older the animal, the smaller and more discrete became the ossification zones and the less intensely did they stain. Rats which had received the alkaline extract for 2 weeks showed in the same areas as in the controls a greater activity in periosteal bone formation evidenced by a laying down of more madder. The bones of the freshly autopsied animals appeared redder in contradistinction to the lighter pink color in those of the control animals. Furthermore, the ossification centers in several of the bones had increased in size as demonstrated by a greater area of coloration. The reaction of the bones to anterior lobe administration consisted of an intensification of the activity of the normal periosteal ossification zones. There was no evidence of abnormal zones being created or stimulated.

On comparing the weight and bone changes in the same animals, it was observed that the amount of madder deposited was roughly parallel to the weight increments, that is, those individuals that gained most weight after anterior lobe administration showed the most intensely stained bones and *vice versa*.

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Parthenogenetic Development of Eggs in the Ovary of the Guinea Pig.

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In 1905 I described,[1] in the ovary of the guinea pig, unusual structures which at first I interpreted as peculiar types of follicular atresia. Further experience, however, convinced me that these structures originated from parthenogenetically developing ova.[2] Since then, long continued study of the ovary of the guinea pig and its various structures has strengthened my conviction that my interpretation was correct.[3] However, a paper by Kampmeier[4] recently expressed the opinion that the structures described by me are not

[1] Loeb, Leo, *Arch. f. mikrosc. Anatomie u. Entwicklungsgesch.*, 1905, lxv, 3.

[2] Loeb, Leo, *Z. f. Krebsforchung*, 1912, xi, 1. *Arch. f. Entwicklgsmech*, 1911, xxxii, 662.

[3] Loeb, Leo, *Science*, 1923, lviii, 35.

[4] Kampmeier, Otto F., *Am. J. Anat.*, 1929, xliii, 45.

embryonic in character but represent abnormal *corpora lutea.*

In view of the great interest in this question and because a fuller publication, for which I had begun to prepare several years ago, has to be delayed, and to prevent the acceptance of erroneous interpretations, I here state briefly the principal reasons which led me to the conclusion (a) that we have to deal in the ovarian structures with embryonic formations and (b) that these embryonic structures owe their origin to parthenogenesis.

(a) The conclusion that we have to deal with embryonic structures is based on the following facts: (1) in 2 animals I observed, within ovaries, early embryos corresponding approximately to the neurula, and in a third case, remains of such structures. One should expect that in the circumscribed area of an ovarian follicle the embryonic development would be very defective; yet, in one case the compression exerted by the rigid wall of the follicle led to only very slight abnormalities, while they were somewhat greater in the second animal. Not only embryonic structures like a neural tube could be readily recognized but, also, the trophoblast was well developed. In more than 30 guinea pigs, we found in the ovary structures closely corresponding to the fetal placenta. These formations are oval or round and the central cavity is lined by an inner layer of cuboidal cells and an outer layer of giant cells and plasmodia; from here chorionic wandering cells penetrate into the surrounding ovarian tissue. They have the tendency to follow the course of the blood vessels and even to penetrate through their wall. This characteristic behavior and the relatively slight resistance offered by such capillaries at the time of oestrus, when there is marked hyperemia, may lead to extensive hemorrhages into the ovary. These bodies are almost identical in character with structures found in the normal embryonal placenta of the guinea pig and with structures found in a case of early extra-uterine pregnancy which I produced experimentally in this species. Moreover, within a single placental body in the ovary, I found combinations of these structures which represent rudimentary trophoblast, and others which represent typical well developed trophoblast of the guinea pig placenta. Another circumstance which gives additional support to my interpretation is the fact that in the ovaries of the same animal we may find in various places multiple new formations representing different types of embryonic structures, namely, in one place a neurula, in another place typical trophoblast with hemorrhage, and in a third place a well developed cystic placental structure. Thus, in a number of cases

multiple structures were found in the 2 ovaries of the same guinea pig.

These facts leave no doubt as to the correctness of our interpretation regarding the character of these bodies. There is certainly not the slightest similarity between these structures and normal or abnormal *corpora lutea;* I have studied the *corpus luteum* of the guinea pig under a great variety of conditions and the various stages in the development of the *corpus luteum* of the guinea pig.[5] Nowhere did I find the slightest resemblance of these embryonal structures to *corpus luteum.* This was also evident in comparing sections of the *corpora lutea* which Dr. Kampmeier found in the dog and which he kindly sent me, with the structures which I found in the guinea pig.

(b) Our conclusion that these bodies owe their origin to parthenogenetic development of eggs and not to fertilized ova, is based on the following facts: (1) In a number of cases the embryonic structures were found in young guinea pigs which had not yet ovulated and were thus sexually immature at the time of examination. This fact alone seems to dispose of the view that we had to deal with fertilization of ova within the ovary. (2) These structures occurred in guinea pigs which had been kept separate from males. (3) They were found in animals during the latter part of pregnancy, and during pregnancy ovulation does not occur. Inasmuch as these embryonal bodies are destroyed through ingrowth of connective tissue after some time, it is improbable that they persist in such a perfect condition for as long a period as 2 months. (4) It is difficult to conceive of a mechanism by which an ovarian fertilization could take place. We would have to assume that following an ovulation, spermatozoa passed through the tube into the peritoneum, that they remained there at least for about 14-16 days and then, at the time of the next ovulation, fertilized the ova. It is very improbable that such a process could occur; however, whether or not this is possible is subject to experimental tests which we intend to make in the near future.

As to the frequency with which these formations occur, all we can state is that they are not exceptional. However, I do not think it of great importance at the present time to make an exact statement as to the frequency of their occurrence. They are not a peculiarity of guinea pigs at any particular locality; they have been found by me in Montreal, Philadelphia and St. Louis. Yet, it is possible that interferences which we applied to produce these bodies

[5] Loeb, Leo, *Anat. Anzeiger,* 1906, xxviii, 102.

experimentally, increased the frequency of their occurrence. In the last few years we have found only one embryonal structure in the ovary of a guinea pig and this was in an animal which had been hysterectomized several weeks previously by Dr. R. J. Crossen in our laboratory. The fact that no intermediate stages between the early irregular segmentation of the ovum and the fully developed embryonal structures have been encountered so far, can easily be understood if we consider the rapidity with which the developing ovum passes through the early stages of development, it then stops when a certain critical stage has been reached at the period of the formation of neurula or embryonal placenta and trophoblast.

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A Reversible Experimental Uremia.

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If the *vena cava* in ♀ albino rats is ligated and cut immediately above the entry of the renal veins there is a temporary cessation of renal function and the blood urea rises to very high levels. By the end of the second day a urine is voided which looks like water. It contains a high concentration of protein and many renal failure casts. Ninety day old rats were used. They were taken from the usual stock diet for the colony, operated upon and given only distilled water after the operation. Groups of 8 or 10 were sacrificed at intervals of from one to 6 days after the operation. The average concentration of blood urea, mgm. per 100 cc., on these various days was as follows: On the first day 268, on the second 413, on the third 278, on the fourth 63, on the fifth 55, and on the sixth 31. These rats excreted normally from 2 to 4 mgm. of protein in the urine in 24 hours but during the first and second days following the operation they excreted from 40 to 55 mgm. per 24 hours. Of the 57 rats used in this part of the work 2 died, giving a mortality of 3.5%. As controls similar animals had the same operative procedure carried out except that the *vena cava* was not ligated or cut, or it was ligated and cut immediately below the entry of the renal veins. The highest concentration of blood urea found in these animals was 34 mgm. per 100 cc., there was little or no increase in the amount of protein excreted, and none of them died.