## **Egg Donor Protocol and Risks**

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Donating eggs for stem cell research is similar in many respects to donating eggs for infertility centers. The goal is to stimulate the ovaries to ripen several eggs instead of just one. The greatest risks are over-response to the ovarian stimulation, and adverse response to anesthesia. A brief review of the normal ovarian cycle will clarify the goals and the risks.

Women are born with on the order of one million eggs. They are quiescent in the ovary in a state of arrested development. The onset of menstruation (Day 1) coincides with the lowest levels of steroid hormones in circulation. The pituitary gland in the brain releases hormones that stimulate the ovary to recruit a quiescent, immature egg to grow and finish maturation. The hormones are termed "gonadotropins" because they stimulate the ovary in women and the testis in men.

In response to the pituitary hormones, the ovary synthesizes and releases estrogen into the blood stream, sending a feedback signal to the pituitary. In response to estrogen feedback, the pituitary produces a bolus of gonadotropin on Day 14 that causes the egg to finish its maturation cycle and be released from the ovary into the female reproductive tract.

In order to mature a cohort of 5 to 10 eggs for research purposes, it is necessary to override the natural pituitary stimulation, and to administer higher than normal amounts of gonadotropins. The pituitary can be suppressed by a variety of hormones, including birth control pills and Lupron. Gonadotropins must be administered by subcutaneous injection, analogous to insulin. High amounts of gonadotropins increase the number of eggs collected, and also the risk of "ovarian hyperstimulation syndrome," a serious potential risk of egg donation.

Uncomfortable side effects of taking Lupron for extended periods of time to suppress other estrogen- responsive conditions, such as uterine fibroids, have been reported by many women. These side effects can be avoided by several approaches, including not using Lupron.

Ovarian hyperstimulation syndrome can be avoided entirely by administering relatively low doses of gonadotropins and carefully measuring the estradiol response in the blood stream. At the first sign of an over response, discontinuing the gonadotropins will eliminate the risk. The long-term risks of taking increased levels of gonadotropins will not be known for another decade or two, but are throught to be low. Risks are further limited by not undergoing more than 2 or 3 cycles of egg collection.

Following about 10 to 12 days of daily gonadotropin injections, eggs are recovered

directly from the ovary a few hours before being spontaneously released into the reproductive tract. This is done under anesthesia, usually not "general" anesthesia, but a short-acting anesthesia. One way to avoid adverse reactions to anesthesia is to accept as donors only women with a record of anesthesia exposure with no problems.

The emotional risks of egg donation include hormone-induced depression and the stress of daily injections and frequent trips to the laboratory for hormone measurements and the doctor's office for ultrasound examinations. The suitability of the donor and her schedule are considered important factors in recruitment.

Donor recruitment includes a full explanation of the science, the risks, the consent form, and a careful assessment that the donor is participating of her own free will out of an interest in moving science forward.

Donating eggs for stem cell research is a serious undertaking, not to be entered into without several months of consideration of all the factors involved.

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