

## When the "Change" Comes Early.

The loss of ovarian function is a gradual process for most women with the hallmark of menopause being the total cessation of menstrual flow. The average age for this event is 51 years of age in the United States. However, 1% of women will experience the loss of ovarian function before 40 years of age. Early menopause or premature ovarian failure (POF) may be accompanied by the classic symptoms of hot flashes, vaginal dryness, or difficulty sleeping. The loss of one's period may also be preceded initially by a shortening of the interval between periods or increased amount of menstrual flow. Subsequently, many women report skipping periods or a decrease in the amount of their menses. However, some women have no symptoms or almost imperceptible changes in their cycles prior to the seemingly sudden onset of menopause. Others may only become aware of this condition when they stop oral contraceptives or attempt to conceive. Often times, these women are faced with this "bad news" when they seek care for infertility and are told that their lab tests indicated that they have poor or absent ovarian function. Up to 10% of women who have difficulty getting pregnant due to infrequent or absent ovulation may have POF.

The classic definition of POF includes an elevation of FSH above 40 mIU/ml measured in the early part of the menstrual cycle on two occasions. FSH is one of the brain regulators of ovarian function and leads to the production of estrogen. Fertility begins to decline dramatically when the FSH is in the teens and pregnancy is unlikely to occur either spontaneously or from fertility treatments when the FSH is above 20. However, rare spontaneous pregnancies have been reported even with levels well above 40. Other hormones, such as anti-mullerian hormone (AMH) or inhibin, as well as ultrasound assessment of small or antral follicles in the early part of the menstrual cycle may also be used to predict one's potential for fertility or ovarian reserve.

One of the confusing aspects of this condition, is that the ovarian function will often "wax and wane". This intermittent function accounts for the occasional return of menses and the rare spontaneous pregnancies. Autoimmunity or immune dysfunction may account for the intermittent nature of this condition. A patient may experience "flares" or immune attacks that only temporarily disable the ovary before resulting in complete failure. Abnormal immune function may also account for the fact that women with POF are more likely to develop problems with other hormonal systems. In fact, ovarian failure may even present as part of a syndrome of multi-glandular dysfunction with other endocrine problems often involving the thyroid or adrenal glands. Surgical removal of the ovaries or damage that occurs as a result of radiation or chemotherapy is a more obvious reason for POF. Other causes such as enzyme deficiencies, chromosome defects, or immune dysfunction are rare and a large percentage of women with POF have no explanation for their condition. In addition to a thorough physical exam, the evaluation of POF may include blood test for chromosomes, thyroid and adrenal function with antibodies, and a diabetes screen. A complete blood count as well as liver and kidney function test are often warranted. More specialized test including autoimmune or genetic screening may be done if symptoms suggest other associated factors. It is also important that the woman with POF, weigh the risk and benefits of hormone replacement

therapy to avoid the serious complications of this early menopause, most notably osteoporosis.

The diagnosis of premature ovarian failure has a tremendous impact on a couple's desire to achieve a successful pregnancy. Although many couples pursue adoption, In Vitro Fertilization (IVF) using donor eggs or oocytes allows a woman to achieve pregnancy in the majority of cases. One may choose to utilize donated eggs from an anonymous donor who matches their family's ethnic background and physical characteristics, while others prefer to rely on assistance from a relative or friend. After an extensive screening and matching process, the donor undergoes an IVF cycle in which she takes fertility medications to stimulate her ovaries. When ultrasound and laboratory testing indicates that the eggs are mature, they are retrieved through the vaginal in an outpatient surgery setting under anesthesia. The oocytes are then combined with the partner's sperm in the IVF lab and monitored for 3 – 5 days before being transferred to the patient's uterus. The recipient of the eggs takes estrogen initially, and then progesterone to prepare the lining of her uterus for pregnancy. Fortunately, the lack of normal ovarian function has no adverse effect on the uterus' ability to carry a healthy, normal pregnancy. In fact, many fertility practices have a comprehensive donor oocyte program with pregnancy rates that approach or exceed 70%. In other words, approximately 7 out of 10 women who undergo a transfer of a donated oocyte experience a successful delivery. Although the donor egg IVF program is not without financial, physical and emotional challenges, this option offers tremendous hope and a high rate of success. One's desire to expand their family can be achieved even when "the change" comes early.