Miscarriage clues identified in new DNA test

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New research shows an alternative DNA test offers clinically relevant genetic information to identify why a miscarriage may have occurred years earlier. Researchers were able to identify chromosomal variants and abnormalities in nearly 50 percent of the samples. This first-of-its-kind study was conducted by researchers from Montefiore Medical Center and the Albert Einstein College of Medicine of Yeshiva University. The results were published in the March issue of *Reproductive Biology and Endocrinology*.

The technique used in this study, called rescue karyotyping, allows physicians to obtain important genetic information from tissue that had not been tested at the time of the miscarriage. As part of standard hospital protocol, tissue from miscarriages is embedded in paraffin for archival use and the karyotyping test is performed on DNA extracted from this tissue.

In this retrospective study of 20 samples from 17 women, genetic testing was successfully performed on 16 samples that had been archived for as long as four years. Of those samples, eight showed chromosomal variants and abnormalities. This is an important alternative when conventional karyotyping is not available or cannot be used for a specific sample.

"Given the ease of obtaining results, even if a delay in testing occurs, this new test may provide a useful technique to gain a better understanding as to why miscarriage occurs in some women," said Zev Williams, M.D., Ph.D., director, Program for Early and Recurrent Pregnancy Loss (PEARL), Montefiore and Einstein, assistant professor of obstetrics &

gynecology and women's health and of genetics at Einstein, and corresponding author of the study. "I have seen women in tears because testing was not done at the time of the miscarriage and they feared they would never learn why it happened. Now we are able to go back and often get the answers we need."

One in five pregnancies ends in miscarriage, with the vast majority occurring in the first trimester. Recurrent miscarriage, which is defined as two or more miscarriages, occurs in up to 5 percent of couples attempting to conceive. Led by Dr. Williams, PEARL is comprised of a team of expert physicians, scientists, genetic counselors, nurses, technicians and staff members who work together to help these women maintain their pregnancies.

"Montefiore and Einstein have worked together to develop an innovative model based on research, which allows us to create novel diagnostic and treatment options and, in parallel, to quickly bring new advances to the clinic," said Dr. Williams. "This represents a new and emerging model in medicine – where the lab and clinic are brought closer in order to speed the pace of discovery and treatment."

"Most miscarriages are caused by an abnormal number of chromosomes in the embryo, accounting for up to 75 percent of first trimester losses," continued Dr. Williams. "This new test can help guide future treatment options but, more importantly, can also help alleviate some of the guilt and self-blame often associated with unexplained miscarriage and can close a door on a painful chapter in a woman's and couple's life."

Dr. Williams is a board certified obstetrician gynecologist with specialty training in reproductive endocrinology and infertility. He received his M.D. and Ph.D. degrees from the Mount Sinai School of Medicine and trained in Obstetrics and Gynecology at Harvard Medical School's Brigham and Women's Hospital and the Massachusetts General Hospital.

Dr. Williams completed a fellowship in Reproductive Endocrinology and Infertility at Weill-Cornell Medical Center.

The title of the paper is "Rescue karyotyping: a case series of array-based comparative genomic hybridization evaluation of archival conceptual tissue." Additional study authors include: Rashmi Kudesia, M.D., Montefiore-Einstein; and Marilyn Li, M.D., Janice Smith, M.D. and Ankita Patel, M.D., Baylor College of Medicine.

Provided by Albert Einstein College of Medicine