

Service. At random examinations of the kidneys of 420 rats (*Mus norvegicus*, *M. alexandrinus* and *M. rattus*) in dark field preparations yielded positive leptospira findings in 139, or 33%. In the vicinity of a stable, 42 of 44 old Norvegicus rats have been found infected. Twenty-two strains have been isolated by guinea pig passage. They all produced fatal infections with icterus on the first, second or third passage. Both the pathological effect and the serological tests in part conducted by Prof. W. A. P. Schüffner identify the rat spirochaetes as *Leptospira icterohaemorrhagica*. Since these preliminary observations have thus far failed to demonstrate *Leptospira canicola* in the rat population, one is justified in concluding that the host relationship of the two spirochaetes recognized in California is the same as in Holland. It has been repeatedly emphasized by Schüffner and Klarenbeek that the dog, the only reservoir for *Leptospira canicola*, causes aberrant human infections. On the other hand, the rat reservoir of *Leptospira icterohaemorrhagica* is equally the source of infections for both man and dog. Canine Weil's disease due to *Leptospira icterohaemorrhagica*, which spreads independently of exposure to rats by simple contact from dog to dog, has not as yet been identified in the United States.

### 9723 P

#### Effect of Prontosil on Blood Cells.

WALTER B. KREUTZMANN AND J. L. CARR. (Introduced by C. L. Connor.)

*From the Pathological Department, University of California, and the Franklin Hospital Laboratory.*

Despite the now voluminous literature on sulfanilamide and prontosil, little has been recorded on the cytological changes in blood or tissues taken from animals given doses of this drug over a prolonged period of time. In order to evaluate the tissue changes following administration of prontosil, the following experiment was undertaken with a desire to demonstrate the cytological changes in parenchymatous organs during the administration of moderate doses of the drug, and to follow the changes in the cellular elements of the blood throughout the experiment.

For this purpose, 12 rabbits were chosen of equal size and age, weighing 1200 gm. apiece. These were mixed males and females

which were kept in well-aired, clean cages during the entire experiment and fed on a normal laboratory diet of rolled oats, alfalfa, fresh green vegetables, and cod liver oil. They were divided into 2 groups, 4 animals being kept as controls and 8 animals were given 10 cc. (0.25 gm.) of prontosil (Winthrop Chemical Company) per kilogram of body weight for 21 consecutive days. The injections were given alternately in either hindleg in the adductor muscle group. This dosage was chosen because it represents an amount slightly in excess of that advised by Long<sup>1</sup> for clinical use. The injections apparently caused no pain and the drug was absorbed very rapidly from the muscle. In 2 to 3 minutes the ears would show a pink coloration and after the first injection, the urine was tinged red by the drug administration. At no time during the experiment did any evidence of pain, edema, soreness or infection develop in the areas of injection.

The color index of the erythrocytes, the erythrocyte count, the hemoglobin percentage, the white blood count with differential studies and the platelet count were done daily throughout the experiment on all animals. At the end of 21 days, the animals were killed by the intravenous injection of 10 cc. of air and necropsied. Tissue sections were made.

Throughout the 21-day period the erythrocyte, polymorphonuclear, and platelet counts ran closely parallel in the treated and untreated animals. The erythrocytes varied between 5 and 6 million, the platelets from 4 to 7 hundred thousand, and the white blood cells from 6 to 10 thousand per cubic millimeter. The hemoglobin level in both groups remained in a narrow zone between 60 and 70%. In the rabbits receiving treatment there was a rise of from 10 to 15% in the number of erythrocytes and in the hemoglobin concentration in the week following the 21-day period of injection. The other elements remained unchanged during this period.

In the differential studies, the treated animals showed an increase of from 10 to 14% of eosinophiles in the peripheral blood over the normally high level seen in rabbits, and in the second week of injection of the drug, increased numbers of stippled erythrocytes were found.

Microscopic examination of the tissues showed a moderate congestion of the splenic pulp with erythrocytes, and an increase in the proportion of single-lobed eosinophiles in the bone marrow.

*Conclusions.* 1. Prontosil given to rabbits in a dosage of 0.25 gm. per kilo of body weight causes no numerical change in the cellular

---

<sup>1</sup> Long, P. H., and Bliss, E. A., *J. A. M. A.*, 1937, **108**, 32.

elements of the blood in 21 days. 2. An increase in stippled erythrocytes and eosinophilic polymorphonuclear cells occurs, suggesting mild bone marrow depression. 3. The parenchymatous organs show congestion of the spleen and an increase of eosinophiles in the bone marrow, suggesting again an early bone marrow depression.

### 9724 P

#### Effect of Theelin on Transplantable Mammary Rat Adenofibroma.\*

LUDWIG A. EMGE, KATHLEEN M. MURPHY AND WALTER SCHILLING.

*From the Department of Obstetrics and Gynecology, Stanford University School of Medicine.*

Murray,<sup>1</sup> Lacassagne<sup>2</sup> and others have shown in males of certain strains of mice that estrogenic hormone may awaken a dormant malignant potentiality in breast tissue. Lewis and Geschickter<sup>3</sup> reported the presence of measurable amounts of estrogenic and gonadotropic hormones in adenofibromas of the human female breast. Numerous investigators have inquired into this phenomenon in relation to other mammalia and contradictory evidence has been forthcoming. Recently Frank and his coworkers<sup>4</sup> reported observations throwing doubt on the influence of these hormones on breast tissue, for other tissues also contain large amounts of estrogenic hormone normally. Heiman and Krehbiel<sup>5</sup> found measurable amounts of estrin in rat adenofibromas, but Mohs<sup>6</sup> not only failed to find appreciable amounts in such tissue but also observed that estrin administration raised the estrin content in these tumors only if high doses of this hormone were given 2 or 3 days prior to sacrifice.

---

\* Aided by grants from the Rockefeller Fluid Research Fund of Stanford University School of Medicine, and from the Scientific Research Committee of the American Medical Association. We are grateful to Parke, Davis and Company for the donation of theelin used in this experiment.

<sup>1</sup> Murray, W. S., *J. Cancer Research*, 1928, **12**, 18.

<sup>2</sup> Lacassagne, A., *Compt. rend. Acad. d. sc.*, 1932, **195**, 630.

<sup>3</sup> Lewis, D., and Geschickter, C. F., *J. A. M. A.*, 1934, **103**, 1212.

<sup>4</sup> Frank, R. T., *et al.*, *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 1665.

<sup>5</sup> Heiman, J., and Krehbiel, O. F., *Am. J. Cancer*, 1936, **27**, 450.

<sup>6</sup> Mohs, F. E., *Am. J. Cancer*, 1937, **29**, 356.