Further Development 14.7

Preimplantation Genetics

One of the consequences of in vitro fertilization and the ability to detect genetic mutations early in development is a new area of medicine called preimplantation genetics. Preimplantation genetics seeks to test for genetic disease *before* the embryo enters the uterus. After that, many genetic diseases can still be diagnosed before a baby is born. This prenatal diagnosis can be done by chorionic villus sampling at 8–10 weeks of gestation, or by amniocentesis around the fourth or fifth month of pregnancy.

Chorionic villus sampling and amniocentesis

Chorionic villus sampling involves taking a sample of the placenta, whereas amniocentesis involves taking a sample of the amnionic fluid. In both cases, fetal cells from the sample are grown and then analyzed for the presence or absence of certain chromosomes, genes, or enzymes.

However useful these procedures have been in detecting genetic disease, they have brought with them serious scientific and ethical concerns. The scientific concern involves the chorion being used as a proxy for the embryo. Recent studies (Coorens et al 2021; Costello and Fisher 2021) have shown that the placenta can sustain many more chromosomal anomalies than can the embryo. The placenta has a much higher percentage of abnormal cells than the embryo does. This could mean that a healthy fetus might be aborted because its placental cells were abnormal.

There are also ethical problems, as well. If a fetus were found to have a genetic disease, the only means of prevention presently available is to abort the pregnancy. The need to make such a choice can be overwhelming to prospective parents.* Indeed, the waiting time between knowledge of being pregnant and the results from amniocentesis or chorionic villus sampling has created a new phenomenon, the “tentative pregnancy.” Many couples do not announce their pregnancy during this stressful period for fear that it might have to be terminated (Rothman et al. 1995).

By using IVF, one can consider implanting only those embryos that are most likely to be healthy as opposed to aborting those fetuses that are most likely to produce malformed or nonviable children. This can be achieved by screening embryonic cells before the embryo is implanted in the womb. While the embryos are still in the petri dish (at the 6- to 8-cell stage), a small hole is made in the zona pellucida and two blastomeres are removed from the embryo. Since the mammalian egg undergoes regulative development (see Chapter 12), the removal of these blastomeres does not endanger the embryo, and the isolated blastomeres are tested immediately. The polymerase chain reaction technique can be used to determine the presence or absence of certain genes to be determined, and fluorescent in situ hybridization (FISH) can be used to determine whether the normal numbers and types of chromosomes are present (Kanavakis and Traeger-Synodinos 2002; Miny et al. 2002). Results are often available within 2 days. Presumptive wild-type embryos can be implanted into the uterus, while any presumptive embryos with deleterious mutations are discarded.

Sex selection and sperm selection

The same procedures that allow preimplantation genetics also enable the physician to know the sex of the embryo. Sometimes parents wish to have this information; sometimes they do not. However, knowing the sex of an embryo prior to its implantation raises the possibility that parents could decide to have only embryos of the desired sex implanted. Sex selection using preimplantation genetics is seen by many as a beneficial way of preventing X-linked diseases, but in fact it is often used as a method of simply choosing one's offspring's sex. Opponents of sex selection point to its possible use as a method of preventing the birth of girls in cultures where women are not as highly valued as men (see Gilbert et al. 2005; Zhu et al 2009). This has created enormous discrepancies in the sex ratio of several regions. Different countries and even different hospitals have different policies permitting preimplantation genetic diagnosis solely for the purpose of sex determination.

Preimplantation Genetic Haplotyping and Editing

In addition to being able to select the sex of one's child, new techniques in molecular biology have promoted a new, variation of PGD, sometimes called Preimplantation Genetic Haplotyping. Here, genes can be screened and some of the normal (not only disease) physical traits of the adult can be predicted. For example, we now know several genes for hair color, and a family might be able to choose to have a son with blond or red hair (see Gilbert et al 2005; Roberts 2006).

There are companies that have begun selling services to patients and hospitals, claiming that their "polygenic risk scores" will enable them to implant the embryos that should be the healthiest. However, this flies in the face of numerous developmental factors, including pleiotropy, developmental plasticity, and genetic heterogeneity and phenotypic heterogeneity (Turley et al 2021). These companies also have claimed that they can measure differences between embryos that relate to their educational attainment decades later. However, the genetic component to intelligence is less than 5% of the total (Snieckers et al 2017).

For some diseases, especially when the organ damage starts while the embryo is still developing, it is becoming possible to replace the missing proteins in utero. Enzyme-replacement therapy (ERT) is being tested on fetuses whose genomes will not produce certain necessary proteins. In the form of Pompe's disease where the fetus lacks acid a-glucosidase, the heart already shows structural anomalies at birth. Replacing this enzyme through intrauterine transfusions, a baby with this genetic prognosis was born with a normal heart (Cohen et al 2022). Moreover, by using CRISPR technology (see pp 88-89), it may soon be able to alter the genes of preimplantation embryos (or germ cells) to give parents a designed baby. This has generated an important ethical debate among scientists and policy makers (see Baltimore et al 2015; Cyranosky 2015; Lanphier et al 2015; Sugarman 2015).

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