PREIMPLANTATION GENETIC DIAGNOSIS (PGD) FOR THERAPY AND DIAGNOSIS IN IVF

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IVF success rates are dependent on a variety of factors. Age of the oocyte, embryo quality, and endometrial lining receptivity are all possible factors. Recently, we have begun to look directly at the embryo from a genetic standpoint as being a factor with respect to success.

For each IVF cycle, the Reproductive Endocrinologist and his/her team must decide which of the many embryos produced are to be implanted and which not. The effectiveness of that decision is the ultimate determinant of the success of the cycle. Recent enhancements in abilities to read the Human Genome have brought greater science to this process of embryo selection.

The improvements mentioned above have found their place in the IVF process through a procedure called Preimplantation Genetic Diagnosis (PGD). 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 Tay Sachs Disease, Cystic Fibrosis or Sickle Cell Anemia. Up to this point, Chorionic Villus Sampling and Amniocentesis have been used to evaluate these abnormalities, however these tests occur after 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. Flourescent 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.

Though PGD is already very beneficial, it is in its infancy and will no doubt be enhanced in the future. There are 14 chromosomes that we do not screen through PGD. At the present time we can only look at 9 specific chromosomes mentioned above for aneuploidy. Newer technologies such as Comparative Genomic Hybridization (CGH) will allow us in the future to look at all 23 chromosomes. Also, there is an obvious concern that ethical standards must be applied to the application of PGD and rigid guidelines for its uses must be established. Further discussions will ensue to address these issues.

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