



## PATIENT'S FACT SHEET

# Side Effects of Gonadotropins

Gonadotropins are fertility medications given by injection. They contain follicle-stimulating hormone (FSH), which is produced naturally by the pituitary gland, alone or combined with luteinizing hormone (LH), also produced by the pituitary gland. A related medication is human chorionic gonadotropin (hCG) which is structurally similar to LH and which simulates the natural LH surge that causes ovulation at midcycle.

Gonadotropins are used to induce follicular development and ovulation in women who do not ovulate. They also are used to induce development and ovulation of multiple follicles in women undergoing advanced reproductive therapies such as in vitro fertilization or superovulation and intrauterine insemination. HCG is commonly used to trigger ovulation once follicles have developed to maturity. There are a variety of gonadotropins commercially available and others in various stages of research and development. Careful monitoring of patients is required when gonadotropins are used in order to minimize the risk of side effects:

**1. Ovarian Hyperstimulation Syndrome (OHSS).** OHSS is characterized by enlarged ovaries and fluid accumulation in the abdomen after ovulation or egg retrieval. It can be either mild or severe. The mild form occurs in 10% to 20% of cycles and results in some discomfort but almost always resolves without complications. The severe form occurs approximately 1% of the time. The chance of OHSS is increased in women with polycystic ovarian syndrome and in cycles resulting in pregnancy. When severe, it can result in blood clots, kidney dysfunction, twisting of an ovary (torsion), fluid collections in the chest and abdomen, and rarely even death. In severe cases, hospitalization is required for monitoring but the condition is transient, usually lasting only a week or two. Occasionally, draining the excess fluid is needed to decrease symptoms. Most patients who are at high risk for severe OHSS are identified by closely monitoring ovulation induction cycles with the daily use of ultrasounds and/or serum estradiol levels. When serum estradiol levels are rising rapidly and/or are too high, or excessive numbers of ovarian follicles develop, one strategy for prevention of severe OHSS is to withhold further gonadotropin stimulation and delay hCG administration until estradiol levels plateau or decline. Alternately, hCG can be withheld so that ovulation fails to occur, thereby preventing severe OHSS. In some IVF cycles in which OHSS is felt to be a high likelihood, a recommendation may be made to administer hCG, retrieve oocytes, but cryopreserve all embryos for use in future cycles.

**2. Multiple Gestation.** Up to 30% of pregnancies which result from cycles involving gonadotropin stimulation are multiple, in contrast to a rate of 1% to 2% without fertility medications. The risk of multiple gestation is dependent upon the number of mature eggs released in an ovulation induction cycle and the number of embryos transferred in an IVF cycle. While most of these pregnancies are twins, a significant percentage (up to 5%) are triplets or higher. Compared to singletons, twins and high order (more than two) multiple gestation pregnancy are associated with an increased risk of pregnancy loss, premature delivery, infant abnormalities, handicap due to the consequences of very premature delivery, pregnancy induced hypertension, hemorrhage, and other significant maternal complications. In general, the risk of severe complications increases as the number of gestations increases. There is a suggestion in some studies that the number of low birth weight in infants may be increased in even singleton pregnancies.

**3. Ectopic (Tubal) Pregnancies.** While ectopic pregnancies occur in 1% to 2% of spontaneous pregnancies in the general population, in gonadotropin cycles the rate is slightly increased. Ectopic pregnancies can be treated with medications or surgery. Occasionally a tubal pregnancy occurs at the same time as an intrauterine pregnancy; this condition is known as heterotopic pregnancy and may be difficult to diagnose.

**4. Adnexal Torsion (Ovarian Twisting).** In less than 1% of gonadotropin cycles the stimulated ovary can twist on itself, cutting off its own blood supply. Surgery is required to untwist or remove the ovary.

**5. Gonadotropins and Ovarian Cancer.** Although early studies suggested that the risk of ovarian cancer might be increased in women exposed to medications for ovulation induction, more recent studies have not shown any such relationship. It is generally felt that gonadotropin therapy does not increase the risk of ovarian cancer.

**6. Adverse Pregnancy Outcomes.** Although the vast majority of pregnancies are entirely normal, recent studies suggest the possibility that complications during pregnancy may be increased slightly. Pregnancy-associated hypertension and abruption of the placenta may be increased. It is not clear if the risks are related to the gonadotropin therapy or are related to the infertility.

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