THE SCIENCE COMMITTEE OF THE British Medical Association.

REPORT CXII.

OBSERVATIONS ON THE PHYSIOLOGY OF THE FEMALE GENITAL ORGANS.

BY

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III.—THE CORRELATION OF THE UTERUS AND OVARIES.—Continued.

RESULTS OF EXPERIMENTS.

SERIES B.

Removal of Uterus and Subsequent Examination of the Ovaries.

ON the whole, we have not been satisfied with the experiments we have conducted in this inquiry. We operated upon two bitches and twelve rabbits. All the animals were about 6 weeks of age at the time of operation. Unfortunately our bitches died of distemper within a few months of the hysterectomies, so that they never reached sexual maturity. We lost five of our rabbits, too, from an epidemic of pneumonia. The rest (about half) that reached sexual maturity were killed at different periods, the longest time that was allowed to elapse between the operation and the examination being eight months. In every case the uterus was removed and the Fallopian tubes as far as practicable. In several cases, when the animals were killed, it was found, however, that the whole of the Fallopian tube had not been removed. It will be understood how difficult it was to effect this in view of the small size of the animals.

In no case did we find any histological change which

corpus luteum. In Fig. 16 is seen a section of an ovary removed from a doe whose uterus had been removed eight months previously, and who had frequently been to the buck. Many sections were cut of this ovary, but nowhere could we find evidence of corpus luteum formation. Ripe follicles and degenerated follicles there were in abundance, but nowhere was there any evidence that a follicle had ruptured. The degeneration, too, of the follicles appears to be of a more cystic nature than in the normal animal. It will be noticed in Fig. 16 that the interstitial cells are as well marked as in the normal ovary. In Fig. 17 is shown a section of the ovary from another doe whose uterus had been removed five months previously. In this case also no corpora lutea can be seen, although in other respects the ovary appears normal.

Heape⁵ has produced evidence to show that the follicles in the normal rabbit's ovary do not rupture unless the doe has connexion with the buck. But in our cases the does that attained maturity had this connexion and apparently came on heat, but in spite of this there was no rupture of Graafian follicles. We must confess that we had fully anticipated that we should find marked changes in the ovary after hysterectomy in spite of the observations of others, and we based this belief on our own clinical experience and on the clinical experience of Abel, Zweifel, and others. But beyond the fact stated above—which may or may not be of importance†—we had no confirmation of our ideas. It is quite possible, however, that a much longer time must be allowed to lapse before changes become apparent, and once more we cannot refrain from saying that, in view of the structure of the rabbit's ovary, comparison with the human ovary is hardly fair. We consider, therefore, that our experiments are inconclusive in this matter, and we shall hope to return to the subject at some future time.

SERIES C.

LIGATION OF THE UTERINE CORNUA.

In this series of experiments we have made observations on (a) the nature of the uterine secretion, (b) the condition of the uterus which had undergone expansion, (c) the condition of the ovaries (in the first experiment).

I.—*Ligation of the Cornua without Removal of Ovaries.*

We performed a large number of these experiments, in order to collect the fluid secreted by the uterus, for exami-

Fig. 15.—Normal adult rabbit's ovary with corpus luteum. × 200.

could have been held to have occurred as the result of removal of the uterus. At the same time there appeared to be the negative effect that in no case could we discover the formation of corpora lutea,* or any evidence that Graafian follicles had ruptured, in spite of the fact that the animals came on heat and had connexion with the buck.

In Fig. 15 is seen a normal adult rabbit's ovary with a

* It is somewhat difficult to define what is meant by "corpora lutea" in rabbits' ovaries since there is no rupture of the follicle without connexion with the buck, but we may recognize three varieties (and we include all three in this term): True and false corpora lutea and the corpus luteum of normal degeneration.

Fig. 16.—Rabbit's ovary after hysterectomy. × 200.

nation and experimental purposes. Consequently we were able to make a number of observations. In all cases we used silk as the ligature material, and usually we doubly ligated each uterine cornu, although it is not necessary to tie the ovarian extremity of the horn, as no leakage occurred in those cases in which we omitted to do so.

(a) *The Nature of the Secretion.*—This we have already dealt with in Paper II.

† Especially in regard to lowered calcium content producing rupture of the follicle.—See Paper II. Compare also C. J. Bond, Experiment XXV (see references).

(b) *The Condition of the Uterus which had Undergone Expansion.*—A section of such a uterus is shown in Fig. 18. One observes a more or less even distension. The endometrium is flattened and thinned from pressure, but the muscular layers do not seem to suffer. It is probable that in those cases in which the muscular layers are well developed gradual distension of the uterine cavity leads to hypertrophy. This is a point of considerable interest,

Fig. 17.—Rabbit's ovary after hysterectomy. $\times 200$.

and very suggestive of the muscular hypertrophy which occurs in pregnancy. We intend to follow the matter up further.

(c) *The Condition of the Ovaries.*—We have been unable to trace any changes in the ovaries as the result of this experiment—microscopical or macroscopical. Bond thought that there were changes, but the condition that he found is probably merely the ordinary result of Graafian degeneration, frequently to be observed in rabbits that come on

resembled that from the virgin uterus, containing less calcium salts than that obtained from a menstruating uterus. We also noticed that in its physiological effect it was not as active as that obtained from the menstruating uterus. (This will be referred to again in Paper IV.) In regard to this inactivity there was a possible source of error, in that it had been kept, sealed in glass capsules, for some little time before being used. We mention this fact

Fig. 19.—Ovary of young doe with hydrometra. $\times 200$.

though we are not ourselves convinced that it is one of any importance.

(b) In Fig. 21 is shown a section of a uterus the horns of which had been tied two and a half months previously, the ovaries having been removed at the same operation. In this particular case the rabbit had had young shortly before. Those experiments on rabbits that had not been recently pregnant gave the same results.

It will be seen from the section that a large hydrometra

Fig. 18.—Hydrometra without removal of ovaries. $\times 200$.

heat but do not have connexion. (Compare Heape, loc. cit.)

Figs. 19 and 20 are sections of young and mature ovaries respectively, removed from does in which hydrometra had been artificially produced. It will be seen that they are quite normal.

II.—Ligation of the Cornua with Synchronous Removal of the Ovaries.

(a) Fluid is freely secreted, the removal of the ovaries making no difference to the quantity. The fluid collected

Fig. 20.—Ovary from young adult rabbit with hydrometra. $\times 200$.

was formed, and that in the process of expansion the endometrium has become much thinned from pressure. It is interesting to note that the muscular layer has not become atrophied to the extent it would have done had the uterine horns not been tied when the ovaries were removed. We think that this is to be explained by the fact that the muscle fibres are called into use to resist the increasing pressure. This view is in harmony with the idea we hold that atrophy of the uterus after removal of the ovaries is primarily due to the consequent inactivity of the uterine muscle, which is, as we have already shown, the first

portion of the organ to be a subject to degenerative changes. It is important to remember that this condition of muscular atrophy recurs seasonally in a physiological manner and degree in wild rabbits.

III.—Removal of the Ovaries followed by Ligation of the Uterine Cornua at a Subsequent Date.

(a) We found that the fluid secreted in these circumstances was as copious as in the last experiment, and closely resembled that secretion in its low calcium content and physiological inactivity. (This was also, however, as in the case of that obtained in the last experiment, kept some time in sealed capsules before being used.)

(b) A typical section of one of the uteri examined is seen in Fig. 22. In this case the animal had been pregnant, and had aborted after removal of the ovaries. Twenty days later the cornua were tied. A month later the animal was killed. In every particular the section of this uterus is comparable with that seen in Fig. 21, and in marked contrast with Fig. 10.

Removal of the ovaries, therefore, whether performed previous to ligation of the cornua or synchronous with that operation, does not affect the quantity of the secretion, while it does appear to alter the chemical nature of

examined the ordinary wild rabbits were breeding. On examination every uterus was found to be in an inactive condition, and the ovaries were all small, and contained no ripe follicles.

It is, of course, possible, that captivity was the cause of this—of the fact that none were on heat; but we incline to the view that it was—in part at least—because the presence of the buck is an exciting factor in the case of wild does in regard to the onset of genital activity early in the year. We were quite unprepared for this result of our examinations, for we hoped to get inactive uteri in the first lot and menstruating uteri in the second, in order to estimate the total calcium in the ash of each lot of uteri. We give this observation for what it may be worth. The great difference between wild animals and domestic animals in their breeding habits is at once a source of wonder and information, and enables us more than anything else to realize how intimate is the association between the genital functions and the general metabolism of the body. The experiments we have described not only indicate that there is this close connexion between the general metabolism and the genital organs, but also that there is a definite interdependence (so long known and recognized, but never defined) of each part of the

Fig. 21.—Hydrometra with synchronous removal of ovaries. $\times 200$.

it, as already indicated by the lowered calcium content and reduced physiological activity.

The histological appearances of the uteri are striking and suggestive, and readily bear the interpretation already put upon them in regard to the hypertrophy rather than atrophy of the muscular layer under these conditions.

We found also in the course of our experiments on hydrometra that unilateral ligation of a cornu does not at all interfere with pregnancy in the other cornu. One of our rabbits in which we made a unilateral hydrometra and stitched it to the abdominal parietes for satisfactory observation subsequently had two litters, both of which appeared at full time, and were reared. We thought, however, that the cyst got smaller during the pregnancies. This bears out Bond's observations as to the absence of secretion from a cornual fistula during pregnancy in the other horn. Indeed, many of our experiments here recorded confirm much of what he has stated in a recent publication. It is only right, however, to mention that our experiments were begun before his paper appeared.⁵

There is one more experiment (for the successful performance of which we are indebted to Mr. James Smith) to which we would like to allude:

One of us arranged with a keeper in Scotland to catch forty wild doe rabbits in February. Twenty of these were immediately killed and the genital organs examined. In every case the uterus was in the inactive or non-contracting state, and was flat and ribbon-like. The ovaries were small, and contained no ripe Graafian follicles. The remaining twenty rabbits were kept in captivity away from bucks for about two months, during which time two died. As far as possible the animals kept in captivity were allowed to lead a natural life, except for the presence of bucks. At the time these were killed and

Fig. 22.—Hydrometra after previous removal of ovaries.

genital apparatus—that is to say, of the uterus and ovaries.

And, finally, these experiments help us to understand the specific changes that occur in each part as the result of interference with the other, or in altered circumstances. They have, in short, enabled us to attempt to define what that specific relationship is, and in coming to our conclusions we wish to acknowledge the assistance we have received from the work of those other observers in the same field of investigation to whom we have already referred.

REFERENCES.

⁵ Heape, W.: Ovulation and Degeneration of Ova in the Rabbit. *Proc. Roy. Soc., Series B*, vol. lxxvi, No. B 509, 1905. ⁶ Bond, C. T.: Some Points in Uterine and Ovarian Physiology and Pathology in Rabbits, *BRITISH MEDICAL JOURNAL*, July 21st, 1906.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

A CASE OF MYCOSIS FUNGOIDES IN THE PRE-MYCOTIC STAGE.

R. F., aged 65, was admitted to Dr. Calwell's wards in the Royal Victoria Hospital, Belfast, on January 2nd, 1909. Fifteen months before admission he noticed the extensor surfaces of both forearms covered with reddish scales. During the succeeding four months this scaliness spread over the whole of his body, and was accompanied by extreme pruritus. Four months previous to admission large patches of brownish pigment appeared on his trunk and extremities.