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

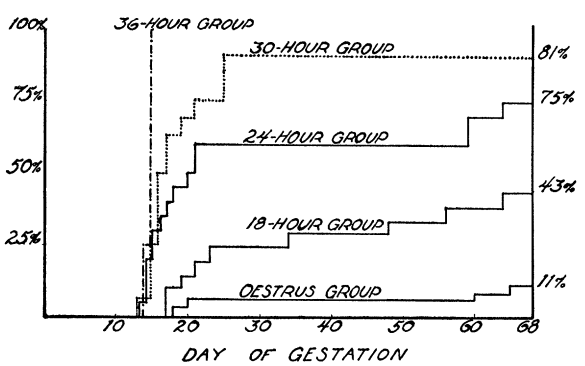

FIG. 1. Time of termination of abnormal pregnancies during the 68-day gestation period.

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.

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[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.

substance was effected by dilution of plasma with 10 volumes of water and acidification with CO_2 to pH 5.8 or with 1 per cent. acetic acid to pH 5.3. The precipitate was collected by centrifuging. After resuspension in 0.85 per cent. NaCl solution to the volume of the original plasma, this substance was as effective as its parent plasma in reducing the clotting time of hemophilic blood. When the precipitate was dried *in vacuo* at room temperature a brown-grey amorphous mass was obtained. Approximately 450 to 600 mgm were derived from 100 cc of citrated plasma. The dried substance was suspended in 0.85 per cent. NaCl solution and centrifuged. The clear supernatant fluid likewise was effective in reducing the clotting time of hemophilic blood both *in vitro* and *in vivo*.

When the above procedure was applied to hemophilic plasma, an approximately equivalent amount of the dried substance was produced, the saline suspension of which, however, had little if any ability to hasten the clotting of hemophilic blood.

Tested against a freshly prepared calcium-fibrinogen system without other coagulation factors, both the normal and hemophilic precipitates were equally active as prothrombin. Our observations seem to indicate that the difference between normal and hemophilic blood is due either to a qualitative difference of their prothrombins or to other substances probably associated with prothrombin. Studies leading to the identification of this substance or to the nature of the prothrombin modification are being made.

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THE ETIOLOGY OF ULCERATIVE ENTERITIS IN UPLAND GAME BIRDS

ULCERATIVE enteritis, or so-called "quail disease," first came to the attention of sportsmen early in 1900 through the exceedingly heavy losses encountered in importations of Mexican quail. The steadily increasing demand for quail for restocking game and shooting preserves has resulted in an increased number of game farms, with a consequent concentration of birds on limited areas. Such concentrations provide favorable conditions for the transmission of the disease, and the majority of game breeders are familiar with the devastating results associated with an outbreak. Although little is known about the prevalence of the disease in wild birds, observations on native ruffed grouse in Minnesota indicate that it may be of wide-spread occurrence.

Ulcerative enteritis is a highly infectious and rapidly fatal disease that affects most species of native upland game birds. Characteristic lentiform ulcers in the intestines are the principal lesions, and the infection is readily transmitted by means of droppings. The average incubation period is about 4 days, though death may occur in 24 to 48 hours and before symptoms or lesions other than those of a toxemia have developed. A diagnosis of the disease can be established by feeding infective intestinal material to test birds. Ordinary cultural methods for isolation of the causative organism yield consistently negative results. A number of contaminating organisms, pathogenic on injection, have been isolated from diseased birds. Since natural infection, however, is contracted by the ingestion of infective material, the feeding test has remained the criterion in attempting to incriminate any organism as the causative agent.

Though a number of investigators, Morse,[1] Barger, Park and Graham,[2] Shillinger and Morley,[3] Pickens, DeVolt and Shillinger,[4] and Levine,[5] have reported on the disease in quail and grouse, no conclusive evidence has thus far been advanced to establish the etiology.

The results of our work, as reported on February 6, 1936, to the North American Wildlife Conference, at Washington, D. C., record for the first time the isolation of an organism from the liver and spleen of diseased birds that is capable of producing death and typical lesions of ulcerative enteritis when fed in pure culture to susceptible quail. Eight strains of the organism, six from bobwhite quail, one from valley quail and one from ruffed grouse, have been studied. Only slight variations in the morphological and cultural characteristics have been noted, but it appears that there may be two or more serological types. The characteristics of the organism causing ulcerative enteritis in quail are as follows:

Corynebacterium perdicum, nov. sp.

Morphology: Primary growth in nutrient broth or agar, short thick rods 0.5 to 0.8 by 2 microns occurring in clumps. Non-motile. Gram-positive. In the tissues and older cultures the organisms are gram-variable. In secondary cultures the rods are of variable dimensions, straight or slightly curved, and show metachromatic granules. Some strains exhibit a marked tendency toward pleomorphism and under certain conditions produce branching filaments, cocci, and intermediary forms.

Cultural and physiological characters: Nutrient broth: Slow growth, with increasing cloudiness and formation of viscid sediment in older cultures. Agar media: No surface growth from tissues on agar media. Primary cultures can be started in semi-solid agar or broth and

[1] G. B. Morse, *U. S. Dept. Agr. Bur. Anim. Ind. Cir.* 109, 11 pp., 1907.

[2] E. H. Barger, S. E. Park and Robert Graham, *Jour. Am. Vet. Med. Assoc.* 84 (n.s. 37): 776.

[3] J. E. Shillinger and L. C. Morley, *Jour. Am. Vet. Med. Assoc.*, 84 (n.s. 37): 25, 1934.

[4] E. M. Pickens, H. M. DeVolt and J. E. Shillinger, *Maryland Cons.*, spring issue, p. 18, 1932.

[5] P. P. Levine, *Amer. Game Conf.*, 19th, Trans., p. 437, 1932.