will register early. The admission to the exhibition will be simplified if members will wear their badges. The attendance is growing so rapidly that it is becoming more imperative to make the exhibition for the membership. However, members will be entitled to bring in the members of their families.

F. C. BROWN,
Director of Exhibits

SPECIAL ARTICLES

OVUM AGE AND THE COURSE OF GESTATION IN THE GUINEA PIG[1]

IN domestic mammals, as the horse,[2] the cow,[3] the ewe,[4,5] the sow[6] and the guinea pig,[7] in which ovulation is spontaneous, it has been found to occur late in the period of heat or even shortly after its end. As a result ova ordinarily are not compelled to await the arrival of the spermatozoa. Whatever waiting is necessary usually falls to the lot of the male cells. That this arrangement may not be without significance is indicated by the lowered fertility of the sow,[6] the ewe,[8] the rabbit[9] and the ferret[10] mated shortly before or soon after ovulation and by the abnormal development of aged sea urchin eggs.[11]

In our studies of the structural and behavioral changes at oestrus in the guinea pig it has been convenient to investigate the relationship between ovum age and the course of gestation and development in this species. A complete report can not be given until preparation and study of the abnormal embryos we have recovered has been possible. In the meantime, though, certain data bearing upon the relationship between ovum age and the course of gestation have accumulated and because of their importance for problems in embryology and the physiology of reproduction they are being reported now.

Exclusive of 21 animals which did not survive the period of pregnancy, 235 individuals were inseminated artificially with spermatozoa freshly removed from the epididymides of normal males and placed in Locke's solution at room temperature. Of these, a control group of 45 were inseminated during heat and prior to ovulation. The remainder were inseminated 18, 24, 30, 36 or 42 hours after the beginning of oestrus, which may safely be assumed to be about 8, 14, 20, 26 and 32 hours respectively after ovulation.[7]

Following insemination the animals were examined twice daily for open vaginal membranes, which usually indicate that impregnation has not occurred, or for bloody vaginal orifices, which have been found to indicate that fetal death has occurred and gestation is to be terminated prematurely. When an instance of the latter was detected the female was killed immediately and the uterus with its contents and the ovaries removed for examination, fixation and subsequent microscopical study. Except for the individuals that were killed because of an abnormal pregnancy, no animal was removed from the colony until the last litter was born. This precaution enabled us to avoid errors of diagnosis in the few cases in which the vaginal membrane opened despite the presence of normal fetuses.

The percentage of impregnations, abnormal pregnancies (embryonic death within the first 20 days, later fetal death followed by abortion before the 66th day and stillbirths at full term) and normal pregnancies are given in Table I. In addition, the average

[1] This investigation was supported by a grant from the Committee for Research in Problems of Sex, National Research Council.

[2] W. A. Aitken, *Vet. Pract. Bull., Iowa State Coll.*, 8: 178, 1926.

[3] J. Hammond, "Physiology of Reproduction in the Cow," Cambridge University Press, 1927.

[4] E. Allen, F. F. McKenzie, J. W. Kennedy and W. K. Beare, Abs., *Proc. Am. Assoc. Anat., Anat. Rec.*, 48, Suppl.: 9, 1931.

[5] J. Quinlan and G. S. Maré, *17th Rept. of the Div. of Vet. Services and Animal Indust., Union of S. Africa:* 663, 1931.

[6] L. L. Lewis, *Okla. Agric. Exp. Sta. Bull.*, No. 96: 3, 1911.

[7] H. I. Myers, W. C. Young and E. W. Dempsey, *Anat. Rec.*, 65: 4, 1936.

[8] J. Quinlan, G. S. Maré and L. L. Roux, *18th Rept. of the Div. of Vet. Services and Animal Indust., Union of S. Africa:* 813, 1932.

[9] J. Hammond, *Jour. Exp. Biol.*, 11: 140, 1934.

[10] J. Hammond and A. Walton, *Jour. Exp. Biol.*, 11: 307, 1934.

[11] A. J. Goldfarb, *Biol. Bull.*, 35: 1, 1918.

TABLE I

IMPREGNATIONS, NORMAL PREGNANCIES, ABNORMAL PREGNANCIES AND LITTER-SIZE FOLLOWING INSEMINATION BEFORE AND AFTER OVULATION

Time of insemination	Number of inseminations	Impregnations	Normal pregnancies	Average litter-size	Abnormal pregnancies	Average number of recovered embryos
During oestrus	45	36 or 80 per cent.	32 or 89 per cent.	2.7	4 or 11 per cent.	2.0
18 hrs. after beginning ...	37	21 or 57 " "	12 or 57 " "	2.0	9 or 43 " "	2.2
24 " " "	41	20 or 48 " "	5 or 25 " "	2.2	15 or 75 " "	1.5
30 " " "	49	16 or 32 " "	3 or 19 " "	1.3	13 or 81 " "	1.6
36 " " "	42	4 or 9.5 " "	0 or 0 " "	0.0	4 or 100 " "	1.0
42 " " "	21	0 or 0 " "	.....	...	.....	...

litter size from normal pregnancies and the average number of recovered embryos and fetuses from abnormal pregnancies are given.

The decrease in the percentage of impregnations as ovum age increases is not unexpected. Interesting, however, are (1) the extreme limit of ovum viability, which is about 26 hours; (2) the limit of ovum age from which any normal individuals may be expected, which is about 20 hours; and (3) the time after ovulation when ovum age effects are first expressed, which is not more than 8 hours.

Also of interest are the smaller average litter-size in animals inseminated after heat and ovulation, and the subnormal number of embryos per female in the case of individuals having abnormal pregnancies. That these deficiencies are not attributable to any chance reduction in the number of ovulated ova is evidenced by the fact that the number of dead embryos removed often was less than the number of corpora lutea. Probable explanations, therefore, are some failures of fertilization, some embryonic deaths at stages earlier than those we have studied or both. If so, what is indicated for ova of different ages in the guinea pig is an entire range of potentialities from the possession of full developmental capacity through subnormal viability to the complete loss of the ability to be fertilized.

Of most importance perhaps is an analysis of the abnormal pregnancies from the standpoint of the time during gestation when the abnormality became evident (Fig. 1). In the guinea pig such pregnancies usually

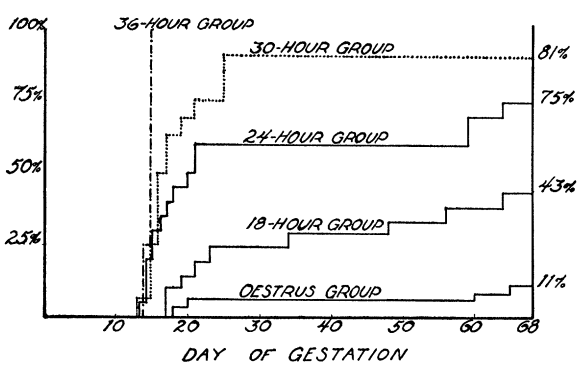

FIG. 1. Time of termination of abnormal pregnancies during the 68-day gestation period.

are terminated near the 18th, the 33rd, the 50th or the 60th to the 64th day following conception,[12] and no important number of exceptions occurred in this experiment. What was noticed, however, was a progressive increase in the frequency with which pregnancies were terminated near the 18th day and earlier as older ova were fertilized. Apparently in the guinea pig ovum age may be one cause of early embryonic death. Later deaths, on the other hand, would seem attributable to some other cause or causes because they are distributed nearly equally in the four groups in which normal litters were born. This latter conclusion, however, must be regarded as tentative until larger numbers of animals can be inseminated.

A continuation and extension of the work is intended to comprehend the gross and finer structure of the recovered dead embryos, the time of death, the nature of the original defect and an analysis of the hormonal relationship between the embryo and the corpus luteum in normal and abnormal pregnancies.

Without the generous assistance given by Messrs. John L. Boling, Edward W. Dempsey, Carl W. Hagquist and Dr. Roy Hertz in the continuous, day and night observation of the animals, completion of the experiments would not have been possible.

WILLIAM C. YOUNG
RICHARD J. BLANDAU
ARNOLD BIOLOGICAL LABORATORY
BROWN UNIVERSITY

[12] W. C. Young, Abs., *Proc. Am. Soc. Zool., Anat. Rec.*, 60, Suppl.: 71, 1934.

THE BLOOD IN HEMOPHILIA[1]

THE identification of a substance or substances contained in normal blood which may supply a clotting factor deficient in hemophilic blood has been the aim of these observations. The procedure consisted of adding to hemophilic blood, both *in vitro* and *in vivo*, graded amounts of normal blood and certain of its separate components. Studies made with normal and hemophilic platelet suspensions in physiological concentration revealed no differences in their behavior regarding clot production.

In normal blood and in citrated normal plasma rendered free from platelets by Berkefeld filtration, there is a substance which in small quantity effectively reduces the clotting time of hemophilic blood. This substance is either greatly diminished or unavailable in hemophilic blood and plasma.

The clot-accelerating substance in citrated normal plasma is stable for at least two months at 5° to 10° C. It is completely inactivated when kept at 56° C. for one-half hour. When normal plasma was dialyzed in Cellophane sacks against distilled water for periods varying from 12 to 72 hours, the clot-accelerating substance was found to be non-diffusible, having many characteristics of globulin. Its suspension in 0.85 per cent. NaCl solution showed a thermolability similar to that of the substance in the parent plasma.

A more practical and uniform preparation of this

[1] Preliminary report. From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard Medical School.