

PREIMPLANTATION GENETIC DIAGNOSIS (PGD) AS BOTH A DIAGNOSTIC AND THERAPEUTIC TOOL IN ASSISTED REPRODUCTIVE TECHNOLOGY

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People who have not undergone a Fertility medical treatment may not know that in In Vitro Fertilization, some of the embryos produced as part of the process are implanted in the would be mother, and the remainder of these embryos may be frozen for possible later use. How many embryos to implant and which ones to implant are decided upon by a Reproductive Endocrinologist and his/her team of experts. The science of this selection process has taken a huge leap forward with the recent improvements in abilities to read the Human Genome.

Success rates in IVF are dependent on a number of factors. Age of the egg, quality of the embryos, receptivity of the endometrial lining are all possible factors. More recently, we have now begun to look at the embryo itself from a genetic standpoint, as being a factor with respect to success.

Recently, the technique, Preimplantation Genetic Diagnosis (PGD) has been utilized in an effort to improve success in Assisted Reproductive Technology. In a PGD procedure one is able to determine either the chromosomal make up of an embryo, or to look at specific single gene defects such as Cystic Fibrosis or Sickle Cell Anemia. Up to this point, Chorionic Villus Sampling and Amniocentesis have been used to evaluate these abnormalities, however these events occur after the pregnancy has been achieved.

The Genesis Network for Reproductive Health, funded by an educational grant from Organon, Inc, recently conducted an IRB approved, randomized, prospective study evaluating three (3) high-risk groups of patients which may be at greater risk for genetically abnormal embryos/aneuploidy. These three high-risk groups include 1.) Recurrent Pregnancy Loss (RPL), 2.) Advanced Maternal Age (AMA), which we define as greater than 38 yrs of age, and 3.) Repeated failed IVF cycles (FC), defined as greater than two (2) failed cycles. A total of 57 patients have been enrolled in phase one of the study from 8/1/01 - 8/30/02. All patients were randomized into either control or PGD. All underwent various stimulation protocols, followed by ultrasound guided oocyte retrieval and ICSI on all mature oocytes. In the PGD group, embryo biopsy and blastomere fixation was done on Day #3 post retrieval on all 6-8 cell embryos. Fluorescent Insitu Hybridization (FISH) analysis for chromosomes 13, 15, 16, 17, 18, 21,22, X and Y were performed at St. Barnabas hospital in New Jersey. Results were received on Day #4-5 post retrieval, and embryo transfer was done on Day #5 post retrieval. In the control group, embryo transfer was done on Day #3 or Day #5 post retrieval, based on physician preference.

Overall, in all 3 groups, 63% of embryos biopsied were abnormal. Approx 30% of women who underwent PGD had no embryo transfer due to all embryos being abnormal.

In the RPL/PGD group, 63.6% achieved pregnancy, as compared to 37.5% of the controls. In the AMA/PGD group 43% achieved pregnancy, as compared to 25% of the controls. Finally, in the FC/PGD group 20% achieved pregnancy, as compared to 0% of the controls. Overall, for all 3 PGD groups, the

pregnancy rate was 43% as compared to 27% for the controls. Although the numbers are still small, it appears that the overall pregnancy rate between the PGD and the control groups approaches statistical significance.

In conclusion, a number of findings were evident.

- 1) PGD confirms that aneuploidy is a common cause of RPL.
- 2) It appears that in patients with RPL, the trend indicates that PGD may be beneficial.
- 3) It is not clear as yet, whether PGD is beneficial in the AMA group.
- 4) PGD clearly offered no benefit in the FC group.
- 5) In view of the large numbers of abnormal embryos in each group, couples may consider alternative options earlier such as donor oocytes, donor embryos, and/or adoption.

There are also drawbacks to PGD. At the present time we can only look at 9 specific chromosomes mentioned above for aneuploidy. Clearly there are 14 other chromosomes that we do not screen. Newer technologies such as Comparative Genomic Hybridization (CGH) will allow us in the future to look at all 23 chromosomes. With the rapid speed that PGD has developed, gray areas remain. The most obvious concern is ensuring that ethical standards are applied to the practice and rigid guidelines are established. Further discussions will ensue to address these issues.

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