

ineffective in bringing about healing. For this purpose monochromatic rays were used; in one experiment a wave length of 2967 Ångstrom units of high intensity was employed. In order to assure ourselves that these antirachitic measures did not lack potency, we made control tests with the standard Sherman-Pappenheimer ration and found that on this diet healing could be readily induced. Moreover, if the calcium ratio in the diet was reduced to 9.5 instead of 11.5, moderate healing could be brought about. Furthermore, if CaCl_2 was substituted for CaCO_3 in equimolar amounts, it was found that the specific agents exercised a curative effect.

Although the rachitic lesions were but little affected by antirachitic agents when they were given for our usual test-period of 9 days, they underwent healing to some degree when these agents were continued for twice this length of time. In other words, the local factor which inhibited calcification was gradually overcome by the prolonged action of potent antirachitic measures.

These clinical observations and animal experiments combine to show that under certain conditions a local disturbance at the epiphyses may play the determining rôle in the pathogenesis and in the cure of rickets. Under such circumstances, the most potent antirachitic agents fail to exert their usual activity, notwithstanding the fact that the concentration and the ratio of the phosphorus and calcium in the blood are at normal levels.

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The Effect of Restricted Diet and Suprarenalectomy on Experimental Tuberculosis in the White Rat.

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It has been previously demonstrated¹ that the albino rat enjoys complete immunity to infection by human tubercle bacilli in spite of the fact that the bacteria remain alive for indefinite periods and apparently multiply in the host.

In the first of these new experiments 36 rats were used and were divided into 3 groups. Twelve of these were inoculated with human, 12 with bovine and 12 with avian strains respectively of the tubercle

¹ Ornstein, George G., and Steinbach, M. Maxim, *Am. Rev. of Tuberc.*, 1925, xii, 1.

bacillus. Six of each of these groups were on a bread and water diet and 6 on a full maintenance diet. Throughout all the experiments the dose used was 1 mgm. diluted with 1 cc. of saline and injected intraperitoneally. The strains were all pathogenic, H. 37, B. 1, and Avian, "pathogenic," and were obtained from Trudeau Sanitarium.

Of these animals those given the human and bovine strains, when autopsied after a suitable interval, showed no macroscopic or microscopic evidence of tissue reaction. On direct smears and tissue stains many of these animals showed the presence of the tubercle bacillus. Most of the animals, however, (82%) which had been inoculated with the avian strain, showed at autopsy extensive macroscopic tuberculosis. The spleen and liver seemed especially involved. These latter results agree with those of Cobbett.²

Each group inoculated was carefully controlled by rats fed on a normal diet. The control animals inoculated with the human strain, at autopsy were, as expected, negative. The bovine group was likewise found negative at autopsy. Of the control group inoculated with the avian strain, 50% were found at autopsy to have extensive tuberculous lesions.

We may then conclude from these experiments that the white rat is immune to the human and bovine strains of the tubercle bacillus even when its resistance is lowered by a deficient diet (white bread and water), but is susceptible to the avian strain. It was noted further that a greater percentage of infections took place among those fed on a restricted diet than among those normally fed.

On the basis of these conclusions, it was decided to investigate the possibility of infection with the bovine as well as the avian strain in animals whose resistance was lowered by bilateral suprarenalectomy. A large number of animals were suprarenalectomized, and were subsequently inoculated on the fifth day post-operative with either bovine or avian tubercle bacilli. Most of the animals died soon after. Of those that remained alive, 16 had been inoculated with the bovine organism and 5 with the avian.

Of the 16 animals in the bovine group, 12 survived for periods ranging from 7 to 22 days. Of these 12, all but one showed definite macroscopic or microscopic (or both) evidence of tubercle formation, and tubercle bacilli were demonstrated in the tissues. The remaining 4 in this group were sacrificed. Three of these showed definite macroscopic lesions. In the fourth, no lesions could be found.

² Cobbett, Lewis, *Causes of Tuberculosis*, Cambridge University Press, 1917, 449-454.

We may say, therefore, that of the 16 animals all but 2 showed definite evidence of tubercle formation as the result of infection with the bovine strain of tubercle bacilli.

Of the 5 suprarenalectomized animals inoculated with the avian bacilli, all were found at autopsy to have extensive tuberculous lesions. In the previous experiment it was shown that only 50% of normal rats inoculated with the avian strain developed characteristic tuberculous lesions. It was, therefore, deemed unnecessary to use additional controls for this group.

It appears then that bilateral suprarenalectomy in the albino rat lowers the resistance so that subsequent inoculation with the bovine tubercle bacillus results in definite tissue reaction, with tubercle formation and caseation, resembling human tuberculosis. This does not occur in normal rats or in rats in restricted diet. Suprarenalectomy and, to a less extent, deficient diet increase the susceptibility of rats to the avian tubercle bacillus.

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Vitamin D in Tuberculosis.

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In 1926 in the course of our vitamin and calcification studies^{1, 2, 3} the question arose repeatedly as to whether vitamins play an important rôle in the etiology and treatment of tuberculosis. Ultra-violet light within recent years has been found of value in the treatment of intestinal tuberculosis; heliotherapy has been used with success in other forms of tuberculosis; calcification often is found in healed tuberculous lesions. These considerations suggested a possible linkage between tuberculosis and the vitamin D content of the diet.

In the older literature, reviewed by Wells, DeWitt and Long,⁴ cod liver oil is mentioned as having value in tuberculosis. The bene-

¹ Shear, M. J., and Kramer, B., *J. Biol. Chem.*, 1926, lxxi, 213.

² Kramer, B., Shear, M. J., and Shelling, D. H., *J. Biol. Chem.*, 1926, lxxi, 221.

³ Shear, M. J., and Kramer, B., *J. Biol. Chem.*, 1928, lxxix, 105, 121, 125, 147, 161.

⁴ Wells, H. G., DeWitt, L. M., and Long, E. R., "The Chemistry of Tuberculosis," Williams and Wilkins Co., Baltimore, 1923.