

(actually 2.92 in Table I) which would ordinarily lead one to suspect a probable significance in the difference noted, such significance is questionable for the following reasons. First, it will be noted (Table I) that while the vaginal opening of the treated non-castrate animals occurred in some cases a day earlier than in some of the treated castrate rats, the vaginas of all treated animals were open by the 35th day. Secondly, in some animals not included in the experiments herein reported, vaginal opening under similar conditions was seen to occur on the 30th day of age. Finally, in experiments reported elsewhere⁸ it was observed that the Graffian follicle under the influence of chronic injections of testosterone propionate was actually inhibited in growth and failed to ovulate.

Conclusions. Testosterone propionate (Perandren-Ciba) stimulates vaginal opening in both non-spayed and spayed immature female rats. This substance, therefore, does have an effect on the vaginal zone which is independent of the ovary. Because such direct effect has been noted and because the age at which vaginal opening occurs in the non-spayed and spayed test groups corresponds so closely it is believed that the intact ovary plays but a negligible part in the process under the conditions of these experiments.

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Effect of Sulfanilamide on Experimental Tuberculosis in the Guinea Pig.

P. H. GREY, H. H. CAMPBELL AND A. W. CULLEY. (Introduced by W. L. Holman.)

From the Department of Bacteriology, University of Toronto, and the Toronto General Hospital.

Sulfanilamide has been found by Rich and Follis¹ to exert a markedly inhibitory effect upon the development of experimental tuberculosis in the guinea pig. These authors noted that 100 mg of sulfanilamide in a single daily dose did not modify the tuberculous process, while 2 daily doses of 100 mg produced considerable inhibition. This was much more marked when 500 mg of sulfanilamide, divided into 4 doses, were given daily. In their experiments treatment was commenced 3 days before the subcutaneous injection of the human tubercle bacilli. Smithburn,² on the other hand, failed to

⁸ Rubinstein, H. S., *J. A. M. A.*, in press.

¹ Rich, A. R., and Follis, R. H., Jr., *Bull. Johns Hopkins Hosp.*, 1938, **62**, 77.

² Smithburn, K. C., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **38**, 574.

find any beneficial effect from the daily administration of 200 mg of sulfanilamide intraabdominally to guinea pigs that had been infected 24 hours before by the intracerebral inoculation of a small number of virulent human tubercle bacilli.

The present report deals with the effect of sulfanilamide upon the tuberculous process in the guinea pig before, and at different intervals after, infection. Forty-eight guinea pigs averaging about 350 g were used in groups of 12. The drug (Prontylin powder, Winthrop Chemical Company) was administered *per os* throughout the experiment in measured doses of 100 mg at 9 a.m., 5 p.m., and 11 p.m. daily, in powdered form with the aid of a nasal speculum, and the animals were found to retain practically all of the drug with this technic. These guinea pigs were infected by the subcutaneous injection of 0.2 cc of a suspension of virulent human tubercle bacilli containing 2 to 6 microorganisms per oil-immersion field. The 12 guinea pigs in group A received sulfanilamide 3 days before, those in group B 17 days after, and in group C 24 days after the infecting injection. At death the treated animals were necropsied and the macroscopic and microscopic findings were compared with those of the control animals that had been infected for a similar period of time. This was made possible by using as controls the animals of groups B and C that died before treatment.

The lesions in the spleens and livers of the animals that had received sulfanilamide before infection were small and few in number in contrast to the many prominent tubercles in the control animals. This difference was even more marked microscopically and but few acid-fast bacilli were found in the lesions compared to those of the controls. The inhibition of the tuberculous process in these organs by sulfanilamide, however, was not quite as marked as that described by Rich and Follis. Furthermore, the extent of the local lesion at the site of the injection was not greatly modified by treatment in this group. In the 2 groups that received treatment 17 and 24 days respectively after infection, there was no appreciable difference noted in the amount or extent of macroscopic tuberculosis. But microscopically the lesions in the treated animals usually could be distinguished from those of the control group in that they presented less extensive necrosis and greater proliferation of endothelial cells.

All of the animals used in these experiments were tested intracutaneously by 0.1 cc of old tuberculin at varying intervals during the infection. The development of sensitivity was not significantly affected in any way by the drug.

The daily administration of 300 mg of sulfanilamide was found to be definitely toxic for the infected guinea pig. This was shown by the fact that the control animals survived longer than those treated. The toxicity of the compound was greatest for pure-white guinea pigs.

Conclusions. Under the conditions of the experiment it was found that sulfanilamide had an inhibitory effect upon the development of tuberculosis in the guinea pig if the drug was administered before the infection was given. When the infection had been present 17 to 24 days, treatment with sulfanilamide did not alter the macroscopic appearance of the tuberculous process. The development of sensitivity to tuberculin was unaltered by sulfanilamide therapy.

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Analysis of Insulin Response of Rabbits After Injection of Diabetic Serum.

F. C. DOHAN. (Introduced by F. D. W. Lukens.)

From the George S. Coz Medical Research Institute, University of Pennsylvania, Philadelphia.

Since the measurement of substances antagonistic to insulin is not possible by direct chemical methods, various indirect physiological methods have been tried. For this purpose De Wesselow and Griffiths¹ used the response of rabbits to insulin before and after the injection of plasma from diabetic patients. Their results suggested that insulin-sensitive and insulin-insensitive types of diabetes might be differentiated in this manner. Our efforts to use this method have led to inconclusive results. An analysis of these results is presented which illustrates the difficulties in interpreting this test. It is probable that equal caution is necessary in appraising any other test where the response to insulin is used. For purposes of comparison the diminution in the response to insulin produced by pituitary extracts has been included.

The fall in the blood sugar of rabbits after insulin was observed before and after the injection of serum from diabetic patients. The test was carried out as described by De Wesselow,¹ except that 10 cc of fresh serum was used instead of 10 cc of plasma. Three

¹ De Wesselow, O. L. V., and Griffiths, W. J., *Lancet*, 1936, **280**, 991.