

If a slightly larger part of the uterus is left back—perhaps one-third or one-fourth its length—the full effects of this operation are not observed, although the life and function of the corpus luteum is somewhat prolonged even under these conditions. In different experiments the ovulation following an incomplete extirpation occurred between a period of twenty-one and thirty-two days following the preceding ovulation, but a delay in the later ovulations was either absent or only very slight. A relatively small part of the uterus can therefore, at least to a great extent, take over the function of the whole uterus. The prolongation of the life of the corpus luteum which occurs even under these conditions may again call forth a proliferation in the mammary gland in some cases. However, there are certain factors in the growth of the mammary gland which need still further investigation.

We believe that this method of prolonging the life and function of the corpus luteum will prove of value in the analysis of the mechanism of the sexual cycle.

Differences in the effect of hysterectomy in different species depend presumably on differences in secondary factors; it is not probable that in principle the effect of the uterus on the corpus luteum differs in different species.

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The mechanism of the sexual cycle and the specificity of growth substances.

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The experimental analysis of the sexual cycle carried out particularly during the last fifteen years makes it possible to state the main factors regulating its mechanism. While this analysis rests largely on experiments and observations in rodents, and especially in the guinea pig, yet in principle conditions seem to be similar in all the mammals.

Two phases can be distinguished in the sexual cycle; the first phase is dominated by an ovarian factor other than the corpus luteum, in all probability by the maturing follicles the wall of which secretes a substance which causes various kinds of circulatory changes and growth processes and in addition certain psychical alterations. Proliferation, under the influence of this substance, occurs in the mammary gland, in the vagina and also in the uterine wall; this substance calls forth changes in the ovary which culminate in ovulation.

These growth processes usually cease in the vagina suddenly with the appearance of oestrus, while in the mammary gland they may continue for a short time longer.

Ovulation leads to the formation of the corpus luteum. The second phase of the sexual cycle is dominated by a substance or substances given off by the corpus luteum. This substance or these substances sensitize the uterus, making possible the production of decidua or of placentomata, or the normal predecidual proliferation and facilitating the fixation and development of the fertilized ovum; they cause growth processes in the mammary gland and prevent proœstrus, œstrus and ovulation; the corpus luteum on the other hand does not prevent the maturation of follicles, at least in rodents. The corpus luteum substance is without a direct effect on vagina, tube or other connective tissue or epithelial structures of the guinea pig. This substance or these substances act on different tissues at different periods of the sexual cycle. The sensitization of the uterine wall is limited to the first half of the life of the corpus luteum. The growth of the mammary gland occurs in the rabbit during the whole period of the life of the corpus luteum; in the guinea pig it begins about on the sixteenth day of the cycle. The substance inhibiting the effects of the maturing follicle acts throughout the whole period of the preservation of the corpus luteum. When degenerative changes occur in the corpus luteum, this function ceases.

Between these two phases, the first phase probably dominated by the maturing follicle and the second, the lutein phase, there may be a short intermission during which the first substance has ceased to act and the second substance has not yet been produced in sufficient quantity to be effective. Certain degenerative processes may occur during this intermission, caused probably

by acute circulatory disturbances and by secondary destructive effects of leucocytes.

We would conclude on the basis of the observations of Long and Evans in the rat that in this species the sexual cycle consists essentially only of the first phase and of the intermission; the lutein phase is here lacking under ordinary conditions, but can be called forth experimentally and is present also during lactation. We would interpret in a similar way the observations of Allen in the mouse.

The specific relation of these growth substances to certain tissues is very pronounced. The corpus luteum substance of the guinea pig acts very strongly on the connective tissue of the uterus, but not at all on that of the vagina; the follicular substance acts on the vagina and on the uterus in a manner quite different from the corpus luteum substance. This specificity is due to the character of these growth substances as well as of the tissues on which they act, and not to the position of the tissues of the body. It can be shown that this specificity is still noticeable in uterine tissue after it has been transplanted subcutaneously.

On the basis of these observations we would propose the following classification of the periods of the sexual cycle. In the various species individual differences exist; thus in the rat and mouse only phases I and II can be recognized.

- I. Follicular phase—
 - a. Prooestrus.
 - b. Oestrus.
 - c. Metoestrus (in some cases).
- II. Intermediate phase (following ovulation and preceding sensitization of the uterus).
- III. Lutein phase—
 - a. Period of sensitization of uterus.
 - b. Period of return to the resting state.
 - c. Period of resting state.