

Estrogen Antagonist

Ant-toga with Easter-egg

It appears that the primary site of clomiphene action is the hypothalamus where it binds to and depletes hypothalamic estrogen receptors, thereby blocking the negative feedback effect of circulating endogenous estradiol. This results in an increase in hypothalamic gonadotropin-releasing hormone (GnRH) pulse frequency and increased serum concentrations of follicle-stimulating hormone (FSH) and luteinizing hormone (LH).

Increased GnRH, LH and FSH Secretion

Up-arrow Gonad-gopher-harmonica, Luge, and Fish

Impairment of estrogen negative feedback signal results in increased pulsatile GnRH secretion from the hypothalamus and subsequent pituitary gonadotropin (FSH, LH) release. This causes the growth of the ovarian follicle, followed by follicular rupture and subsequent oocyte extrusion. This then allows the egg to become fertilized.

Induction of Ovulation

Egg released

The ovarian actions of clomiphene are secondary to the effects of elevated FSH and LH on ovarian follicular development. These hormones promote the growth of the ovarian follicle, luteinization of the follicle, rupture of the follicle wall, and release of a fertilizable ovum.

Side Effects

Multiple Gestations

Multiple Children

Multiple gestations, or multiple pregnancies, refers to pregnancies with two or more fetuses. Induction of ovulation with Clomiphene increases the probability of multifetal pregnancy.

Visual Disturbances

Wavy Eyes

Visual symptoms, such as blurring, double vision, and/or scotomata, develop in 1 to 2% of women and are usually reversible. The mechanism of visual disturbances is not well understood, it has been thought to represent retinal toxicity but some studies show that clomiphene appears to affect the visual cortex rather than the retina. Physicians should actively check for visual changes in a patient receiving clomiphene. If no other cause of visual disturbances is identified, clomiphene should be replaced with another drug.

Hot Flashes

Burning Flash

Hot flashes are common, occurring in 10 -20% of women. They are mediated by thermoregulatory dysfunction at the level of the hypothalamus and are induced by estrogen withdrawal. Clomiphene occupies hypothalamic estrogen receptors and disturbs the feedback mechanisms of the hypothalamic-pituitary-ovarian axis.