Recombinant Gonadotropins Used in Fertility Treatments [1]

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First manufactured in 1988 by Serono laboratories, recombinant gonadotropins are synthetic hormones [5] that can stimulate egg [6] production in women for use in fertility treatments. Recombinant gonadotropins are artificially created using recombinant DNA technology, a technology that joins together DNA from different organisms. In vertebrates, naturally-occurring gonadotropins regulate the growth and function of the gonads, known as testes [7] in males and ovaries in females. Medical professionals can derive female gonadotropins from the urine of pregnant and post-menopausal women, often using it to facilitate fertilization [9], or IVF. With the rapid development of assisted reproductive technologies like IVF, demand for human-derived gonadotropins rose to a global yearly demand of 120 million liters of urine by the beginning of the twenty-first century, which resulted in a demand that could not be met by traditional technologies at that time. Therefore, researchers created recombinant gonadotropins to establish a safer and more consistent method of human gonadotropin [10] collection that met the high demand for its use in fertility treatments.

Within vertebrates, the endocrine system is responsible for creating naturally-occurring gonadotropins. Endocrine glands, such as the pancreas or the ovaries, secrete chemical messengers known as hormones [8] into the blood, where they flow throughout the body and influence cells that have a hormone’s corresponding receptors. Two of the main gonadotropic hormones [8], luteinizing hormone [11], abbreviated LH, and follicle-stimulating hormone [12], abbreviated FSH, are produced by a pea-sized gland in the brain called the pituitary gland [13]. Gonadotropic hormones [8] regulate the primary reproductive organs, also known as gonads. Those organs are the ovaries in females and the testes [7] in males. On a monthly cycle for most females, the pituitary gland [13] naturally produces FSH and LH in order to stimulate the ovaries to produce a single mature egg [6].

The bodies of some women who experience problems with fertility may produce insufficient or abnormal amounts of gonadotropins like FSH and LH. In fertility treatments such as IVF, fertility specialists can administer injections of FSH and LH to stimulate women’s ovaries to grow egg [6] follicles, or fluid-filled sacs containing immature eggs. For fertility treatments such as that, fertility specialists often proceed with administering an injection of human chorionic gonadotropin [14], shortened to hCG or HCG, in order to push those egg [6] follicles to maturity for collection and later for use in fertility treatment. Fertility specialists need to collect mature eggs from the woman’s body for IVF because non-mature eggs are not capable of successfully producing an embryo upon insemination. As of 2020, hCG is colloquially known as the pregnancy [15] hormone [12] because it is produced by the placenta [16], an organ attached to the uterine lining that nourishes the growing fetus [17] and is used to detect pregnancy [18] in urine testing strips.

Modern research on gonadotropins dates back to the early twentieth century. Two researchers from Germany named Selmar Aschheim [18] and Bernhard Zondek [19] found in 1927 that the blood and urine of a pregnant woman contains an egg-maturing substance, which is modernly known as hCG. In 1929, two years after that initial discovery, Zondek hypothesized that the pituitary gland [13] produces two gonad-stimulating hormones [5], later named FSH and LH. Zondek’s hypothesis was partially founded on his previous research where he implanted pituitary glands taken from cows and humans [20] into prepubescent animals, causing rapid onset of sexual development. Shortly thereafter, other researchers began to investigate whether gonadotropins derived from animals could benefit women who had clinically under-functioning ovaries.

Beginning in the 1930s, researchers investigated animal sources of gonadotropins intended for clinical use in infertile patients who cannot produce adequate amounts of gonadotropins. For many women with under-functioning ovaries, they can lose their ability to produce mature eggs, or ovulate, and therefore cannot become pregnant. Researchers investigated the use of pregnant horse [21] urine as one of the first animal-derived sources of gonadotropins. Pregnant horse [21] serum gonadotropin [10], or PMSG, for example, was first described by researchers Henry Cole and George Hart from the University of California, Davis in Davis, California, in 1930. Commercially-produced PMSG was available on the market in 1938, but was later discontinued because women who took PMSG did not always develop mature eggs as a result of the treatment. In general, animal-derived gonadotropins for clinical usage were primarily discontinued in the 1950s due to the dangers of antibody formation, or a reaction of the immune system to what it perceives as foreign invaders. With the use of some animal-derived gonadotropins, women would experience severe allergic reactions. Others would often only result in a biological neutralization of the gonadotropin [10], meaning the woman’s body nullified the hormone’s effects. However, some animal gonadotropin [10] medications were still available in a few countries in Europe as late as 1998. Beginning around the 1950s, researchers shifted to collecting and purifying human gonadotropins directly from human sources, such as human urine and pituitary glands.

In the decades before 1995, scientists collected human gonadotropins from human urine and pituitary glands harvested from
Sources


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