**<FURTHER DEVELOPMENT 14_05>**

## The IVF procedure: In Vitro fertilization procedure and risks

Worldwide, over nine million children have been conceived through assisted reproductive technologies. In Europe, as many as 6% of newborns have been conceived this way (De Geyter et al 2018; ESHRE 2020).

The IVF procedure has four basic steps, outlined below.

- **Step 1: Ovarian stimulation and monitoring.** Having several mature eggs available for IVF increases the possibility that at least one will result in a pregnancy. Typically, women are injected with gonadotropins or anti-estrogens over a period of days or weeks to "hyperstimulate" the ovaries to produce several mature oocytes.
- **Step 2: Egg retrieval.** Once the follicle has matured (but not yet ruptured), the physician attempts to retrieve as many eggs as possible. Although they are usually called eggs, the female gametes about to be ovulated are actually metaphase II oocytes (see Chapter 19). The physician retrieves the oocytes surgically, guiding an aspiration pipette to each mature follicle and sucking up the oocyte. Once the oocytes are recovered, those that are mature and healthy are transferred to a sterile container to await fertilization in the laboratory.
- **Step 3: Fertilization.** A semen sample is collected from the male partner approximately 2 hours before the female partner's oocytes are retrieved. These sperm are then processed (a procedure called sperm washing) using various techniques. Sperm washing capacitates the sperm and selects only the healthiest and most active sperm in the sample. The selected sperm are then placed in a petri dish with the oocytes, and the gametes are incubated at body temperature. In general, each oocyte is incubated for 12-18 hours with 50,000 – 100,000 motile sperm. The success rate for fertilization is between 50-70%. If fertilization is successful, the eggs will begin to divide, and the resulting embryos will shortly be ready to be transferred into the uterus
- **Step 4: Embryo transfer.** Embryo transfer is not a complicated procedure and can be performed without anesthesia or surgery. It is usually done 3 days after egg retrieval and fertilization. The physician looks for healthy embryos (those that have divided well,

containing 6 – 8 cells). The embryos are sucked into a tubular instrument called a catheter. The physician then inserts the catheter through the female partner's vagina and cervix in order to place the embryos directly into the uterus. Normal implantation and maturation of at least one embryo is required to achieve pregnancy.

In cases in which fertilization has been achieved in vitro, but after a number of cycles, implantation into the uterus fails, the physician may suggest "assisted hatching," in which a small hole is lysed in the zona pellucida prior to inserting the embryo into the uterus  This procedure ensures that the embryo will be able to hatch from the zona pellucida in time to adhere to the uterus.

**Ethical issues concerning IVF**

IVF and other means of assisted reproductive technology (ART) began as a way of allowing infertile couples to become pregnant. This technique has been successful, in that the rates of deliveries are just about equal to those achieved by normal fertilization. However, this technology has raised several ethical (and legal) concerns (see Purdy 2001; Pinto-Correia and Gilbert 2017).

- **Whom does it assist?** States differ widely in their mandating that insurance companies cover infertility treatments. Couples may pay $10,000 for a cycle of IVF in the United States. Couples often pay between $50,000 and $200,000 to achieve a single pregnancy (Andrews 1999; Caplan 2005). Is ART only for the wealthy? If a woman with infertility knows that she could possibly have a genetically related child if she were wealthy, does this frustrate more women than it helps? If curing infertility is our goal, then should our focus be on high-tech medicine or on public health efforts to eliminate sexually transmitted diseases (one of the leading causes of infertility)?
- **Is there a "right" to have a genetically related child?** Are procedures designed to allow 50-year-old women to have babies the best use of our medical resources?

- **Why is there a "need" to have genetically related children?** Is this desire "biological" or is it being manufactured by the advertising done by fertility clinics competing with one another in the present market?

- **What is the status of a frozen embryo?** Is throwing away the extra embryos produced by IVF equivalent to abortion? Who has the right to keep the embryos if the couple should divorce? (And is the biological father obligated to make child support payments if the embryo is implanted and comes to term?) It is estimated that there are 400,000 frozen embryos currently in storage (Hoffman et al 2003).

- **Are current ART procedures safe for mothers and offspring?** While the link between hormones and reproductive cancers has been known for years, it is not known whether women undergoing extensive cycles of ART are at risk for cancers (see Pappert 2000.) The first step of the IVF procedure involves the hyperstimulation of the ovaries. About 5% of the women who are hormonally hyperstimulated acquire a syndrome involving the enlargement of the ovaries, nausea, vomiting, and stomach cramps. In severe cases of ovarian hyperstimulation syndrome, the woman will experience persistent nausea and vomiting, dizziness, severe abdominal pain, rapid weight gain, and respiratory distress that might require hospitalization (Mayo Clinic 2014; 2019).

Another complication comes when more than one embryo is implanted into a woman's uterus. Medical complications are associated with twin and triplet pregnancies for both the woman and her babies. Twins are often born prematurely, and they have more risk of having developmental anomalies such as spina bifida, cerebral palsy, and heart defects. Women carrying twins or triplets have higher risks for anemia, hypertension, and miscarriage (JHUMed 2021). With improved techniques of IVF, physicians are now implanting fewer embryos than in previous years. Most singleton babies born from IVF are as healthy as those born through natural conception (Squires and Kaplan 2007; Hart and Norman 2013). However, the oldest IVF-conceived people are now only in the fourth decade. It is not yet known if they will have metabolic changes as they grow older (Naraparedy et al 2020).

- **Should infertility clinics be regulated?** In contrast to Great Britain, where there are strict laws regulating what infertility clinics can do and how they must report their results, infertility clinics in the United States are not under federal or state regulations. It is often difficult to compare success records or health records between clinics. Indeed, what is an "experimental" treatment in one hospital might be considered "standard" treatment in another.

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