Studies on Human Reproduction; Ovarian Activity and Fertility and the Billings Ovulation Method®

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Ovarian Activity and Fertility

Ovulation - the release of an ovum by the ovary and therefore the only time during the cycle when the ovum is exposed for fertilization--is the central event of the fertile ovarian cycle. It determines the time when pregnancy can occur from an act of intercourse which is the period of 3-4 days (rarely 5-6 days depending on the cervical mucus) before ovulation determined by the fertilizing life span of the sperm and up to 24 hours after ovulation determined by the fertilizable life span of the ovum. Outside this time period a woman cannot conceive from an act of intercourse no matter how hard she tries. Even within this time period, pregnancy from an act of intercourse is not a certainty, the chances vary depending on the couple and the timing of intercourse in relation to ovulation. Maximum fertility is reached during the period of 24 hours before ovulation and several hours afterwards. If the chances of pregnancy at this time are 70% per cycle, it takes two cycles for 90% of couples having intercourse on the most fertile day to achieve pregnancy. If the chances at the beginning of the fertile period are 10% per cycle, it takes 24 cycles for 90% of couples having intercourse at this time to achieve pregnancy.

Many authorities would say that the chances are much less than the figures given. Even with in vitro fertilization (IVF), which many would like to think is the ultimate in assisted pregnancy, most health funds allow up to six cycles of treatment. Thus, couples who do not follow the rules of the Billings Ovulation Method® (BOM) and do not become pregnant should not conclude that the rules do not apply to them, chance has been on their side. Alternatively, if they have had intercourse on the most fertile day they should not expect pregnancy to follow as a certainty. In animals, Nature has ensured a maximum fertilization rate (but not 100%) by restricting intercourse to the most fertile day of their cycle by the phenomenon of oestrus. Thus, the assessment of ovarian activity and the accurate timing of ovulation are basic requirements in natural family planning (NFP) for avoiding pregnancy and under all circumstances including IVF for achieving it.

Physiology of Ovulation

Ovulation occurs over a period of about 15 minutes and even when more than one ovum is released, as in a twin pregnancy, the multiple ovulations occur very close together in time. Thus, ovulation is the one event in the menstrual cycle with a very precise time frame. The ovulatory mechanism produces the two ovarian hormones, oestradiol and progesterone. The ovum is contained within an ovarian follicle and matures as the follicle goes through its rapid growth phase. During this rapid growth phase, the follicle produces increasing amounts of oestradiol. This oestradiol stimulates the glands of the cervix to secrete a particular type of mucus ("mucus with fertile characteristics") which is essential for the sperm to pass through the

cervix to reach the ovum. Oestradiol also stimulates growth of the endometrium which lines the body of the uterus, i.e., the womb ("proliferative phase").

After rupture of the follicle and release of the ovum, both progesterone and oestradiol are secreted by the corpus luteum which forms from the ruptured follicle. The rapid rise in progesterone secretion strongly counteracts the effect of oestrogen on the cervix and vaginal epithelium and thus causes the progesterone change (PC) in the mucus pattern which occurs near ovulation and defines the Peak day (the last day of mucus with fertile characteristics before the change). Progesterone also acts on the oestrogen-primed endometrium making it suitable for implantation of the fertilized ovum ("secretory phase"). In the absence of pregnancy, secretion of oestradiol and progesterone reaches a maximum approximately 7 days after ovulation and then declines. This leads to shedding of the endometrium as menstrual bleeding 11-16 days after ovulation.

The cyclical changes in ovarian activity are controlled by the secretion of two hormones by the pituitary gland situated in the brain, follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Production of these two hormones is controlled in turn by an area of the brain called the hypothalamus. The hypothalamus acts as a computer, analysing nervous signals from other areas of the brain including those generated by the emotions and by environmental factors, such as stress and nutrition; it also analyses hormonal signals (oestradiol and progesterone) generated by the ovaries and other endocrine glands and transmitted by the blood stream. The sum total of these effects determines the quality of the ovarian activity produced.

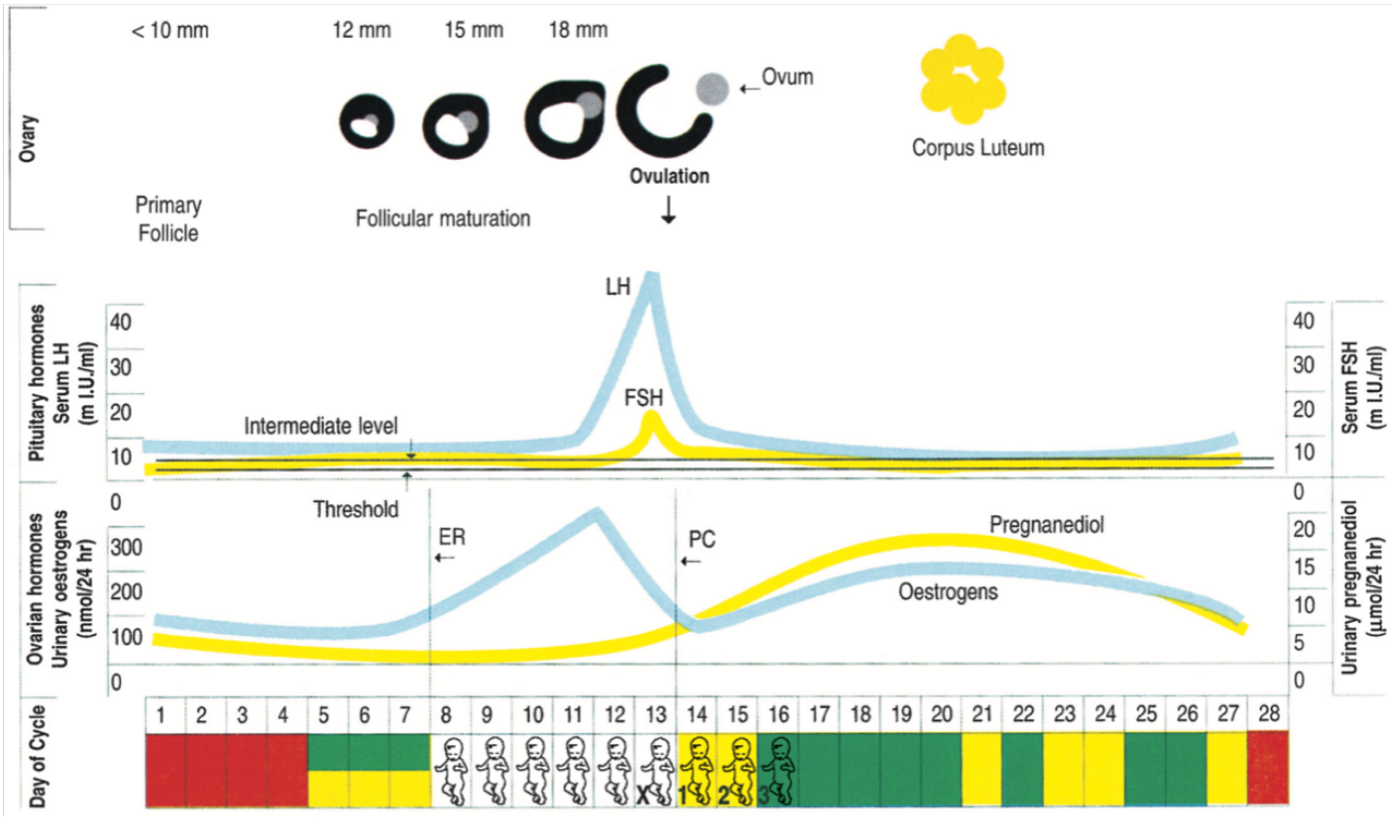

Figure 1. Relationship of the hormonal events of a woman's reproductive cycle to the stamp record. In the pre-ovulatory infertile phase in a cycle of average length the woman will observe dryness (green) or an unchanging discharge (yellow). In an extended pre-ovulatory phase either of the two infertile patterns may occur at different times. Er, oestrogen rise. Pc, progesterone change. X = peak day.

The ovulatory cycle proceeds in a well-ordered series of events (see Figure 1). During the latter half of the preceding cycle, the high output of oestradiol and progesterone by the corpus luteum acting via the hypothalamus suppresses the production of FSH and LH by the pituitary gland. The waning production of oestradiol and progesterone at the end of the cycle removes this suppression and the FSH levels begin to rise. The follicles within the ovaries have a threshold requirement for FSH below which all remain dormant. Initially, the amounts of FSH reaching the follicles are suppressed below this threshold but as the suppression is removed the FSH levels rise and reach the threshold for a few of the most sensitive follicles which include those with the best blood supply. These follicles begin their rapid growth phase while the remaining follicles whose thresholds have not been reached remain in the dormant state. This is an essential mechanism for conserving follicles so that the initial store at birth lasts for the reproductive life span of the individual. This is the recruitment phase of the ovarian cycle.

Once a follicle begins its rapid growth phase it has only two outcomes. Either it progresses to its ultimate destiny, ovulation and the potential production of a new individual, or it fails in the race to ovulation and dies in the process of atresia. It cannot return to the original follicle pool. Several days of growth are required before the growing follicles secrete sufficient oestradiol into the blood stream to provide the signal to the hypothalamus/pituitary that their threshold for FSH has been reached. There is also an intermediate level of FSH production which must be exceeded before a follicle is finally boosted into its full ovulatory response, and a maximum level which must not be exceeded otherwise too many follicles are caused to develop and multiple ovulations occur. The maximum level is only 20-30% above the initial threshold so that the FSH must rise slowly and precise feedback control by the estrogen produced by the developing follicles is essential.

Selection of the follicle which will ovulate is achieved by the following process. As a follicle develops, its content of granulosa cells increases and it produces rapidly increasing amounts of oestradiol and at the same time its requirements for FSH to maintain its rapid growth diminishes, that is, its threshold for FSH decreases. Thus, the most advanced follicle quickly gains the advantage in that it becomes the major producer of oestradiol, and this reduces FSH production by the pituitary at a rate sufficient to maintain its own rapid growth but the levels drop below the thresholds of its less advanced competitors so that they stop growing and atrese (die). Only when two or more follicles are exactly equally matched in the race to ovulation do multiple ovulations occur. The fall in FSH levels caused by the rising oestradiol output also turns on a maturing mechanism within the dominant follicle which makes it receptive to the second pituitary gonadotrophin, LH, while its competitors have not reached this stage.

The high oestradiol levels also activate a positive feedback mechanism in the hypothalamus which causes the pituitary to release a massive surge of LH. This surge of LH is the trigger which initiates the ovulatory process and rupture of the follicle (ovulation) occurs approximately 36 hours after the beginning of the surge or 17 hours after its peak. Ovarian production of oestradiol reaches a peak (the pre-ovulatory oestrogen peak) approximately 36 hours before ovulation and then falls as the ovulatory mechanism progresses. This fall is an important marker because it signals the end of the rapid growth phase of that

follicle, whether it is proceeding to ovulation or atresia. The LH surge causes some luteinization of the follicle before rupture and this leads to the beginning of progesterone production. Thus, a woman monitoring her oestrogen and progesterone output sees a marked rise in oestrogen production to reach a peak followed by a fall. She knows that ovulation will occur within 24 hours after identifying the day of the fall and that this is the most fertile day of her cycle. If ovulation is actually occurring, i.e., the LH surge has occurred and has triggered the ovulatory process, she also sees on the day of the fall a small rise in progesterone output. The actual level of progesterone output associated with the moment of ovulation can be specified within a small range which applies to most women, and this, in the presence of an estrogen fall, is a very accurate marker for timing ovulation.

However, if the fall happens to signal the end of the rapid growth phase of a follicle which is not going to ovulate, no rise in progesterone is seen (anovulatory cycle) or a small rise is seen which is not progressive (luteinized unruptured follicle). After the ovulation, the ruptured follicle is transformed into the corpus luteum, and production of progesterone increases rapidly (approximately doubling each day) together with a second rise in oestradiol output. The rise in progesterone levels causes the progesterone change in the cervical mucus which allows the Peak day to be calculated. The decrease in the progesterone levels towards the end of the cycle causes the bleeding - menstruation. Oestradiol output also falls at the end of the cycle, but this fall is less important in inducing bleeding than the fall in progesterone output. Bleeding always follows the post-ovulatory rise and fall in progesterone output but a corresponding rise and fall in oestradiol output without the production of progesterone, as in anovulatory ovarian activity, may or may not be followed by bleeding.