

free organisms could be demonstrated in the aspirated fluid. Polymorphonuclear cells were present in large numbers and phagocytosis was intense. The virulent type D, on the other hand, gains its foothold primarily by reason of the late appearance of phagocytes following its intrapleural injection.

The occurrence of the low-virulent type G would seem to afford an excellent opportunity for the investigation of the properties or products of secretion which give the parent D type its characteristic of high virulence.

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## II. The prevention of the development of rickets in rats by sunlight.

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In June, 1919, Huldchinsky<sup>1</sup> reported that the ultraviolet ray exerted a curative action in rickets. The criterion on which he relied was the evidences furnished by the X-ray of calcium deposition at the ends of the long bones. He found that there were definite signs of calcium deposition after four weeks of treatment and that at the end of eight weeks healing was almost complete. In May, 1920, Huldchinsky<sup>2</sup> again reported the curative effects of treatment with the ultraviolet ray in rickets in a series of thirty children, aged between one and one half and six and one half years, who exhibited all clinical manifestations of the disease. In all, healing was accomplished after twenty-two to twenty-six treatments covering a period of two months. In April, 1920, Putzig<sup>3</sup> corroborated the findings of Huldchinsky. He obtained

<sup>1</sup> Huldchinsky, K., *Deutsch. Wchnschr.*, 1919, xlv, 712.

<sup>2</sup> Huldchinsky, K., *Zischr. f. orthop. Chir.*, 1920, lxxxix, 426.

<sup>3</sup> Putzig, H., *Therap. Halbmonatschr.*, 1920, viii, 234.

cures by means of the quartz lamp in premature infants suffering from rickets. In July, 1920, Riedel<sup>1</sup> further confirmed Huld-schinsky's findings in a series of one hundred children suffering from rickets. In June, 1921, Hess<sup>2</sup> confirmed Huld-schinsky's findings in a series of six cases.

The favorable influence of sunlight in rickets has been recognized by some students of the disease for a long time, notably by Palm<sup>3</sup> (1890), and experimental evidence of its beneficial effect on mineral metabolism in the puppy has been furnished by Rac-zynsky<sup>4</sup> in 1912. Huld-schinsky made use of sunlight together with the ultraviolet ray in two cases of his series and Riedel relied on treatment with sunlight in some of his cases, supplementing with the quartz lamp ray only on sunless days. Hess<sup>5</sup> was the first, so far as we are aware, to demonstrate, by means of the radiograph, that sunlight alone exerts the same curative action as the ultraviolet ray. All the investigations which have been made up to the present time in regard to the curative effects of both the ultraviolet ray and sunlight in rickets have been made on human subjects of the disease and all the evidence has been furnished by means of the radiograph. In order to satisfy ourselves concerning the action of light in rickets as well as actually to see the changes produced in the bones we performed the following experiments.

Eighteen rats about six weeks old and weighing between forty and fifty grams were placed on diet 3,143 which, as previous experience<sup>6</sup> has shown, produces rickets comparable in every respect to the rickets manifesting itself in human beings. The ration has the following composition:

Wheat.....	33.0%
Maize.....	33.0
Gelatin.....	15.0
Wheat gluten.....	15.0
NaCl.....	1.0
CaCO <sub>3</sub> .....	3.0

<sup>1</sup> Riedel, G., *München. med. Wchnschr.*, 1920, lxvii, 838.

<sup>2</sup> Hess, A. E., and Unger, L. J., *Am. J. Dis. Child.*, 1921, xxii, 186.

<sup>3</sup> Palm, T. A., *The Practitioner*, 1890, xlv, 270-279 and 321-342.

<sup>4</sup> Rac-zynski, J., *Compt. rend. de L'Association Internationale De Pédiatrie*, Paris, 1913, p. 308.

<sup>5</sup> Hess, A. F., and Unger, L. J., *J. A. M. A.*, 1921, lxxvii, 39.

<sup>6</sup> McCollum, E. V., Simmonds, Nina, Shipley, P. G., and Park, E. A. *J. Biol. Chem.*, 1921, xlvii, 507.

It contains nearly twice the optimal content of calcium, and is decidedly below the optimum in its content of phosphorus and in fat soluble A. Otherwise, it is well constituted.

Twelve rats placed upon this diet were sent to New Haven, there to be exposed to sunlight. The remaining six rats were retained in Baltimore to be kept as control animals under ordinary laboratory conditions in a large, well-ventilated room completely screened with windows of ordinary glass. The animals treated with the sunlight were divided into two groups and placed in fairly large wire mesh cages. Each clear day the cages were carried out of doors and placed in the sunlight. At first, the weather being warm, the rats were exposed to the sunlight for two short periods of twenty minutes each. Soon, however, the periods were lengthened to six or even more hours. During the experimental period, which covered between sixty-two and sixty-seven days, the rats were exposed to the sunlight on every day except nine. The total exposure to sunlight during the experimental period varied between two hundred and forty-two and two hundred and seventy-three hours. The average daily exposure was four hours.

When first exposed to sunlight, the albinos developed conjunctivitis; the ears of all, in particular the albinos, began to peel; the skin of the tails became sunburned and rough; the hair of some of the albinos acquired a yellowish tint. Long before the experiments were completed it became evident that the animals treated with sunlight were not developing rickets. Though they did not grow normally, they remained extremely active, climbing and darting about the cages. Toward the end of the experiments the males became sexually active; one of the females became pregnant.

The control rats, killed at the expiration of two months, showed all the gross and microscopic evidences of rickets, the characteristic deformities of the thorax, enlargement and distortion of the costochondral junctions, fractures of the shafts, enlargements at the wrists, ankles and knees, and the ends of all the long bones. The bones cut with diminished resistance. On section a deep rachitic metaphysis entirely free from calcium was exposed. Into it the proliferative cartilage extended in irregular prolongations. The trabeculae were surrounded with broad zones of osteoid.

The rats exposed to the sunlight, on the other hand, showed none of the evidences of rickets. The thorax was not deformed; the costochondral junctions were normal. There were no fractures of the ribs. The ends of the long bones were not enlarged. The long bones cut with great resistance. On microscopic examination the cartilage was normal. The proliferative zone was completely calcified. The trabeculæ were completely calcified. The condition found was normal except that both microscopically and grossly the bone was more delicate than in the rat of corresponding age reared on satisfactory diets. Though the sunshine completely prevented the development of rickets, it did not entirely compensate for the deficiency of phosphorus in the diet, either as regards the growth and development of the rat as a whole or of the skeleton.

There were some noteworthy findings outside the skeleton. An abundance of fat was present. In the control rats the fat was scant. The thymus was only partially involuted. In the control rats it was completely involuted. The spleen was not enlarged.

#### DISCUSSION.

Sunlight effectually prevents the development of rickets in the rat. We have already shown,<sup>1</sup> as has also Pappenheimer, that cod-liver oil prevents the development of rickets in the rat. As nearly as we can judge from the radiographs furnished by Huldchinsky and others the mode of healing at the cartilage-shaft junction induced by the ultraviolet ray (sunlight) is exactly analogous to that which occurs after the administration of cod-liver oil, as determined by Howland and Park.<sup>2</sup> The time relations are also similar. Huldchinsky found that the ultraviolet ray produced definite evidences of healing at the end of four weeks, and at the end of two months almost complete healing. Howland and Park found that cod-liver oil first gave rise to evidences of healing at the junctions of the cartilage and shaft of the long bones three weeks after the administration was begun and that at the end of about two months the calcification of the diseased ends of

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<sup>1</sup> Shipley, P. G., Park, E. A., McCollum, E. V., and Simmonds, Nina. *Proc. Soc. Exper. Biol. and Med.*, xviii, 227, 1921.

<sup>2</sup> Howland, J., and Park, E. A., *Arch. Pediat.*, 1920, xv xvii, 411.

Howland, J., and Park, E. A., *Bull. Johns Hopkins Hosp.*, November, 1921. (To be published.)

the shafts seemed to be complete. Moreover, as the result of the gross and histological examinations made on the rats fed the rickets-producing diet 3,143 but exposed to sunlight it is possible to say that the changes produced by sunlight in the skeleton do not differ in any important respect from the changes produced when the animals are kept in room light but on a diet supplemented by cod-liver oil. Cod-liver oil contains something which is essential for optimal cellular function. Light also contains something which is essential for optimal cellular function. Cod-liver oil or light when made available to an organism previously deprived of either permits the organism to put into successful operation adaptations or defense mechanisms which otherwise would have been ineffectual. Neither cod-liver oil nor light meets the defects in the composition of the diet directly by supplying to the body either calcium or phosphorus but meets them indirectly by so raising the potential of cellular activity as to secure the most efficient utilization possible of those substances available in the body which are directly or indirectly concerned with ossification and calcification.