products. However, that is not the purpose of this paper. It was the aim of the authors to report, in the JOURNAL literature, an analysis of pharmaceutical cod liver oil extracts which are being offered in the American market for the manufacture of so-called cod liver oil tablets, wines, elixirs and other proprietary preparations, so that the industry may be acquainted with the composition of these extracts.

Thanks are due Messrs. McKee and Larson of the Standard Laboratories, Chicago, Illinois, who were kind enough to furnish the materials used in this investigation.

EPSTEIN & HARRIS, CONSULTING CHEMISTS,
CHICAGO, ILLINOIS.

NEW LIGHT ON COD LIVER OIL.*

BY BERNARD FANTUS, M.D.

There is one disease in which the special value of cod liver oil is now well established. This disease is rickets. Though the opinion of clinicians regarding its curative value in this disease had long been well crystallized, it remained for experimental demonstration upon laboratory animals to furnish not only unequivocal proof of this but also the key to its mode of action.

VITAMIN D CURES RICKETS.

The recent rapid development of our knowledge in this field we owe to the fact that lower animals, and among them rats, are susceptible to rickets; and that large numbers of experiments can so easily be conducted upon rats. These experiments have shown not only that cod liver oil is curative of rickets; but also that a concentrate could be prepared representing all the antirachitic activity of the original oil (Funk, 1924). They have shown that the antirachitic principle is entirely stable to saponification, in other words that the oil can be boiled with strong alkali so as to destroy the fats completely without impairment of the antirachitic potency. This points to the desirability of subjecting to intensive study the unsaponifiable substances isolated from this fat. It has been suggested, but not yet proved, that sterols, cholesterin in animals and the phytosterols of plants, carry the activity.

In the present state of our ignorance of the essential chemical nature of this antirachitic factor, it is classed among the vitamins; and recent studies have forced the designation "Vitamin D" upon it. At first, the antirachitic factor was not distinguished from vitamin A, as both are oil-soluble; and both are contained in cod liver oil. More recently it was shown that they differ from each other. Thus, while butter fat promotes growth and prevents xerophthalmia—in other words, contains vitamin A—it is of little use in the prevention of rickets. Coconut oil, on the other hand, can prevent rickets, but does not promote growth or prevent xerophthalmia. Furthermore, it has been shown by E. A. Park and his associates at Johns Hopkins that, by limited oxidation of cod liver oil, one can destroy vitamin A without destroying the antirachitic factor. Hence, the antirachitic factor is different from vitamin A. It has provisionally been designated vitamin D.

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ULTRAVIOLET RAYS CURE RICKETS.

Rickets is a disease found only in civilized communities, most especially in large cities; and in animals kept under artificial conditions. In farming districts the disease is very rare; among savages, practically unknown. Wild animals likewise are free from it. It is incurred most especially during winter. It has, on the other hand, long been known that "open air" treatment cures rickets.

It remained for the observations of Huldschinsky (1919) to prove, by laboratory demonstration, that light, or rather the ultraviolet rays of it, are the specific preventive and curative agent. Light filtered through glass is of no value because glass, though it transmits the visible light rays, does not permit the ultraviolet rays to pass through. This has led to the establishment, on a firm basis, of the treatment of this disease not only by sunlight but also by the ultraviolet (or actinic) rays, which can be produced artificially by means of a quartz mercury vapor lamp and employed when exposure to the sun is impossible.

The puzzle how two such dissimilar agents as sunlight and cod liver oil came to have identical effects has apparently just been solved by two independent investigations that approached the problem from different angles.

IRRADIATED OILS CURE RICKETS.

Harry Steenbock[1] and his associates at the University of Wisconsin made the surprising observation about 1923 that, when animals exposed to ultraviolet radiations, were kept in the same cage with nonirradiated animals, neither developed rickets, though both groups were on a rickets producing diet. They first assumed that secondary radiations emanating from the irradiated animals might be responsible. But experiments soon decided that it was the excreta of these animals that had become activated; and that enough of these was taken in by the others to obtain the required antirachitic factor. About the same time, English investigators (Goldblatt and Soames[2]) showed that livers taken from rats which had been exposed to the quartz mercury vapor lamp were able to induce proper growth in rats, while livers taken from nonirradiated rats were inactive. Assuming that light synthesized the antirachitic factor, the investigators exposed the food and later various oils to quartz mercury light for thirty minutes. Much to their surprise they found that various foods and fats, such as lard and olive oil and others, previously devoid of the antirachitic factor, had become antirachitic. They also found that excessive illumination caused these oils and even cod liver oil to lose their antirachitic activity. This shows how unstable this vitamin is in respect to radiant energy. Still, when properly kept, in well stoppered bottles in the dark it seems perfectly stable.

ULTRAVIOLET RAYS PRODUCE VITAMIN D.

It is evident that, when light shines directly on the animal body, it acts in part at least by virtue of the fact that it makes antirachitic certain substances already present. It is also reasonable to assume that cod liver oil owes its antirachitic activity to solar irradiation. Its exceptionally high degree of action could hardly

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[1] Harry Steenbock and Amy L. Daniels, "Irradiated Foods and Irradiated Organic Compounds." *Jour. A. M. A.*, Vol. 84 (April 11) p. 1093 (1925).

[2] H. Goldblatt and K. M. Soames, *Biochem. J.*, 17, p. 446 (1923).

be due merely to direct insolation of the cod fish. It is more probable that both the oil-soluble vitamins A and D are chiefly formed by green plants, for their own use, with the aid of the ultraviolet rays of the sun. When these are eaten by fish the surplus of the vitamins that are oil-soluble is stored in oil, most especially in the liver. Cod fish receive the vitamins indirectly by eating other fish; and, as may be expected, the liver oils of many other fish besides the cod have similar properties.

The same thing happens with land plants and animals though the vitamin concentration of these does not seem to become quite as great. Birds store a liberal supply of antirachitic vitamin in the yolk of the egg for use by the developing bird. It is not surprising, therefore, to find that yolk of egg is a good preventive of rickets. The young mammal receives vitamin D in the milk, though cow's milk is relatively poor in it, especially during the winter season when the animals do not obtain green food. Human milk is richer in vitamin D than cow's milk. This is why breast-fed babies are so much less liable to rickets than the bottle-fed.

VITAMIN D PRODUCES ULTRAVIOLET RAYS.

A fascinating theory as to the probable mode of action of the substances curative of rickets has been advanced by Kugelmass and McQuarrie[1] who find that such bodies emit ultraviolet rays on oxidation. When they expose cod liver oil, yolk of egg, sperm oil to a current of oxygen and cover the container with a photographic plate protected by glass, the plate is not blackened. When, on the other hand, the sensitive plate is protected by quartz, blackening occurs. The necessary conclusion is that, upon oxidation of these bodies, ultraviolet rays are produced. As these bodies are oxidized in the animal system, they must yield ultraviolet rays to its cell. A considerable number of substances not curative of rickets did not emit such radiation, when exposed to the same experimental conditions.

These observations may not only give us a method of measuring the therapeutic potency of substances to be used in the treatment of rickets, but they also offer a basis for wide-reaching speculations.

We have known for a long time that all life requires a certain amount of heat. Plants, during their growing period, store excess heat in the form of starch and other organic compounds, to be liberated by oxidation of these compounds during periods of growth, when there is a deficiency of heat. The higher animals have developed this second part of the mechanism to such perfection that they can carry on active existence in the presence of an external temperature so low as to paralyze all vegetable life. They do this by making use of the caloric energy providently stored in the plant for its own use and that of its offspring.

Now it seems that the same thing is true of radiant energy.[2] That the growth

[1] I. N. Kugelmass and I. McQuarrie, "The Photoactivity of Substances Curative of Rickets and the Photolysis of the Oxy-Products by Ultraviolet Radiation." *Science*, 60 (Sept. 19), 272 (1924).

[2] It might perhaps be well to explain that radiant energy is entirely different from heat. Heat is a movement in the molecules of matter; radiant energy, a wave motion in the all pervading ether. All the force the sun sends out is in the form of radiant energy, which is *not* heat—for the space through which it traverses is bitter cold—though it can be converted into heat when it strikes molecules of matter.

and proper development of plants depend upon radiant energy, such as that emitted by the sun, is a well known fact. We believed, however, that animal cells were independent of the necessity of direct irradiation for proper growth. The observations cited may make it necessary for us to revise this opinion. The far reaching generalization is dawning upon us that, without radiant energy acting directly upon it, no organism can grow properly.

An interesting parallel is to be found in connection with the clinically well established value of cod liver oil in tuberculosis. This disease is, like rickets, a disease of civilization and of darkness. Out-door-life and sunshine have a therapeutic value in both, and so has cod liver oil. Cod liver oil is, of course, not curative in tuberculosis as it is in rickets, because in the latter it supplies the deficiency that causes the disease, while the former is a much more complicated process, being a fight between the tissue cells and the tubercle organisms. How the cod liver oil helps in this fight whether, by favoring through its vitamins, the proper maturing of tissue cells and the walling off of the germs, or in some other manner, remains to be determined by future studies.

A PARTIAL ANALYSIS OF THE FRUIT OF EUPATORIUM URTICÆFOLIUM.

BY F. S. BUKEY.

Eupatorium urticæfolium Reichard[1] (*Eupatorium ageratoides* L.f.) is known by the common names of white snakeroot, rich weed and white sanicle. The name white snakeroot is the most commonly used. The plant is very widely distributed. Its range extends from Canada to Georgia and westward to Kansas and Nebraska. The plant appears to be most common in Indiana, Illinois, Ohio, Pennsylvania New York and the New England states. The conditions best suited to its growth are rich woods bordering streams, or in shaded mountain woods usually on the northern slopes. In northern Ohio the white snakeroot is found mostly on the northern slopes of wooded hillsides. The plant is a member of the Composite family, and of a genus in which there are some nineteen species in the region covered by "Gray's Manual" (seventh edition). Many of these species resemble each other so closely as to render recognition extremely difficult.

Eupatorium urticæfolium is a herbaceous perennial one to two meters in height. The surface of the typical plant is practically free from trichomes and other hairy growths. The leaves are opposite on long, slender, very much branched stems. They vary from five to fifteen centimeters in length, and from three to eight centimeters in width. They are netted-veined, palmately three-nerved. The blade is thin and broadly ovate, having an acuminate apex, dentate-serrate margin and a truncate or cordate base which in the smaller leaves may be abruptly narrowed into a slender petiole. The petiole is usually three to seven centimeters in length. The inflorescence is a compound corymb, each head having from ten to thirty flowers. The receptacle is flat. The involucre is of narrow lanceolate

[1] The species was identified by Dr. E. E. Stanford, Head of the Department of Pharmacognosy, Western Reserve University School of Pharmacy.