HUMAN OVULATION AND FERTILITY

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HUMAN OVULATION AND FERTILITY

TO AUGUSTA

AND

OUR THREE CHILDREN

Preface

The primary purpose of the author in this book is to present the results of a decade of experiment on basic problems of human ovulation and the practical application of some of these results. The information has aided many childless couples in obtaining their greatest desire—the conception and the birth of a child.

My previous book (1950) deals with the causes and the alleviation of sterility in the husband; it presents this aspect of our work in complete and integrated form. This volume deals chiefly with the female.

The desire for children is one of man's most deep-seated emotions. It has existed in all peoples and in all eras. The inability to have them is one of his greatest disappointments and humiliations. My experience with childless couples verifies that there is hope for most couples to reproduce, when the findings of these years of research are applied.

An interesting fact gleaned from hundreds of interviews with couples was their slight knowledge of the process of reproduction. Obviously, therefore, a preliminary step is careful and thorough discussion with them, to gain their co-operation and confidence. They acquire from this an intelligent understanding which ultimately results in their following, willingly and carefully, instructions and routines that are frequently irksome and tedious.

Normalcy of both the male and the female, as revealed by their histories and examinations, has not always resulted in conception. In such couples, the cause of the failure must be singled out. There must be a reason for childlessness.

If this book encourages the physician to try the methods described in it, along with or in place of those he already employs for the solution of troublesome sterility problems, the effort to complete it will have been worthwhile.

Objectively, it is my sincere hope that these years of research and the findings resulting therefrom may prove to be another milestone on the path to the joy of family fulfillment.

EDMOND J. FARRIS

Acknowledgments

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My thanks are due to the hundreds of childless couples who endured the annoyance of a long waiting list and provided a generous supply of research material, as well as financial aid.

My appreciation is due my colleagues and friends for their unstinting aid in various investigations reported throughout the book. Without their understanding, co-operation and interest, many of the studies never would have been accomplished. It is with pleasure that I list the names of some of these collaborators: Dr. Douglas Murphy; Dr. Warren H. Lewis; Dr. Margaret R. Lewis; Dr. Robert A. Kimbrough, Jr., and many members of his present and former staff at the Graduate Hospital of the University of Pennsylvania, including Dr. Craig Muckle, Dr. Charles Freed and Dr. Howard Balin; Dr. Carl Bachman and Dr. Franklin Payne and their entire staffs at the University of Pennsylvania Hospital; the staff of the Department of Obstetrics and Gynecology at the Philadelphia General Hospital; Dr. Eugene Pendergrass and Dr. Richard Chamberlain of the Radiological Department of the University of Pennsylvania; Dr. George W. Corner of the Carnegie Institution of Washington and his son, Dr. George W. Corner, Jr.; Dr. A. E. Rakoff; Dr. J. Gershon-Cohen; Dr. M. B. Hermel; Dr. Sophia Kleegman; Dr. Ephraim Shorr; Dr. Samuel Gurin; Dr. Alfred McShan; Dr. Stuart Mudd; Dr. Donald S. Murray; Dr. Ernest Schwenk; Dr. M. G. Sevag; Dr. Werner Vandenberg; Dr. Louis Farris; Dr. Sabin W. Colton, 5th; Dr. Helen Fornwalt; Dr. George Fornwalt; Dr. Eleanor Yeakel, and many others.

To my successive secretaries, Mrs. Beatrice Herold and Mrs. Margaret Steidel, my deepest gratitude is expressed. To them has fallen the burden of typing, indexing and handling the numerous details associated with such an undertaking. To Mr. Adolph Marfaing, photographer, credit is due for the excellent diagrams and photography included in the book. To Laura S. Thompson, R.N., one of my laboratory assistants, my thanks are due for her co-operation in summarizing some of the studies.

To my publishers my deep appreciation is extended. They have helped me to produce an accurate, and I hope useful, book.

EDMOND J. FARRIS

Contents

1

Activity at the Time of Ovulation

INTRODUCTION

Mating, ovulation and conception occur during estrus in most mammals. It is a well-known fact that a considerable increase in general physiologic activity is exhibited during this period of time. Wang ('23) showed that the bursts of activity of the female white rat occur during estrus. The peak of this activity coincides with the height of estrus, as verified by vaginal smear and mating tests. Slonaker, et al., ('24) found that the peak of the rat's activity curve corresponded with the vaginal cornified cell stage, at which time the female will accept the male. Using an automatic recording device, Farris ('41) demonstrated that estrus in the rat was characterized by bursts of running activity which coincided with the different stages of estrus, during which times variations occurred in the receptivity of the female to coitus. Altman ('41) showed that sows in estrus manifested twice their normal activity. In most cases, this increase in activity continued for 1 to 3 days prior to the sow's return to normal estrual activity. Bond ('45) found activity of a 4-day cyclic nature in the golden hamster which may correspond to the estrus cycle. Farris ('54) demonstrated increased activity in dairy cattle during estrus.

Human beings and the higher primates do not exhibit estrus. The menstrual cycles of both humans and primates re-occur about every 4 weeks and coitus may occur at any time during the cycle. Ovulation does not take place during the normal menstrual flow, but a few days prior to the middle of the cycle. There is little if any correlation between the estrus period of lower mammals, which may be defined as the period of sexual activity, ovulation and conception, and the ovulation period of the human female.

It was due to my early experience in observing the activity of female rats and other mammals that my attention was directed to the fact that periodically certain female technicians would become extremely active in their duties around the laboratory. These girls would exhibit bursts of energy, voluntarily cleaning up the laboratory, scrubbing the table tops, approaching many of their problems and duties enthusiastically, in contrast with the lackadaisical and disinterested approach to the same problems a few days previously. There was a definite willingness at times and a lack of enthusiasm at other times.

Veering from elation and happiness with an increase in activity to melancholy and indifference, these extreme emotional states offered an interesting subject for investigation. Therefore, the walking activity of 15 healthy women, 9 married and 6 unmarried, was measured. For purposes of comparison, the walking activity of 6 men was measured.

A New Haven pedometer was employed to record the distance the individual walked from arising until retiring. The women wore the pedometers on a garter belt, the men carried them in their watch pockets. By doing this, the pedometer in each case was suspended over the lower right abdomen. In most cases, each individual wore the same pedometer throughout the test period. The instrument was checked periodically for accuracy.

OBSERVATIONS

Three peaks of activity were observed in most of the women during their 45 menstrual cycles which covered a period of 1 to 6 months. The unmarried women in this series consisted of girls from 19 through 36 years of age. They were employed in different capacities, such as technicians, scientists or student aides. The married women ranged in age from 22 through 34 years. The menstrual cycles ranged from 24 to 42 days in length, averaging 29 days. The average daily walking distance per menstrual cycle was 6.5 miles.

A mid-cycle activity peak (Fig. 1) was evident on cycle day 15, ranging from cycle day 10 to 21 and averaging a walking distance of 10.1 miles. On the average a menstrual activity peak occurred on cycle day 4 with a range of cycle days 1 through 6 and with an average walking distance of 9.6 miles. A late cycle activity peak occurred on the average cycle day 24, with a range of days 18 through 38 and an average walking distance of 9.8 miles.

In contrast, the walking activity of the 6 male subjects was followed over a period of 18 months and for intervals as long as 29 days. The men walked an average of 4.3 miles, with a range of 3 to 6.6 miles per day. Figure 1 shows diagrammatically the peaks of activity in women in comparison with the uniform activity of the men, who did not exhibit evidence of peaks. The men represented different occupations: 2 junior medical students, 1 arts college freshman, 1 executive, a supervisor in charge of shell loading at a war plant and America's most physically fit marine.

The differences in the activity behavior between the male and the female was strikingly emphasized in our rat experiments. Figure 1 shows diagrammatically the activity cycles of the female rat. Every

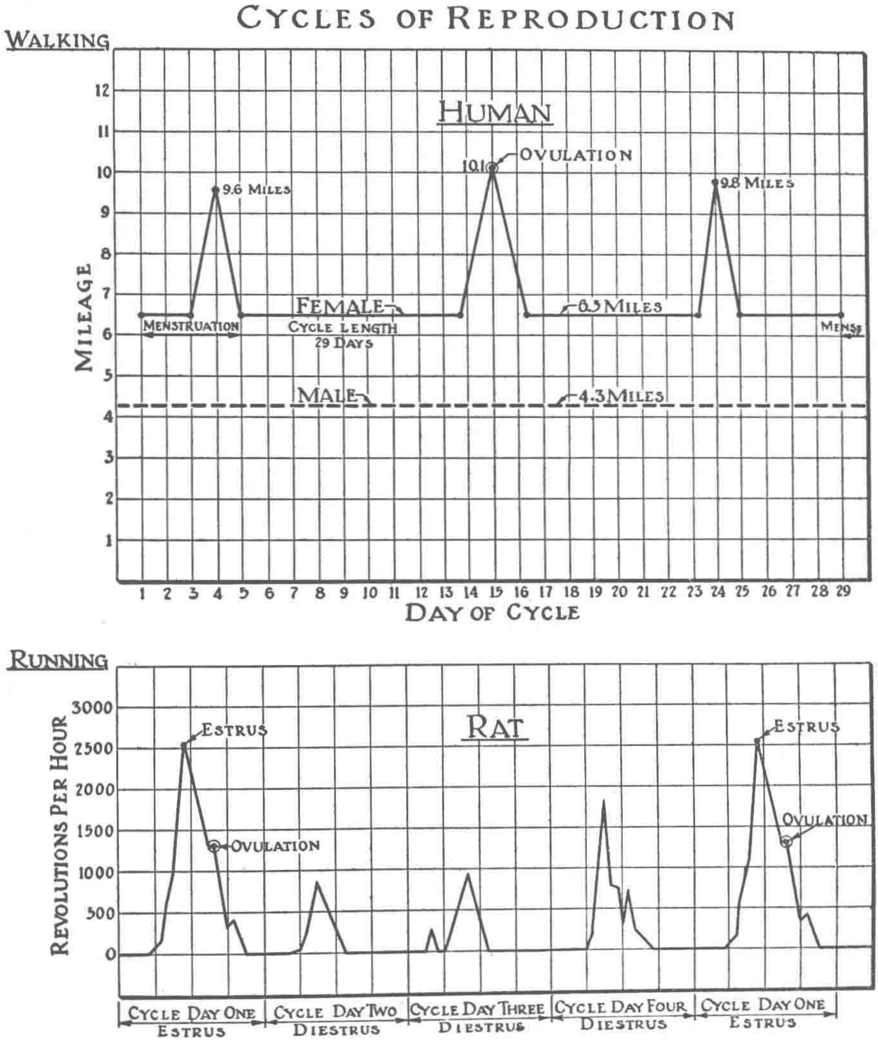

FIG. 1. A comparison of activity cycles between the human and the rat. The human female showed 3 increased walking activity peaks during a cycle: during the menses, averaging 9.6 miles; during the mid-period, averaging 10.1 miles; and late in the cycle, averaging 9.8 miles. The women walked an average of 6.5 miles daily. The males averaged 4.3 miles daily and did not exhibit peaks of activity.

The female rats showed peaks of running activity during estrus which occurred usually on the 5th day.

4th or 5th day the animal would come into estrus, at which time she would run about 24,000 revolutions, in comparison with 11,700 revolutions for the 24 hours during diestrus.

In contrast, the male rat would run very little. In fact, the average number of revolutions run by the male rat during a life span totaled approximately 333,000 revolutions. For the equivalent time, the females ran as much as 3,800,000 revolutions.

Our endocrine experiments (Farris, unpublished), based on increased running activity peaks in female rats, suggested that the peaks of activity in the human female may be hormonal in reaction and may be associated directly with the process of reproduction.

Various hormones known to be associated with the reproductive processes, such as gonadotrophins, estrogen, progesterone, thyroxine, etc., were tested on female rats to determine their effects on running activity. We learned that injections of a follicle-stimulating hormone of the pituitary gland stimulated the ovary to produce estrogen which caused increased running activity in female rats.

In an effort to establish the cause of the increase in the activity of women, studies were undertaken to locate endocrine factors responsible for it. Eventually, hormones were identified in the urine of women on the days the activity increased. This bio-assay method of identification of gonadotrophic hormones became the new test for the recognition of the time of ovulation and the gonadotrophin (Farris, unpublished) was found to be one of the factors responsible for the activity response.

The intensive study which followed this finding has resulted in the material that is incorporated in this book.

WALKING ACTIVITY AND THE RAT HYPEREMIA TEST

Figure 2 illustrates the mid-period walking peaks of women who had menstrual cycles ranging from 22 to 42 days. Subject N.M. showed a mid-period activity peak of 21.3 miles on cycle day 13.

Under this subject's mid-period activity graph are a series of symbols representing results of the bio-assay test. On cycle days 10, 11, 15, 16 and 17, there are a series of zeros; on cycle days 12, 13 and 14 there are 3 consecutive reactions of 1. These reactions will be explained fully in the next chapter and are referred to as the rat hyperemia test.

The rat hyperemia test is based on the observation that at about the time of ovulation the urine of a woman produces a hyperemia in the ovaries of an immature rat when administered to the animal subcutaneously. It has been established that at the mid-period, a series of consecutive positive reactions preceded and followed by negative

WALKING ACTIVITY IN RELATION TO RAT HYPEREMIA TEST

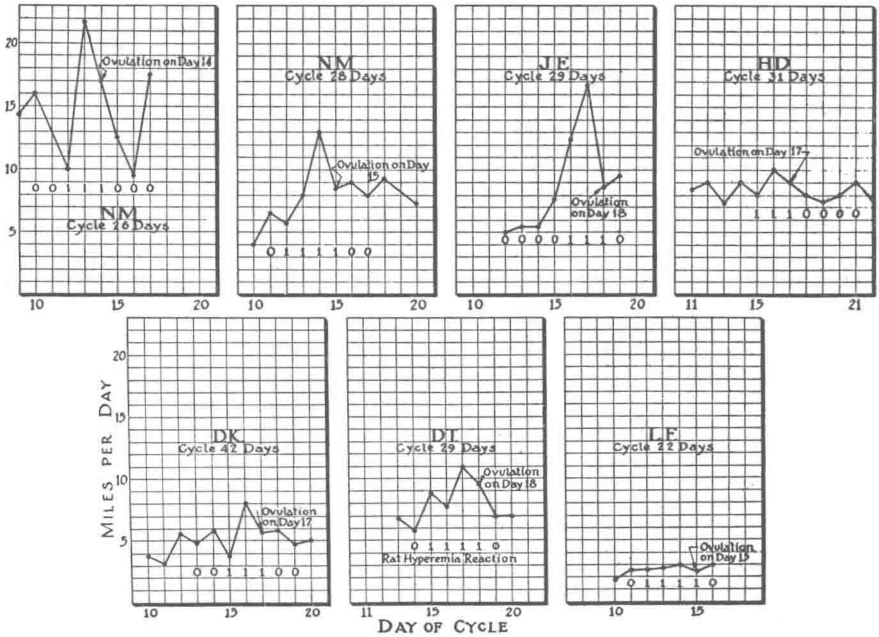

FIG. 2. These 7 records reveal an increased walking activity peak at about the mid-period, ranging from 4 to 21.3 miles. Ovulation took place the day following the activity peak, as indicated by the last day of the hyperemia reaction, which is the usual day of ovulation.

reactions indicates that ovulation is taking place. Usually ovulation occurs on the last day of the positive reaction. If for any reason the urines for the early days of the ovulation testing are not available, ovulation may be estimated by picking the last day of the series of positive reactions.

A hyperemia of short duration may occur briefly at other times in the cycle, but it does not last as long as the normal ovulation reaction of 3 to 7 consecutive days. For example, in the record of N.M., the mid-period activity peak of 21.3 miles occurred on cycle day 13, and ovulation occurred on cycle day 14, the last day of the hyperemia reaction. Hyperemia was also found on the first day of the menses, at which time she walked 12.5 miles and on cycle day 24, the late cycle peak, she walked 15.9 miles. During this particular cycle, she walked an average of 11.3 miles per day and showed three peaks—on the first day of the menses, on cycle day 13 and again on cycle day 24.

Other illustrations in Figure 2 indicate that ovulation is associated with a definite hormonal change, as indicated by the rat hyperemia reactions which are shown under the individual graphs. In all of these instances, ovulation occurred the day following the highest activity peak. Ovulations occurred from cycle days 14 through 18. The mid-period activity peak ranged from 4 to 21.3 miles.

Figure 3 illustrates walking activity in relation to the rat hyperemia test, with ovulation occurring at the peak of activity, rather than the day following, as was evidenced in Figure 2. Subject E.M. had a cycle 32 days in length. The mid-period peak of 5.4 miles occurred on cycle day 13, the last day of the hyperemia test and the usual day of ovulation. Although not illustrated, subject E.M. showed a late activity peak on cycle day 23, walking 4.6 miles. She also showed a hyperemia for one day, by rat test. Her average daily activity was only 3 miles. A pedometer was not worn during the menstrual cycle when the first peak is usually evidenced.

Subject E.Y., lower right record in Figure 3, showed a cycle 32 days in length. Her mid-period activity peak of 11.8 miles was reached on cycle day 18. This was the 4th day of the consecutive hyperemia reaction. It is of interest to note that as evidenced in this case, the 4th consecutive day reaction proved later to be one of the most common of the hyperemia reactions, indicating ovulation probably on cycle day 18. Her first, or menstrual activity peak for this cycle, which is not shown in the graph, occurred on cycle day 4 and was 13.2 miles. Her late cycle activity peak was on day 25 with 9.5 miles. She walked an average of 7.8 miles daily.

Figures 2 and 3 indicate a definite relationship between increased walking activity and the hyperemic reaction, caused by hormones found in the urines at these times. Later, the mid-period activity peak proved to be associated with the process of ovulation.

Figure 4 illustrates the walking activity of a husband and of his wife during her cycle in which conception occurred. Without exception, in the tests on all of the couples the wives outwalked the husbands. Many arguments took place between the husband and the wife regarding who walked farther. In this particular couple, the wife walked 135 miles in 28 days, averaging 4.8 miles per day, while during the same period, the husband walked 132 miles, averaging 4.7 miles. In most instances there was a marked difference in the mileage walked between the husband and the wife.

Figure 4 shows that the peak of 10.2 miles was on cycle day 12. Intercourse took place on cycle days 11 and 13. In view of our findings, illustrated in Figure 2, we believe that conception took place on cycle day 13, the day after the peak of activity. The pattern of the