

Ipsilateral Versus Contralateral Ovary Selection of Dominant Follicle in Succeeding Cycle

JEROME H. CHECK, MD, CAROLE DIETTERICH, RT, RDMS, AND
MARY ANNE HOUCK, RT, RDMS

There is still confusion as to whether ovulation in a succeeding cycle is a random event or is more likely to occur at the ipsilateral or contralateral ovary. Both histologic and sonographic data support alternating ovulation. Some ultrasound studies have suggested that ipsilateral ovulation is more likely in succeeding cycles, and another found right-sided ovulation to be more common. Because many of the studies are based upon small numbers, we initiated a large study to determine the more likely side of ovulation. Furthermore, the present investigation attempted to confirm biochemically the true existence of the dominant follicle by demonstrating appropriate serum estradiol levels. Evaluation of natural cycles (286 pairs) demonstrated 52.4% ipsilateral ovulation and 47.6% contralateral ovulation. Right-sided ovulation occurred in 54.5% of cycles. Our data suggest that the side of ovulation in successive cycles is not influenced by the side of ovulation in the preceding cycle. (*Obstet Gynecol* 77:247, 1991)

Whether ovulation in succeeding ovulatory cycles is a random event or is more likely to occur at the ipsilateral or contralateral ovary has been a topic of considerable research and debate. According to several standard gynecology and reproductive endocrinology texts, ovulation in the succeeding cycle will occur more frequently in the contralateral ovary.^{1,2} Support for the concept of alternating ovulation was reported by Gougeon and Lefevre,³ based on dating the corpora lutea histologically during the preceding four or five cycles. Other studies have also provided evidence for the alternating ovulation theory in cynomolgus⁴ and rhesus monkeys.⁵

However, there are other reports that question the

alternating ovulation theory, favoring ipsilateral,⁶ random,^{7,8} or right-sided ovulation.⁹ Many of the studies suffer from small numbers of subjects. We initiated a larger study to better evaluate ovulation patterns in consecutive cycles.

Materials and Methods

Sequential sonographic follicular maturation studies were evaluated in pairs of consecutive ovulation cycles in 92 consecutive infertile women who had a history of regular menses and were not receiving ovulation-inducing drugs. Seven were eliminated because they did not have a minimum of three ovulatory cycles evaluated; 16 others were excluded because of known tubal or peritoneal disease. The remaining 69 couples consisted of 30 with male factor exclusively, 25 with luteal phase defects exclusively, seven with male factor and luteal phase defects, five with cervical factor, and two with unexplained infertility.

The dominant follicle was defined as the cystic structure that first attained an 18-mm average diameter associated with a serum estradiol (E2) level above 200 pg/mL. A follow-up sonogram was performed 2-3 days later to document collapse of the dominant follicle. Each ultrasound scan was performed by one of four experienced sonographers using real-time ultrasound equipment (Advanced Technology Laboratory, Inc., Bothell, WA).

We included in the study only pairs of cycles in which single ovulation occurred during both cycles. Cycle 1 was always considered the initial side of the ovulation cycle; cycle 2 was considered the side for the succeeding cycle when compared with cycle 1 but the initial side when compared with cycle 3. No more than six cycles were evaluated in any subject. Patients with previous ovarian surgery were excluded. Statistical analysis was performed by χ^2 test, with $P < .05$ considered significant.

From the Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Cooper Hospital/University Medical Center, Robert Wood Johnson Medical School at Camden, University of Medicine and Dentistry of New Jersey, Camden, New Jersey.

Presented at the 38th Annual Clinical Meeting of The American College of Obstetricians and Gynecologists, San Francisco, California.

Results

A total of 572 natural cycles were evaluated. When ovulation was initially on the right ($N = 156$), 56% ($N = 88$) demonstrated right-sided ovulation in the succeeding cycle, compared with 44% ($N = 68$) on the left. Similar data were found when the initial side of ovulation was the left ($N = 130$), in that 52% ($N = 68$) demonstrated right-sided and 48% ($N = 62$) had left-sided ovulation ($P = .57$). Chi-square analysis failed to demonstrate any statistical significance for ipsilateral or contralateral ovulation following initial left-sided or right-sided ovulation.

In natural cycles, counting both the initial and succeeding cycles, 312 of 572 ovulations (54.5%) were on the right (not statistically significant). Two women had right-sided ovulation in all six cycles, two had left-sided ovulation in all five cycles, and one had five in a row on the right after initial ovulation on the left. The eight patients with four consecutive ovulations on the ipsilateral side did so in 38 cycles.

To eliminate a possible bias due to unequal numbers of analyzed cycles in different patients, we normalized the data by calculating the probability of alternating ovulation in each patient. The mean (\pm standard deviation) probability of ovulation on the contralateral side during the subsequent cycle was 0.52 ± 0.27 , which is not significantly different from the probability that the side of ovulation is a random event (0.50).

Discussion

Using pelvic sonography, Marinho et al¹⁰ reported evidence for alternate ovulation, with 80% of all ovulations in natural cycles occurring on the alternate side. This led to the theory that ovulation is more likely in the ovary with the lowest levels of progesterone in the ovarian effluents, which is the contralateral ovary.^{1,11,12} The hypothesis suggests that progesterone antagonizes estrogen action through depletion of estrogen receptors, thus inhibiting estrogen-dependent follicular mechanisms. Another explanation for alternating ovulation is based upon differences in the ovarian hormonal milieu, such that a 5-day asynchrony exists in the population of follicles developing in the "ovulating" ovary and the contralateral one.¹³ It was proposed that follicles 2-5 mm in diameter are especially active in the late luteal phase and, in all probability, the dominant follicle is selected from this group. Local factors inhibit growth of ipsilateral follicles, so that selection of the follicle for the next cycle is likely to occur in the contralateral ovary with larger follicles.²

Despite the elegant hypotheses as to mechanisms

explaining contralateral ovulation, there are contradictory ultrasound data. Werlin et al⁶ concluded that after ovulation in one cycle, there is a 75% chance that ovulation will occur in the ipsilateral side. In fact, a case was reported of a woman who ovulated 12 consecutive times from the same ovary (side of occluded tube) until she was superovulated.¹⁴ In another ultrasound study, the investigators also disagreed with the alternating ovulation theory and instead concluded that ovulation from the right ovary was the most likely to occur.⁹

Our data support some earlier studies in nonhuman primates indicating that the side of ovulation in succeeding cycles is a random event uninfluenced by the location of ovulation in the previous cycle. Perhaps the histologic method used by Gougeon and Lefevre³ to propose alternate ovulation was not accurate in determining the age of previous corpora lutea. Although there have been reports of persistent ipsilateral ovulation in some women, we found only one case, as compared with nine of 39 women in the study by Werlin et al.⁶ These investigators might fortuitously have selected nine unusual patients (chance should have led to no more than one) as the basis for their conclusions.

Our study also demonstrated a slight, but not significant ($P = .15$), predilection for right-sided ovulation, similar to the findings of Potashnik et al.⁹ Our ultrasound data were supported by serum E2 levels, thereby assuring that the follicle seen sonographically was a true mature follicle. Some of the reports may be conflicting because the presence of follicular maturity was unconfirmed by serum sex steroid determinations, leading to the false conclusion that some other cystic structure present was the dominant follicle.

The conclusion that ovulation is a random event was drawn in the elaborate primate studies of Goodman and Hodgen.¹⁵⁻¹⁷ However, subsequent data in humans seemed to have created some confusion as to the sequencing of ovulation. Our sonographic data in humans confirm the previous finding of Goodman and Hodgen that the hormonal events in one cycle do not influence the side of the dominant follicle in the next cycle. Thus we similarly conclude that "in the presence of the active corpus luteum or dominant follicle, growth of follicles is arrested to a similar degree on both ovaries and the contralateral ovary contributes little, if at all, to the regulation of gonadotropin secretion or to the function and life-span of the corpus luteum."¹⁶ However, we studied only infertile women, and it is theoretically possible that the results might be different in a fertile population.

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Address reprint requests to:

Jerome H. Check, MD
7447 Old York Road
Melrose Park, PA 19126

Received July 20, 1990.

Received in revised form October 25, 1990.

Accepted October 31, 1990.

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