and in all but one estrus reappeared in from 8 to 20 days after retransplantation.

It is evident that the failure to maintain cycles is not due to inhibition of ovarian ability to ripen follicles and form corpora lutea, but to an inhibitory effect on ovarian products depending on the circulatory path from ovary to pituitary or uterus.

These findings serve to explain the marked difference in effectiveness of a given dose of estrogen given orally when compared with parenteral injection. Other applications to clinical problems are not difficult to find.

Further work on the rôle of the liver in estrogen inactivation is being carried on.

10206 P

Eclampsia-like Syndrome Occurring in Pregnant Dogs and Rabbits Following Renal Artery Constriction.

L. V. DILL AND C. C. ERICKSON. (Introduced by D. H. Sprunt.)

From the Department of Pathology, Duke University School of Medicine, Durham, N. C.

Liver lesions in the experimental animal resembling those seen in eclampsia have been reported by several investigators, and associated renal injury has been noted following the injection of Vasopressin.[1]

Greene[2] has reported spontaneous eclampsia occurring in the rabbit, demonstrating liver lesions in a large number of animals. The spontaneous disease in sheep and guinea pigs has also been reported. In no instance, to our knowledge, has anything comparable to the spontaneous eclamptic complex with its anatomical lesions been produced experimentally.

We wish to record our observations on the rapidly fatal course and pathological findings in pregnant dogs and pregnant rabbits following constriction of the renal arteries. The suggestive significance of pregnancy as a factor in the fatal effect of renal arterial constriction is emphasized by the remarkable rapid recovery of animals if they are delivered.

Eight pregnant mongrel dogs from the stock colony were used for the experimental procedure. All animals were in good condition at

1 Byrom, F. B., *J. Path. and Bact.*, 1937, **45**, 1.

2 Greene, H. S. N., *J. Exp. Med.*, 1937, **65**, 809.

the beginning of the experiment and were maintained in the animal quarters on routine stock diet.

Renal artery clamps modeled after the Goldblatt[3] clamp were applied in such a manner as to produce minimal to moderate constriction of the renal arteries in the pregnant animals. A single renal artery clamp was applied on about the 15th and 20th day before the probable date of delivery in 2 pregnant dogs. The second clamp was applied approximately 10 days later. In 6 pregnant dogs 2 renal artery clamps were applied simultaneously, 2 to 30 days before the expected date of delivery. Periodic blood pressure determinations were obtained by direct arterial puncture. Qualitative urinary examination and blood determinations for N. P. N. and uric acid were made at intervals. Complete autopsies were performed immediately after death except in 2 instances in which there was a delay of more than 4 hours. Two dogs were sacrificed by administration of illuminating gas through inhalation.

Five non-pregnant female and 2 male dogs were used for the control series. Both renal arteries were moderately or severely constricted in these animals, but otherwise they were treated as the animals in the experimental group.

The significant limitation of survival time in the pregnant animals is noteworthy. Within 48 to 120 hours following constriction of the renal arteries the pregnant dogs developed weakness, lassitude, coma, and convulsions, and all exhibited hypertension, hematuria, albuminuria, and nitrogen retention. Death occurred in 5 pregnant animals in from 5 to 15 days, and 2 were sacrificed after 4 and 7 days.

In 2 of the pregnant animals operation was followed by the rapidly progressing toxic signs and symptoms which proved to be characteristic of these pregnant animals. One animal delivered 24 hours later with subsequent rapid improvement, and the animal is now living and well after 8 months with a sustained hypertension. The other animal delivered 5 stillborn and macerated fetuses 48 hours after operation followed by rapid improvement and with all the appearances of ensuing well-being. N. P. N. was 29 mg per 100 cc and uric acid was 1.1 mg per 100 cc 24 hours after delivery. The animal was killed at this time.

Of the control group, despite severe renal artery constriction, one male is living after 11 months, and one female is living after 6 months with both animals maintaining a sustained hypertension. In no instance did we produce in the controls the rapidly fatal clinical

[3] Goldblatt, Lynch, Hanzal, and Summerville, *J. Exp. Med.*, 1934, **59**, 347.

course with minimal arterial constriction such as occurred in the pregnant animals. In 4 control dogs it was necessary to increase the severity of the renal artery constriction at subsequent operations. This group of dogs died in uremia 3 to 30 days following the severe renal artery constriction. These observations suggest that some factor other than simple renal insufficiency is concerned in the production of the rapid and fatal course noted in the pregnant animal.

The significant autopsy findings in the 7 pregnant dogs with constricted renal arteries were evidences of terminal acute cardiac failure with pulmonary edema (with infarction in some instances), hemorrhage and infarction in the myocardium, and scattered hemorrhages in the gastro-intestinal tract. The kidneys showed changes characteristic of renal ischemia with lobular renal necrosis where renal artery branches had been occluded. Alterations noted in tissues of one animal were impossible to interpret microscopically due to terminal invasion by gas bacilli. Of the remaining 6 pregnant animals, all showed suggestively significant widespread liver lesions. In 2 pregnant animals conspicuous large areas of coagulation necrosis were present with hemorrhage, laked red cells and fibrin. These lesions imitate closely those described by many as typical of human eclampsia and which are known to consist primarily of periportal necrosis with hemorrhage and periportal "laking". In addition to this more specific lesion there were in the pregnant animals all degrees of liver injury varying from simple periportal cloudy swelling, dilatation of sinusoids, and hemorrhage to occasional periportal necrosis and even more conspicuous focal necrosis. These lesions appear to have developed in a manner comparable to that which obtains in human eclampsia and indeed they resemble the hepatic lesions of this disease.

In the control animals small hemorrhages in the myocardium were occasionally seen. The liver showed only an intense central congestion. The kidneys and lungs did not differ from those of the experimental animals.

In another experiment with groups of pregnant and control rabbits and in which a similar but modified technic was used our results were remarkably comparable to those recorded in the dog experiments. In pregnant rabbits we noted a uniformly characteristic response. Death occurred usually within 48 to 120 hours and autopsy showed lesions involving kidneys and liver comparable to those described in spontaneous eclampsia of rabbits (Greene[2]).

These preliminary observations indicate that experimentally produced renal ischemia or renal injury in pregnant dogs and pregnant

rabbits results in an eclampsia-like syndrome, characterized by a rapidly fatal clinical course and significant pathological lesions in the liver and kidney.

We wish to suggest the probability of a correlation between the physiological and pathological processes underlying these observations and the mechanism of human eclampsia. These and further observations will be reported more fully when experiments now under way have been completed.

10207 P

Further Observations on the L Organism of Klieneberger.

LOUIS DIENES.

From the Department of Pathology and Bacteriology, Massachusetts General Hospital, Boston.

The L organism which Klieneberger[1] isolated from the cultures of *Streptobacillus multiformis* and more recently directly from pathological lesions of rats presents many characteristics which are not observed in bacteria. It has a marked similarity to a group of microörganisms, the main representative of which is the causative agent of pleuropneumonia bovis. The relation of this group to the well characterized classes of microörganisms is obscure. The L organism starts to grow in very small units which pass readily through a coarse bacterial filter. Later the small forms develop into large yeast-like bodies. Probably the small bodies are reproduced by the disintegration of the large forms. In all stages of development the organism is very fragile and its form can be seen only by using special technic. Since pleuropneumonia-like organisms occur in different animals[2] and probably also free in nature,[3] their occurrence in rats is not unexpected. However, it is very surprising to find such organisms regularly in the cultures of a bacillus.

Klieneberger regards the connection between the L organism and

[1] Klieneberger, E., *J. Path. Bact.*, 1935, **40**, 93; 1936, **42**, 587; *J. Hyg.*, 1938, **38**, 458; Klieneberger, E., and Steabben, D. B., *J. Hyg.*, 1937, **37**, 143.

[2] Shoentensack, H. M., *Kitasato Arch. Exp. Med.*, 1934, **11**, 277; 1936, **13**, 175 and 269) (Quoted after Klieneberger).

[3] Seiffert, G., *Zbl. Bakt. I. O.*, 1937, **139**, 337; Oerskov, J., *Zbl. Bakt. I. O.*, 1938, **141**, 229.