and Tyrode's solution did not support the survival of vaccine virus at 37°C. for many days. If, however, a mixture of vaccine virus, kidney tissue killed by freezing and thawing, serum, and Tyrode's solution was placed on one side of a collodion sac, and a preparation of living minced kidney tissue, serum, and Tyrode's solution was put on the other side, the survival of the virus was far better than that in the first set of experiments described above. In fact, there seemed to be complete survival, if not multiplication of the virus. The results were so striking that further work is in progress to ascertain the nature of the factors responsible for the survival of the virus, and to determine if multiplication of the virus can take place under such conditions.

4647

Observations Suggesting a Local Factor in Pathogenesis and Healing of Rickets.

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The pathogenesis of rickets is a moot question. By many it is believed that this disorder is entirely of systemic origin and that the local lesions at the epiphyses are secondary in nature. This point of view has been fortified by the demonstration that a low concentration of inorganic phosphorus in the blood is one of the most constant phenomena of rickets in infants and in animals. There can be no doubt of the participation of the systemic factor. However, as we have pointed out from time to time, rickets may come about occasionally in infants and in animals in spite of the fact that the calcium and the phosphorus in the blood have remained at normal levels. In rats this relationship was noted most often when about 10% dried milk was added to the standard rickets-producing ration. Furthermore, it was observed that the lesions of rickets may fail to become manifest in some infants and animals which are poorly nourished, although the phosphorus in the blood is definitely below the non-rachitic level. This incongruity was noted in some instances among rats which had been fed the Sherman-Pappenheimer diet, which is deficient in several nutritional factors.

Last year this subject was again brought to our attention by the occurrence of a mild degree of rickets in some infants, notwithstand-

ing the fact that they were well nourished and that the calcium and phosphorus content of the blood remained practically unaltered. These infants should have been fully protected as they were fed irradiated dried milk. On further investigation, it was found, however, that this milk had been insufficiently activated, due to a technical error in the course of irradiation.

More recently we found that the subject was open to investigation by means of animal experiment. Our first step was to induce rickets by means of a diet in which there was a marked excess of calcium. This was accomplished by substituting yellow corn meal for the yellow corn in the standard Steenbock rickets-producing ration. By this means the ratio of Ca:P was rendered exceptionally high, about 11.5:1, due to the low phosphorus content; the excess of base over acid was about 520 cc. of 0.1 N alkali. The next step was to administer an antirachitic agent. It was found that in spite of very large amounts of cod liver oil or of irradiated ergosterol, the rachitic lesions in the epiphyses remained unaffected, whereas the blood showed normal or even excessive concentrations of inorganic phosphorus and calcium; in some instances the ratio was normal, in others the one or the other element was disproportionately great.

In many instances in which rickets was brought about by this means, the multiple of Ca $\times$ P of the blood was above rather than below normal. It has been held that if this multiple is as high as 45, rickets will not develop. In some animals this multiple was even as high as 80 or 90 and nevertheless rickets persisted.

The presence of rickets was diagnosed by the typical radiographic picture. In many instances, the diagnosis was confirmed by means of histological examination. In still others it was further substantiated by an analysis of the bones. The ash was found to be low; instead of the normal percentage of about 50, it was approximately 30%.

Not only was a form of "local rickets" developed, but, as stated, these lesions were extraordinarily resistant to treatment with specific antirachitic measures. Healing could not be brought about by cod liver oil, even in amounts as high as 40 times the curative dose. Various standard brands of cod liver oil were fed. Nor was egg yolk effective in bringing about healing; 0.5 gm. was fed daily. Irradiated ergosterol also proved ineffective, even when 200 or 20,000 times the minimum curative dose was fed daily. It may be added that when very large amounts of irradiated ergosterol or cod liver oil were fed, the percentage of ash in the bones was lower than when lesser quantities were given. Ultraviolet irradiation was also

ineffective in bringing about healing. For this purpose monochromatic rays were used; in one experiment a wave length of 2967 Ängstrom 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.

4648

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

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It has been previously demonstrated[1] 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 Tuber.*, 1925, xii, 1.