221 (2181)

The effect of extirpation of the uterus on the life and function of the corpus luteum in the guinea pig.

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It is usually assumed that extirpation of the uterus is without any noticeable effect on the ovaries, outside perhaps of cystic degenerative changes which have sometimes been observed to follow this operation and which evidently are due to interference with the blood supply of the ovary following injury of the uterine vessels.

Experiments in the guinea pig have however convinced us that a complete or almost complete extirpation of the uterus may be followed by a very characteristic effect, namely a long continued preservation and function of the corpus luteum. Instead of beginning to degenerate fourteen or fifteen days after ovulation, the corpus luteum may remain well preserved and even show attempts at mitotic proliferation for sixty days, or perhaps even as late as eighty days after the last heat. We have not yet determined the limit of preservation of the corpus luteum under these conditions. The cyclic corpus luteum thus equals or perhaps surpasses in vitality the corpus luteum of pregnancy which latter has in the guinea pig a duration of about sixty-five days.

In order to demonstrate this effect we extirpated the uterus a few days after ovulation. The corpus luteum which develops as a result of ovulation remains preserved for a long time following this operation. If we extirpate the uterus in very young guinea pigs at a time when an ovulation has not yet occurred, the first ovulation takes place, notwithtanding the extirpation of the uterus. In various experiments we observed this ovulation to occur as early as nine days and as late as twenty-nine days following the operation. The corpus luteum which thus originates remains then preserved for a long period of time and mitotic figures may often be seen in the lutein cells. In ovaries of these young animals, which ovulated for the first time fol-

lowing hysterectomy, there is usually no remnant of retrogressing corpora lutea representing former ovulations visible. In one case, however, we found such a body side by side with a well preserved corpus luteum. This was probably due to the fact that one of the corpora lutea formed during an ovulation may retrogress earlier than the others.

We see then that extirpation of the uterus does not prevent ovulation as such, but that it has such an effect only indirectly by preserving the life of the corpora lutea. Also in other respects the ovaries in hysterectomized guinea pigs are normal. Follicles grow in the normal manner, mature and undergo atresia. The maturation of follicles is not interfered with under those conditions.

These corpora lutea not only live, but they also function. They prevent the occurrence of an ovulation during the whole period of their life; but if the corpora lutea are extirpated completely, a new ovulation takes place at an early period notwithstanding the absence of the uterus. This is an additional proof that the hysterectomy as such does not prevent ovulation. On the other hand, if we prevent the maturation of follicles through underfeeding, a new corpus luteum does not develop in a young guinea pig, which has not yet ovulated, even after extirpation of the uterus.

This marked prolongation in the life and function of the corpus luteum may not only be obtained after a complete hysterectomy, but even in cases in which a very small amount of uterine tissue has been left back, an amount sufficient to give rise to the development of a placentoma. In such a case we observed as late as forty-six days after ovulation mitotic proliferation in placentomatous tissue without the presence of pregnancy.

In these hysterectomized animals the mammary gland develops quite markedly and mitotic proliferation may be observed in such glands as late as seventy-four days after the last ovulation. In one case we found sixty days after ovulation milk production in a mammary gland which had previously proliferated. During the prolonged period of function of the corpus luteum prooestrus and oestrus are prevented and thus growth processes do not occur in the vagina. The epithelium of the vagina becomes therefore very vacuolar and polynuclear leucocytes migrate through the mucosa into the lumen in hysterectomized guinea pigs.

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.

222 (2182)

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.