MedicalXpress

A procedure used in preconception diagnosis can lead to problems with pregnancies

April 7 2011

A new study demonstrates that a procedure used in preconception diagnosis to identify eggs that are free of genetic disease might not work well in all cases. The research, published by Cell Press in the April issue of the *American Journal of Human Genetics*, highlights the issues associated with analyzing the amount of mutant mitochondrial DNA in supporting cells as a proxy for eggs prior to in vitro fertilization.

Preimplantation genetic diagnosis (PGD) and preconception diagnosis (PCD) are services that have been very useful to couples who have a genetic defect in their family. "PGD and PCD represent alternatives to conventional prenatal diagnosis for couples who have a high risk of giving birth to a child affected with a serious genetic disorder … and can prevent the anxiety associated with a prenatal diagnosis procedure and the optional termination of the pregnancy," explains lead study author Dr. Julie Steffann from the Université Paris-Descartes and Hôpital Necker-Enfants Malades in Paris, France. The processes involve performing genetic diagnostics on a cell removed from a developing embryo, in the case of PGD, or from a cell called a polar body, which supports the unfertilized egg, in the case of PCD. Those embryos and eggs that are found to be free of mutations are then considered safe to proceed with through pregnancy.

Dr. Steffann and colleagues Nadine Gigarel, and Jean-Paul Bonnefont, and Arnold Munnich from the Université Paris-Descartes and Hôpital Necker-Enfants Malades and David Samuels from Vanderbilt University Medical Center in Nashville, TN show that assuming the polar body has

a genetic make-up that matches that of the unfertilized egg can be complicated in some cases. The polar body divides from the egg when the egg develops, so it was thought that it could serve as a proxy for the egg and that testing it would allow a genetic diagnosis to be made without harming the egg. This is true for genes in the nuclear DNA, but the authors show that things are different for genes in the mitochondria.

If a person has a mutation in mitochondrial DNA, it can be present in all of the mitochondria or in a percentage of the mitochondria. This is referred to as mutant load. If the mutant load is high, the person can have the disease associated with that mutation, but if the mutant load is low enough, the person can be healthy. For these reasons, clinicians performing PCD want to select eggs with a low mutant load. In this work, Dr. Steffann and colleagues show that there is a poor correlation between the mutant load of mitochondrial DNA in an egg and that of its polar body. Finding a low mutant load in a polar body doesn't mean that the mutant load will be low in the associated egg; this could lead to incorrect conclusions regarding which eggs are safe to use for pregnancy.

"Our findings argue against the use of the polar body as a diagnostic material for mtDNA disorders, unless the purpose is for the selection of embryos that are completely mutation free," concludes Dr. Steffann. "Indeed, all mutation-free polar bodies were found to be associated with mutation-free eggs. Unfortunately, because the number of mutation-free eggs is low in women who have mtDNA mutations, the PCD option would dramatically decrease the successful pregnancy rate."

Provided by Cell Press

preconception-diagnosis-problems-pregnancies.html