

DEMENTIA PRÆCOX AND VITAMINS.*

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THE progress made in recent years in the study of vitamins has been phenomenal in that many disorders previously regarded as of infective origin have been shown to arise from deficiency of some particular item of the diet, which quantitatively is infinitesimal in relation to the total bulk of food taken. Although some five vitamins have been identified and their value established, as yet only one has been isolated in pure form and has acquired the distinction of a chemical formula. This vitamin—fat-soluble D—has a powerful influence in the prevention and cure of rickets; and its relation to dentition and caries of the teeth has been established by careful and prolonged experiment. So far as we know at present vitamin D can be obtained by the body from three different sources. The effects on health of sunlight and ultra-violet rays on the skin have been shown to arise from the capacity of the cells of the sebaceous glands of the skin to manufacture under these influences, from the various sterols they contain, a substance—vitamin D—which is then picked up by the blood-stream and distributed throughout the body. The second source is the fat taken in the diet, butter and cream being particularly rich in this respect. It has also been proved that food exposed to ultra-violet radiation acquires in an added degree the capacity to ward off the ill-effects of vitamin D deficiency. The third and, from the point of view of accurate laboratory control, the most important source is that in the form of ergosterol, a compound related to cholesterol, produced by extraction from yeast and other substances. Ergosterol can be obtained in more or less pure form, and after being subjected for a definite time to irradiation by ultra-violet rays becomes converted into a substance which has all the effects of vitamin D.

At present we know very little of the causative relation of any vitamins to mental and nervous disorder, but it is known that a form of multiple neuritis is part of the symptom-complex of beri-beri arising from deficiency of the water-soluble vitamin B. Vitamin D is not to our knowledge associated with any dysfunction of the nervous system, unless it be that the irritability and general nervous restlessness arising from prolonged exposure to sunlight or

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ultra-violet rays is due to excess production of it in the skin with consequent toxic effects.

The presence of cholesterol in all cells of the body, and especially in the cells of the brain and nervous system, has for a number of years focused our attention on this substance. On the whole the results of these investigations have been unsatisfactory, but perhaps the most significant observations in this connection have been the finding of cholesterol or excess of cholesterol in the cerebro-spinal fluid in destructive brain affections. It may now, however, be questioned whether the cholesterol so found has any significance.

Rosenheim and Webster have shown that ordinary cholesterol as we know it is not a pure chemical substance, but is probably a mixture of substances of similar nature. They found that if after irradiation cholesterol was subjected to a separation process, a highly active fraction could be identified which would effectively prevent or cure rickets in rats, and that the cholesterol residue had no such effect. It is possible therefore that the previous work on cholesterol would have been more productive of results in relation to mental disorder had it been possible to take other, now known, similar chemicals into account. And although irradiated ergosterol cures rickets, the practical importance of vitamin D is by no means limited to the prevention and cure of rickets and the prevention of dental caries, but applies also to other ill-defined conditions causing greater or less ill-health and suffering. The undoubted effect of sunshine on general health, nervous stability and mental ease is too well known to be emphasized here.

It is, however, quite a different matter to pass from these benefits to the assertion of a definite relation between vitamin D sufficiency and mental disorder in its grosser and more serious forms. Such a strong assertion is not justified by the known facts. But it can nevertheless be demonstrated that vitamin D has a definite effect on certain blood reactions that occur in mental disorders, more especially in dementia præcox. Not only is this so, but the same effect is found when there is an apparent sufficiency for the normal body needs of vitamin D obtained from natural sources. These observations were made by testing the effect of certain substances on the hæmoclastic crisis which is found to occur in a proportion of cases of mental disorder.

The hæmoclastic crisis, first described by Widal as occurring in conditions of known hepatic disorder, has since been found to occur in other diseases of a very different clinical nature. Dr. Isabella Robertson's results, obtained at the Maudsley Hospital, showed that a hæmoclastic crisis occurred in 94% of dementia præcox, in

85% melancholia, in 75% of chronic mania cases, and in over 60% of early psychotic and neurotic patients (*vide Journ. Ment. Sci.*). These results were later confirmed by me, working at the Rampton State Institution in conjunction with Dr. Lascelles, by tests carried out on 300 mental defectives, 200 of whom had shown mild or transient mental disorders (*vide Journ. Ment. Sci.*).

The value and reliability of this reaction has been questioned by many competent observers, but I think the balance of opinion is now strongly in favour of the real existence of these definite hæmic changes. In order to satisfy myself that a normal person does really give on every occasion a leucocytosis, over a period of fourteen months 360 separate tests were carried out on a control, each test being done on separate days, under similar conditions and exactly at the same hour.

One result was doubtful, and on 359 occasions a definite leucocytosis occurred (a negative reaction). These tests go far to prove that the blood reaction is reliable and subject to accurate laboratory observation. A case of dementia præcox that had previously given a hæmoclastic crisis was selected, and this subject and the control referred to above were kept under similar ward and fresh-air conditions for a period of eighteen months. All substances intended to influence the reactions were given fifteen hours before each daily test. A number of drugs and extracts are known to influence the hæmoclastic crisis, but the dosage and the period over which the effect could be maintained has not, so far as I know, been established. The subject for test, a case of dementia præcox, was found to give thirty-nine positive reactions in a series of forty-five daily tests. The six negative reactions (leucocytosis) were given on single days at more or less regular intervals.

Sodium nitrite given in 2-gr. doses daily produced a complete and permanent reversal of the crisis, but took several days to produce its effect.

Anabolin, an extract of liver, containing a depressor principle, produced in daily doses of three tablets a complete reversal to normal over a period of nearly four months. In one- and two-tablet doses the reversal was partial only, some reactions being positive and some negative. This liver extract is stated to contain no cholesterol or allied substances.

Cholesterol itself, given suspended in a small quantity of olive oil, produced an irregular reversal in doses of $\frac{1}{2}$ gr., but $\frac{1}{4}$ gr. given daily maintained a permanent reversal of the abnormal reaction. As it has been shown that cholesterol as hitherto known is mixed with very small portions of other cholesterol-like substances which when irradiated have the same effect as vitamin D, the

further tests were conducted with irradiated ergosterol—the preparation being that known as radiostol.

Radiostol has a definite effect on the hæmoclastic crisis. One pellet containing 1 mgrm. ($\frac{1}{8}$ gr.) of radiostol produced a partial return to the normal reaction, the test results being positive and negative in about equal proportions. Two pellets given daily maintained a permanent reversal of the hæmoclastic crisis. If we accept the hæmoclastic crisis as being significant—the crisis occurs also in hepatic disorder and in certain chronic gastric conditions—it is reasonable to assume that the administration of a substance known to have a profound influence on body metabolism indicates that in dementia præcox and in some other mental disorders there is an actual body deficiency of vitamin D. As the vitamin D in similar doses had no apparent effect on the health of the control, it may be assumed that the deficiency was not due to a badly arranged diet or lack of exposure to such sunlight as may be available. The food intake being approximately equal in both subject and control, it is apparent that the vitamin D obtained from this source is in one case sufficient and in the other inadequate.

The effect of ultra-violet radiation of the skin on the hæmoclastic crisis was next investigated. The subject was exposed at a distance of 3 ft. to the rays from a mercury quartz lamp. On the first day the patient was given full body exposure, four minutes front and four minutes back, and on each subsequent day the period was increased by one minute to fifteen minutes back and fifteen minutes front. This period was then maintained. Owing to the risk and actual occurrence of burning, treatment was limited to four days weekly. The effect on the hæmoclastic crisis would appear to be equal to that produced by 1 mgrm. ($\frac{1}{8}$ gr.) of irradiated ergosterol given daily. From the results obtained I would judge that the amount of vitamin D formed in the body was fairly constant, and that the effect of increasing periods of exposure was offset by the protective action of increasing pigmentation of the skin. Only partial reversal of the hæmoclastic crisis occurred, so that in order to produce a complete reversal, at least 1 mgrm. of irradiated ergosterol had to be given daily to supplement the treatment by ultra-violet radiation. It is of course assumed that the amount of vitamin D obtained from food remains fairly constant, but a point of vital importance is that an excellent diet, plus sunlight in plenty, or ultra-violet rays, does not produce sufficient vitamin D to reverse the hæmoclastic crisis in this particular case of dementia præcox. These results may have no more significance than that, as in the case of certain other substances, an excess of vitamin D, while not necessary to the body economy, yet has a strong effect on certain

blood reactions, but it is equally possible and much more likely that the vitamin D is of some as yet unknown value in cases of mental disorder.

Sodium nitrite, by its dilating action on the blood capillaries of the skin, produces an increase of the flow of blood through the capillaries serving the sebaceous glands, and it is suggested that its effect will be an increased activity of these organs with a consequent increase of vitamin production under the action of the proper stimulants.

The fact that the hæmoclastic crisis occurs also in hepatic disorder suggests that in this condition there is some loss on the part of the liver of its ability to store ergosterol, and owing to the occasional association between liver disorder and mental and nervous disease one is rather tempted to read these experiments as showing that many mental disorders have a cause or effect relation with the storage or catalytic action of the liver. As our knowledge of the mode of action of vitamin D, beyond its influence on calcium and phosphorus metabolism, increases, we may find some explanation of the phenomena here recorded. At the moment it can merely be said that irradiated ergosterol has an effect on a particular blood reaction in dementia præcox. So far as I am aware, no work has been done on the clinical effects in mental diseases of the known vitamins, but it would certainly be interesting to carry out a series of clinical observations on the effects of irradiated ergosterol on the course of early mental disorders, and it may be that vitamin D, in common with liver extract, has a corrective or antitoxic action in these and allied disorders.

Conclusions.

(1) Irradiated ergosterol causes a reversal of the abnormal blood reaction known as the hæmoclastic crisis in a case of dementia præcox, and the dose required to establish a permanent reversal is 2 mgrm. ($\frac{1}{5}$ gr.).

(2) There was no evidence in the control case of any deficiency of vitamin D obtained from the skin and from the food supplied.

(3) Ultra-violet radiation does not increase the production in the body of vitamin D sufficiently to produce a reversal of the reaction, and the quantity thus provided appeared to be roughly equivalent to 1 mgrm. of irradiated ergosterol.

(4) The vital significance of this vitamin to the body economy suggests the possibility of some relation between it and mental disorder, either directly or through some as yet unknown function of the liver.