

columnar and 3 hypertrophic cells, the columnar cells being somewhat increased over the normal and indicating an energetic resumption of growth. The metaphysis was well vascularized. The spicules were of normal length and width, and they were covered by thick layers of large polygonal osteoblasts. Repair was accomplished more rapidly in females than in males.

Adult Animals. In control animals the epiphyseal disc was composed of a small amount of inert degenerated cartilage, sealed off on both sides by a bony plate. The bony shaft and the epiphyseal spicules were lined by large, ovoid osteoblasts. In the mice kept on the deficient diet for 4 and 5 weeks, no changes were noted in the growth zone. However, the number of osteoblasts was decreased, and the bony structures were covered

by a discontinuous layer of spindle-shaped cells.

Summary and Conclusions. In growing mice, riboflavin deficiency decreases both the rate of growth and of ossification, but intensifies the degeneration of the cartilage. These changes represent the histological basis for the inhibition of lengthwise growth seen in riboflavin-deficient animals. As compared with the changes seen in pantothenic acid deficiency, lack of riboflavin inhibits the proliferation of the cartilage to a lesser extent, whereas it produces degeneration of the cartilage, not seen in pantothenic acid deficiency. As in pantothenic acid deficiency, males are more sensitive to the lack of the vitamin than are females.

In adult mice, the endosteal and peritrabecular osteoblasts undergo atrophy.

15601 P

Infection Experiments with the Hookworm (*Bunostomum phlebotomum*) in Calves.

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The calves used in these experiments were obtained from the L. S. U. Dairy Department as soon after birth as possible, usually within 36 hours, and raised under parasite-free conditions in the animal building of the Veterinary Science Department.

Three animals 2½ to 13 months old have been inoculated with infective larvae by mouth. All had begun passing eggs by between 64 and 83 days after receiving the larvae. One animal developed a diarrhea lasting about 10 days at approximately 30 days after inoculation.

Three other calves were inoculated by placing larvae on the skin of the flank. These animals were then fastened in stanchions in such a manner as to prevent licking the larvae from the skin, in one instance for 42 days, another 67 days, and in the case of the 3rd for 97 days. Two of these calves developed a very severe bloody diarrhea 31 and 38

days after the application of the larvae, which continued for 10 days in one, and for 18 days in the other. A very marked skin irritation developed over the area of application of the larvae in all 3 animals. Two of these animals began passing eggs on the 57th and 65th days after the application of the larvae. The third calf with the most severe diarrhea and which became the most emaciated, remained negative to the end of the experiment, 133 days.

Three additional calves began passing hookworm eggs at between 60 and 115 days of age after being raised under conditions free of parasitic infection. The animal that was positive at 115 days was not examined between the 78th and 115th day and it is believed that a positive examination could have been secured earlier than the 115th day. It seems evident that these 3 animals secured their infective larvae during the few hours

between birth and their transfer to the Veterinary Science Department.

Summary. These experiments indicate that infection with the hookworm parasitic in calves takes place by way of the skin

as well as orally and that the larval stages are capable of producing severe symptoms of parasitosis. The prepatent period may be as short as the 57th day and may extend to at least 79 days.

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Derivatives of Diphenylsulfone, Related Sulfoxides and Sulfides in Experimental Tuberculosis.*

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Many investigators have reported favorable results in experimental tuberculosis with derivatives of 4,4'-diaminodiphenylsulfone, including promin and diasone, and the related sulfone, promizole. In the following experiments several new derivatives of diphenylsulfone, a number of related sulfoxides and other allied compounds were evaluated for their effect in experimental tuberculosis, both *in vitro* and *in vivo*. An effort was made to determine the relationship between chemical structure and chemotherapeutic activity.

Methods. The bacteriostatic studies were initially performed on the avirulent strain of tubercle bacilli, No. 607, using Proskauer and Beck synthetic media, at a pH of 7.2. The chemical compounds were dissolved in propylene glycol to make 0.5% solutions. Subsequent dilutions were made directly into the media. Each tube was inoculated with one loopful of fresh culture of tubercle bacilli. The appearance of a pellicle was taken as the criterion of growth; the cultures were read at the end of 2 and of 4 days. Compounds showing a favorable bacteriostatic action were repeated, using the virulent

culture H37Rv. The cultures were read at the end of 3 weeks. As the differences between the bacteriostatic effect on the avirulent and the virulent cultures were insignificant, only the results of the experiments performed with the avirulent culture are reported.

Animal Experiments. Approximately 9 guinea pigs, averaging 350 g weight, were used to evaluate each compound. The animals were inoculated in the left groin with 0.01 mg of H37Rv tubercle bacilli. The drugs were administered either orally or hypodermically. For oral administration, in most cases, the finely ground drug was mixed with ground rabbit pellets; in the other cases the drugs were suspended in tragacanth solution and given with a pipette. The food was supplemented by fresh vegetables. For hypodermic administration the drugs were ground with either cotton seed oil or a 1% beeswax-sesame oil mixture. All experiments were terminated at the end of 6 weeks. Pathology was evaluated numerically by the method of Sweany, Sher, and Kloeck,¹ in which the maximum gross involvements of the organs were given the following numerical ratings: lymph nodes 8, spleen 24, liver 28 and lungs 40. Hemoglobin determinations were made at the end of the experiments.

Results. The *in vitro* bacteriostatic results are recorded in Table I. The com-

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¹ Sweany, H. C., Sher, B. C., and Kloeck, J. M., *Am. Rev. Tuberculosis*, 1946, **53**, 250.