ings were taken at 24, 48 and 72 hours and the size of the area of inflammation was recorded as well as the degree of redness and edema. The last reading was used for final evaluation.

No significant changes were found in the male group. In the female group, however, the majority of the individuals showed considerable variation in intensity of the reaction. These changes involved the area and the degree of redness as well as the extent of edema; if one or more of these criteria was more pronounced whereas the others remained stable, the whole reaction was listed as more severe in our records. On the basis of such an interpretation it was found that of 9 Schick-positive individuals, 6 exhibited a severer reaction at the beginning of the menstrual period than during the interval while one reacted less strongly and 2 showed no change whatsoever. Among the 4 Schick-negative reactors, 3 remained negative on repeated injections; however, one individual who had given a completely negative reaction during the interval showed a distinct but mildly positive reaction at the beginning of the menses. Two individuals in the Schick-negative group gave pseudoractions to the heated toxin. In one instance this pseudoraction remained unchanged; in the other, a definite increase in severity was noted at the time she was menstruating.

The above data are of interest in demonstrating that susceptibility to a capillary poison, like diphtheria toxin, may be increased during the onset of menstruation.

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Sulfanilamide in Experimental Tuberculosis.*

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Rich and Follis[1] reported an inhibitory effect of sulfanilamide on experimental tuberculosis in guinea pigs. Doses of 200 and 500 mg were given daily, beginning 3 days before the animals were infected subcutaneously with human tubercle bacilli, and treatment

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1 Rich, A. R., and Follis, R. H., Jr., *Bull. Johns Hopkins Hosp.*, 1938, **77**, 621.

was maintained throughout the experiment. Similarly, Greey, Campbell and Culley,[2] using human bacilli, observed some inhibitory effect in guinea pigs, on a dosage of 300 mg of sulfanilamide; while Buttle and Parish[3] obtained very favorable results with 250 mg administered *per os*. Ballon and Guernon,[4] after experimenting with doses up to 680 mg, found that daily treatment with 340 to 380 mg of sulfanilamide was tolerated by guinea pigs, and had an inhibitory effect. However, Dietrich,[5] using prontosil (100 mg per kilogram of body weight), observed no favorable influence of this drug on guinea pigs infected with human bacilli, although he treated his animals 14 to 16 days before infection. Smithburn[6] used sulfanilamide in doses of 250 mg (50 mg less than Rich and Follis' most successful dosage) and obtained no beneficial results; while Kolmer *et al.*[7] treated guinea pigs with 6 derivatives of sulfanilamide, in the form of sodium salts, using doses varying from 200 to 500 mg, and were equally unsuccessful. An early trial on a small number of animals suggested to us that sulfanilamide was not effective in experimental tuberculosis; but after learning of the results achieved by Rich and Follis,[1] we decided to repeat our experiment on a larger scale.

Experiment I. Fifty-four guinea pigs, averaging 365 g in weight, and negative to tuberculin, were infected subcutaneously in the groin with 0.0001 mg of virulent bovine tubercle bacilli (BI). Twelve animals remained untreated and served as controls. Forty-two animals were treated with sulfanilamide (Merck & Co.). The treated animals were divided into the following 3 groups: Group I: 14 guinea pigs received 100 mg sulfanilamide daily in 2 divided doses, 7 by oral administration and 7 by subcutaneous injection. Group II: 14 guinea pigs received 200 mg sulfanilamide daily in 2 divided doses, 7 *per os* and 7 by subcutaneous injection. Group III: 14 guinea pigs received 300 mg sulfanilamide daily in 3 divided doses, 7 *per os* and 7 by subcutaneous injection. At the end of the 5th, 6th, 7th and 8th week, animals from each group were sacrificed in consecutive series. In the first 3 series, one guinea pig from each group and 2 control animals were killed; the fourth

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

[3] Buttle, G. A. H., and Parish, H. J., *Brit. Med. J.*, 1938, **4058**, 776.

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

[5] Dietrich, H. F., *Am. Rev. Tuberc.*, 1938, **38**, 389.

[6] Smithburn, K. C., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 574.

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

series included all the remaining guinea pigs. Macro- and microscopic readings were made from the lung, liver, spleen, and the mesenteric, superficial and deep inguinal lymph glands, in order to determine the extent of the lesions.

Results. Series 1: Eight guinea pigs were autopsied 35 days after infection. Macroscopic examination showed early tuberculosis in all the animals. The treated guinea pigs did not differ in any significant manner from the untreated. The regional glands were slightly enlarged, with a small degree of caseation evident in all but the control animals. In the guinea pigs which had received daily doses of 200 and 300 mg of sulfanilamide by injection, the livers were clear, but the spleen showed early tubercles. Lungs were congested, but no tubercles were found.

Series 2: The 8 guinea pigs of this series were autopsied 41 days after infection. Macroscopic examination revealed no significant variation between the animals treated with sulfanilamide and those left untreated. Lungs were clear in all but one control animal. Regional glands were much enlarged, with beginning caseation. Involvement of the livers and spleens varied considerably in individual animals, but this variation extended throughout the entire group.

Series 3: Autopsy readings were made on these 8 guinea pigs 48 days after infection. Again macroscopic examination revealed no significant variation among these animals. Lungs were all slightly involved; the regional lymph glands were very much enlarged and showed moderate caseation. The least involvement was observed in the animals from Group I. Spleens were enlarged and contained tubercles in every instance.

Series 4: The remaining guinea pigs were autopsied 54 days after infection. No significant difference in the extent or the degree of infection was seen between the treated animals and the untreated controls.

Microscopic examination of slides prepared from the lungs, livers, spleens, and lymph glands corresponded with the macroscopic findings.

Experiment II. Twelve guinea pigs were divided into 2 groups of 6 animals. Group I was treated for 3 days with sulfanilamide in 100 mg doses administered orally 3 times daily. These guinea pigs were then injected subcutaneously with 0.0001 mg bovine strain (Bl) tubercle bacilli, and the sulfanilamide treatment continued throughout the course of the experiment. The animals in

Group II were infected but remained untreated for control purposes. One guinea pig from each group was autopsied during the 6th week after infection, and the rest of the animals during the 7th week.

Results. Set 1: Two guinea pigs were autopsied 37 days after infection. Macroscopic readings of the necropsy findings were similar in the 2 animals, although the tuberculous lesions of the untreated guinea pig were perceptibly more advanced than those of the sulfanilamide-treated guinea pig. Lungs were clear in both instances, and the regional lymph nodes were equally involved, enlarged and slightly caseous. The tubercles on the surface of the liver were fewer, and the spleen was smaller, in the treated animal than in the control.

Set 2: The 10 remaining guinea pigs were autopsied 44 days after infection. Macroscopic examination revealed no significant difference between the treated and untreated animals, extent of infection being remarkably similar. Tubercles were found in the lungs in several instances. Livers and spleens were all extensively involved. Regional lymph glands were enlarged and caseating in every case.

Microscopic examination revealed no difference in histopathology between treated and untreated animals.

Summary and Conclusion. (1) Sulfanilamide treatment initiated on the day of infection and maintained throughout the experiment failed to affect the course of experimental tuberculosis in the guinea pig. (2) Guinea pigs treated with sulfanilamide before the infection and treated daily thereafter showed no evidence of being benefited by the drug. (3) It is therefore concluded that, under the conditions of our experiments, sulfanilamide is ineffective as a means of protection against infection with the bovine tubercle bacillus in guinea pigs.