start. They should be followed up with a [cholesterol](#) check. This isn't done regularly today, but it should be done regularly in the future. The use of statins during pregnancy is not recommended now, but several [clinical studies](#) are looking more closely at this and are showing that pravastatin, for example, can be safe to use during pregnancy," says Silva.

More information: Gabriela Brettas Silva et al. Cholesterol Crystals and NLRP3 Mediated Inflammation in the Uterine Wall Decidua in Normal

and Preeclamptic Pregnancies, *Frontiers in Immunology* (2020). DOI: [10.3389/fimmu.2020.564712](https://doi.org/10.3389/fimmu.2020.564712)

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