Explosive compound reduced blood pressure in the female offspring of hypertensive rats

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The explosive organic compound pentaerythritol tetranitrate (PETN) might one day allow pregnant women to protect their daughters from developing high blood pressure before they're born, according to an animal study published in the American Heart Association's journal *Hypertension*.

Researchers assessed the effect of PETN on pregnant rats with high blood pressure and their offspring. Pregnant rats were fed food mixed with 50 mg/kg of PETN every day during pregnancy and lactation periods.

Researchers found that PETN had no effect on blood pressure in the parent rats. However, surprisingly the researchers did observe a drop in blood pressure in the female offspring but not in male offspring. The systolic blood pressure (top number) of the female offspring rats were about 10 mm Hg to 13 mm Hg lower compared to the offspring of pregnant rats not given PETN.

PETN is in the same chemical family as nitroglycerin (component in dynamite) and nitrocellulose (main component in gunpowder).

"Like nitroglycerin, PETN is an organic nitrate and an explosive compound," said Dr. Huige Li, M.D., Ph.D., co-author of the study and professor in the Department of Pharmacology at the University Medical Center, Johannes Gutenberg University in Mainz, Germany.

"In the clinic, both compounds are used in treating coronary heart disease. For the relief of acute chest pain, nitroglycerin is preferred because of its rapid action. For the prevention of chest pain as a long-term medication, however, nitroglycerin is not continuously effective because of the phenomenon known as nitrate tolerance. PETN has an important advantage in chronic use. At least in animal studies, PETN doesn't cause nitrate tolerance."

The fact that PETN had no effect on blood pressure in the parent rats, but reduced blood pressure in the female offspring, suggests that PETN is not directly responsible for the blood pressure lowering effect observed in the study. Rather researchers believe PETN may have modified genes in the female offspring to produce more molecules that help relax blood vessels; ultimately lowering blood pressure in the offspring rats.

"While the pre-birth programming effect of PETN shows promise for future clinical implications, we must be careful about generalizing findings from animal studies to humans," Li said.

PETN was part of a past human clinical trial involving 111 pregnant women with a condition that reduced the blood flow going to and from the placenta (abnormal placental perfusion). Results in the German study showed that PETN treatment may have helped decrease the risk of preterm birth and poor growth of a baby while in the mother's womb.

"As promising as these early results are, medications during pregnancy should be used with great caution," Li said. "We should first evaluate the blood pressure development and the long-term safety in the children of such PETN-treated patients, before considering maternal PETN treatment as a therapy option for hypertension in humans."