son, and Loomis[1] state that 1-2 mg of crystalline progesterone daily are required to maintain the adrenalectomized rat. It is interesting, in view of the toxic effects of estrin in such animals, that the flourishing corpus luteum produces a sufficient amount of progestin to replace cortical hormone and also to overcome the effects of whatever estrogenic substance is being produced. The ovaries of the animals on the lower dose were apparently able to secrete progestin equivalent to 5% of their own weight daily. Further experiments are under way to determine, by means of continued injection, for how long a time the corpora are able to maintain this high level of progestin output.

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Sulphanilamide and Related Compounds in Experimental Tuberculosis.

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It was previously[1] shown that sulphanilamide—300 mg per animal per day—had an inhibitory effect upon the development of experimental tuberculosis in the guinea pig when the drug was administered before the injection of virulent human tubercle bacilli. These results were similar to those of Rich and Follis,[2] and Buttle and Parish.[3] However, we found no difference in the extent of macroscopic tuberculosis in treated and control animals when sulphanilamide was administered 17 and 24 days after the establishment of the tuberculous infection. But Ballon and Guernon[4] did find definite differences when the drug was given both 5 and 10 days after the infection. The latter 2 authors also found some evidence of bacteriostasis *in vitro*.

[1] Gaunt, Robert, Nelson, W. O., and Loomis, Eleanor, PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 319.

[1] Greey, P. H., Campbell, H. H., and Culley, A. W., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 22.

[2] Rich, A. R., and Follis, R. H., Jr., *Bull. Johns Hopkins Hosp.*, 1938, **62**, 77.

[3] Buttle, G. A. H., and Parish, H. J., *Brit. M. J.*, 1938, **2**, 776.

[4] Ballon, H. C., and Guernon, A., *J. Thoracic Surg.*, 1938, **8**, 184 and 188.

Dietrich[5] has recently reported that Prontosil soluble does not modify the tuberculous process in guinea pigs even when given before the animals were infected. Similarly Kolmer, Raiziss and Rule[6] found that sulphanilamide and 6 derivative compounds given intramuscularly had no demonstrable beneficial effect in the treatment of experimental tuberculosis of guinea pigs. However, their method of administration of sulphanilamide and dosage were not entirely the same as those used in our experiments. Buttle and Parish,[3] using a bovine strain of tubercle bacilli, found that sulphanilamide had but little effect in guinea pigs, and none in rabbits.

The present report deals with a comparative study of the effect of sulphanilamide and related substances upon the tuberculous process in the guinea pig and rabbit. The following substances were studied and their effect compared with the result obtained with sulphanilamide: Prontosil soluble, Prontosil base, the dimethyl derivative of disulphanilamide (Uleron), diacetyl diamino diphenyl sulphone and p-benzylamino benzenesulphonamide (Septazine).*

(a) *In Guinea Pigs.* The total daily dose of the drugs was divided into 4 equal doses and administered at 9 a.m., 1 p.m., 5 p.m., and 10 p.m. *per os* by means of a nasal speculum. The drugs were administered in the following amounts per guinea pig per day: sulphanilamide, diacetyl sulphone, Uleron and Septazine 300 mg each, Prontosil base 50 mg, Prontosil solution 2 cc of a 2½% solution. Eight guinea pigs were used for each compound while 20 untreated animals served as controls. The various compounds were administered for 3 days, then all the animals were infected by the subcutaneous injection of 0.2 cc of a suspension of virulent human tubercle bacilli containing 2-6 microörganisms per oil immersion field. Only multicolored guinea pigs weighing about 350 g were used. At death the treated animals were necropsied and the macroscopic and microscopic findings were compared with those of the sulphanilamide-treated and control animals that had been infected for a similar period of time.

Again it was found that in the animals treated with sulphanilamide the lesions in the spleens and livers were small and few in number in contrast to the many prominent tubercles in the control

[5] Dietrich, H. F., *Am. Rev. Tuberc.*, 1938, **38**, 388.

[6] Kolmer, J. A., Raiziss, G. W., and Rule, A. M., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 581.

* The following compounds were generously supplied by: Winthrop Chemical Co., Prontosil base, sulphanilamide, Uleron and diacetyl sulphone; Poulenc Frères Ltd., Septazine and diacetyl sulphone; E. B. Shuttleworth Chemical Co., sulphanilamide.

animals. The lesions in the animals treated with the other compounds, however, were equal to and in some instances exceeded in number and size those in the controls.

All the compounds proved to be toxic in the doses used, in that half of the treated animals died before the end of the fourth week and on several occasions it was found necessary to decrease the daily dose of the compounds for 2 days in order to overcome toxic symptoms.

(b) *In Rabbits.* In this experiment each of the aforementioned compounds were administered to 2 rabbits 4 times daily at the same hours as the guinea pigs were treated. Six rabbits served as controls. The compounds were administered for 3 days and then all 18 rabbits were infected by an intravenous injection of 1 cc of a light suspension of virulent bovine tubercle bacilli. The rabbits selected for use weighed about 1.2 kilos and the compounds were administered in the following total daily dose per animal: sulphanilamide, diacetyl sulphone, Uleron and Septazine 1 g, Prontosil base 200 mg and Prontosil solution 8 cc of a 2½% solution.

The treated and untreated animals died during the third to fourth weeks after the injection of bovine tubercle bacilli. At necropsy all the rabbits showed widespread tuberculous infection of the lungs and no difference could be noted between the lesions of the treated animals and of the controls. Several microscopic sections were prepared from the kidneys of both the treated and untreated animals. Examination failed to reveal any difference in the renal lesions in the treated animals from those occurring in the controls.

Conclusions. Under the conditions of the experiment sulphanilamide was again found to inhibit the tuberculous process in guinea pigs infected with human tubercle bacilli. The large doses necessary to obtain such results preclude clinical application. In guinea pigs similarly infected but treated with Prontosil soluble, Prontosil base, the dimethyl derivative of disulphanilamide (Uleron), diacetyl diamino diphenyl sulphone and benzylamino benzene sulphonamide (Septazine) the tuberculous process was not inhibited. The above compounds, including sulphanilamide, exerted no influence upon the course of the tuberculous infection induced in rabbits by the intravenous injection of bovine tubercle bacilli. The renal lesions in the treated and control rabbits showed no differences.