We do not know whether or not the dosages used were excessive, but it should be mentioned that monkeys 1, 2 and 3 received corpus luteum extract equivalent to 360, 400 and 450 gm. respectively and while showing some modification of the endometrium were not nearly so favorable as animals 4 and 5, whose protocols are given. The accompanying figures do show, however, that it is possible to produce premenstrual changes in the uterus of castrate monkeys through the combined use of follicular and corpus luteum hormones.

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Physiology of Corpus Luteum VII. Maintenance of Pregnancy in Rabbit After Very Early Castration, by Corpus Luteum Extracts.

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In a recent series of papers[1] we have described the preparation and effects of an extract made from the *corpora lutea* of swine. When administered to recently spayed adult rabbits, or to immature rabbits whose uteri have been brought to the mature resting state by injections of oestrin, the *corpus luteum* hormone (progestin) induces alterations of the endometrium characteristic of pregnancy. If female rabbits are mated and castrated 18 hours later, while the fertilized ova are still in the Fallopian tube, the extracts substitute for the removed ovaries so completely that the embryos are nourished, become implanted, and develop in the uterus exactly as in normal pregnancy under the influence of the mother's own *corpora lutea*. In the third of our previous reports we have described 2 animals which were carried to the 13th and 19th days of pregnancy respectively. The demonstration of normal implantation with normal foetuses in these animals at autopsy led us to attempt to carry other animals through the full term, with the results now to be reported.

The procedure in general was as follows: A doe was mated, usually to 2 bucks, and was subjected to bilateral double oöphorectomy 18 hours after mating. The number of ruptured follicles in each ovary was noted. Administration of the extract by subcu-

[1] Corner, G. W., *Am. J. Physiol.*, 1928, lxxxvi, 74; Corner, G. W., and Allen, W. M., *Ibid.*, 1929, lxxxviii, 326; Allen, W. M., and Corner, G. W., *Ibid.*, 1929, lxxxviii, 340.

taneous injection was begun on the day of operation and was continued daily thereafter. The preparation used was the crude oily extract described in our second paper. About the 8th to the 12th day of the experiment the animal was again explored under ether anesthesia, for the purpose of determining whether or not implantation had taken place. This procedure enabled us to conserve the costly extract in case the pregnancy had not continued. If the animal was found to be pregnant the experiment was continued, until terminated by spontaneous delivery or by a third laparotomy, as indicated below. In those experiments in which pregnancy did not continue to full term the extract was again tested on another rabbit by the test given in our previous paper (No. 2 of the series).

Four animals which received from 0.2 cc. to 0.5 cc. daily of an extract known to be fully potent, went to spontaneous delivery on the 29th, 32nd, 28th and 32nd day respectively (usual duration of normal pregnancy in our colony 33 days). Two of these animals received the extract daily throughout the whole experiment, and 2 received it for 21 days only. This should not, however, be taken to demonstrate that the hormone is unnecessary during the last week of pregnancy in the rabbit; the extract used in these experiments is a heavy oil which is absorbed very slowly, and therefore the 2 animals which received only 21 injections may have possessed subcutaneous stores sufficient to carry them during the last week.

Two animals which received respectively 1 cc. and 0.5 cc. of a potent extract daily throughout the whole term failed to give birth to their young on the 33rd day. By means of Caesarian section on the 34th and 36th days respectively, fully developed dead foetuses were found *in utero*, together with others already undergoing resorption. From the size of the better-preserved foetuses and from other signs it appeared that in one case the young had grown until the 26th day, in the other until the 32nd or 33rd day.

In 8 animals the embryos did not survive. In 5 of these cases no implantation occurred, and in 2 others the embryos became implanted but were resorbed soon after. In all of these cases the extract when subsequently tested was discovered to have lost potency.

Another animal which received a potent extract in adequate dosage, did not implant her embryos at all, as demonstrated by exploration on the 9th day; this was the only unexplained failure in the series.

These experiments demonstrate that our crude extract of pigs' *corpora lutea* is able, when administered in a fully potent condition

and in adequate dose, to maintain pregnancy in rabbits, spayed at the 18th hour after mating, until full term.

Experience obtained during the course of this work enables us to state certain precautions which must be used in similar experiments. We find that the crude extract does not always maintain its potency longer than one week when kept in the oily state, and therefore we now keep our stock of extract dissolved in 95% ethyl alcohol, distilling off weekly a supply for immediate use. The dosage necessary to insure implantation and maintenance of pregnancy is larger than that required to produce progestational proliferation according to our standard test of potency. Usually 0.1 cc. of the crude extract daily for 5 days, or a total of 0.5 cc., contains one rabbit unit; but to insure maintenance of pregnancy 0.5 cc. should be given daily. In all cases in which pregnancy terminates prematurely, the extract used should be tested for potency on another rabbit.

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Influence of Tyramine on the Number of Red Corpuscles in the Circulating Blood.

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Rabbits were given tyramine subcutaneously in single doses of various sizes, in hourly doses and in daily doses. With but few exceptions the effect was to increase the number of red corpuscles per cubic millimeter in the circulating blood. The hydrochloride was used. This was dissolved in 0.9% sodium chloride solution in such proportion that 1 cc. contained the dose per kilo of body weight, and the solution warmed to body temperature before injection.

Single doses of from 0.1 mgm. to 20.0 mgm. per kilo of body weight were used. The average results of these are given in Table 1. A dose of 0.5 mgm. per kilo caused an increase in the red blood corpuscle count of 18.46% and was selected as an average effective dose.

Each of 4 rabbits was given 0.5 mgm. per kilo of body weight and the dose repeated at intervals of one hour until 4 doses had been given. The results are summarized in Table II.