VITAMIN B COMPLEX IN RELATION TO NEUROPSYCHIATRY.*

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IN this paper it is my intention to give a broad survey of vitamin B complex deficiencies and their influence upon neuropsychiatric abnormalities generally, whilst Dr. Hardwick will discuss in greater detail the syndromes more specifically associated with such deficiencies, amplifying his remarks by reference to cases we have treated in recent years.

Throughout the war and in the uneasy days that have followed it, public propaganda has tended to over-emphasize the importance of vitamins generally, so that the thinking members of the community are somewhat sceptical when such deficiencies are discussed, and it is with this healthy scepticism that our investigations and studies on this subject have been carried out.

In mental ill-health deficiency in vitamin B may show itself in two ways. It may manifest itself in neuropsychiatric syndromes solely due to such deficiencies, which resolve after specific treatment; or it may colour and confuse the symptoms of the ordinary psychoneuroses and psychoses. I emphasize this latter state because I do not think it is generally recognized. In new admissions suffering from such unrelated mental disorders as arteriosclerotic dementia, manic-depressive psychosis, schizophrenia, general paresis, anxiety and hysterical states, one frequently comes across cases where a greater or lesser degree of vitamin deficiency has rendered diagnosis difficult. Only after the exhibition of appropriate B complex factors has the underlying basic psychosis been clearly revealed. In any case showing symptoms of some mental confusion, greater or lesser, it is, in my opinion, advisable to search for such somatic abnormalities as rawness of the tongue, even if only confined to the tip, rashes, particularly involving the face, back of the neck, back of the hands and wrists, sensory changes, muscular tenderness, tremors, etc.

Of the better known factors which make up the B complex—thiamine, nicotinic acid, riboflavine, pantothenic acid and pyridoxine—the first two are, in our present state of knowledge, predominantly the factors whose loss causes abnormal neurological and psychological states.

Thiamine plays an important part in the fundamental processes of oxidation in the living cell, as a coenzyme in the oxidation of carbohydrate by the cell. Since the C.N.S. obtains its energy chiefly from the oxidation of glucose, the importance of adequate amounts of thiamine for normal neuronic metabolism can be clearly understood. The study of the metabolism of cerebral

* Read at the Quarterly Meeting of the Royal Medico-Psychological Association held on February 14, 1946, at 11, Chandos Street, W. 1.

https://doi.org/10.1192/bjp.92.387.305 Published online by Cambridge University Press

tissues removed from avitaminotic animals reveals that there is a reduced oxidation of glucose and glucose breakdown products, such as pyruvic acid and lactic acid, whilst the addition of thiamine to these tissues restores the normal oxygen consumption. This diminished ability of avitaminotic tissues to oxidize carbohydrates is a result of their decreased cocarboxylase content, i.e. the diphosphoric ester or active form of vitamin B1.

Nicotinic acid is chemically related to nicotine. In the body nicotinic acid amide combines with adenine, phosphoric acid, etc., to form a coenzyme essential for the transference of oxygen in the fundamental processes of the cell ; animal cells cannot synthesize nicotinic acid, and without it coenzyme formation is impossible. The direct effect of nicotinic acid amide on brain metabolism is difficult to demonstrate. Investigations upon the cerebral tissues removed from dogs suffering from " black tongue "—a syndrome due to a nicotinic acid amide lack—show no decrease of the coenzymes, whilst cerebral oxygen utilization is unchanged. Other tissues hold on to the coenzyme equally as tenaciously, and in obvious pellagra the nicotinic acid content of whole blood may not fall below that found in normal controls. It follows that storage by the body of nicotinic acid appears better than that of thiamine.

Riboflavine is a component of the coenzymes essential in the intermediate stages of carbohydrate metabolism. Although at the present there is no definite evidence that it is directly responsible for neuropsychiatric conditions, it is found that dogs suffering from chronic riboflavine deficiency may show myelin degeneration of the peripheral nerves and posterior columns of the spinal cord, progressively increasing in severity with the length of time they are on the deficient diet.

It is probable that pyridoxine mobilizes riboflavine from storage, or dissociates it from some combination in which it is physiologically inactive, whilst pantothenic acid may have a similar action.

The pathological changes to be found in the C.N.S. in B-complex deficiencies are reversible, and the more obvious are most commonly due to thiamine lack. The nerves in a polyneuropathy show a degenerative demyelination, and at no stage is there evidence of an active inflammatory cellular reaction, and for this reason it is inaccurate to refer to the condition as a neuritis.

Regardless of the underlying cause of the deficiency, a small percentage of patients with a polyneuropathy develop demyelinating lesions in the spinal cord. Usually the posterior columns only are involved, the column of Goll being more frequently destroyed than the column of Burdach. These posterior column lesions are preceded by demyelination of the posterior nerve roots. The pathological appearances of these deficiency disease lesions are very similar to those of tabes dorsalis, and although no claim is made for a common aetiology in these conditions, it is possible that a common disturbance of cellular metabolism may result in such similar morbid changes. In Wernicke's encephalopathy, lesions of a haemorrhagic and later cellular invasive nature are found in the paraventricular grey matter of the third ventricle, the mammillary bodies, para-aqueductal region, the corpora quadrigemina beneath the ependyma of the fourth ventricle, the olives and in the cerebellum.

There are no specific changes to be found in the C.N.S. in nicotinic acid

https://doi.org/10.1192/bjp.92.387.305 Published online by Cambridge University Press

deficiency, but the occurrence of primary irritation of large nerve cells, such as the Betz and the anterior horn cells, either alone or in combination with hyaline changes in cerebral blood capillaries and Wallerian degeneration of the posterior and lateral tracts of the spinal cord, are highly suggestive.

In experiments with chicks, it has been shown that pantothenic acid is essential for the preservation of the spinal cord, whilst other factors of the vitamin B complex are not able to compensate for such a deficiency, although it must be admitted that so far it has not been demonstrated that the health of the nervous system in other animal species is influenced by an inadequate supply of this factor.

To summarize: The distribution and order of frequency of lesions in thiamine deficiency is more or less the reverse of nicotinic acid lack. In some forms of B1 loss (beri beri) the peripheral nerves are the primary seat of damage, while in pellagra the brain seems to be the early focus of disturbance. As the condition advances, the processes tend to extend centripetally in beri beri and centrifugally in pellagra.

As yet one cannot be assured as to the best methods for the biochemical estimation of deficiencies of the various B factors.

In B1 deficiency states the thiochrome content of the blood or urine can be measured by the thiochrome method or by a yeast fermentation test, whilst the blood cocarboxylase content gives a good indication of the thiamine saturation of the body. At the present the estimation of the dextrose, pyruvic acid and lactic acid content and changes in the blood, following oral or intravenous glucose, appears to furnish the most reliable results.

The estimation of the urinary content of nicotinamide methochloride is probably at the present the method of choice in estimating nicotinic acid body saturation, but further reference will be made to the fallacies of such an estimation later in the paper.

One must now discuss conditions which may cause these deficiencies. Succinctly they are (1) a lack of the factors in the ingested food, (2) failure in their absorption, (3) an inability to store them, and (4) an upset in the body cell's ability to utilize them. An inadequate ingestion of vitamin B is likely to occur in food faddists, diabetics, dyspeptics, widowers or single people living on their own who neglect to cook for themselves or collect their rations, and in war time, commonest of all, mothers who have sacrificed their ration for the good of the family. In such chronic wasting diseases, as tuberculosis, diabetes, hyperthyroidism and neoplastic diseases, secondary deficiency states may occur even when an adequate diet is being taken.

Before dealing with defects in absorption I must mention the recent work of Ellinger, Coulson, Benesch and Kay on the biosynthesis of nicotinic acid in the human gut by the intestinal flora. Most of this research has been carried out at West Park Hospital. It had been found that thiamine could be synthesized by the intestinal flora, whilst the considerable discrepancies between the quantities of nicotinic acid daily ingested and eliminated suggested to these workers that a similar mechanism for the production of nicotinamide might be at work. They found that when the bowel was "sterilized" by succinyl sulphathiazole, the output of urinary nicotinamide methochloride

https://doi.org/10.1192/bjp.92.387.305 Published online by Cambridge University Press

dropped, on an average 60 per cent., but returned to normal on the cessation of the " sulpha " drug. That this was not due to the destruction of nicotinamide by the drug was proved by the controls who received sulphathiazole only. Benesch found that aerobic cultures of caecal organisms synthesized considerable quantities of nicotinic acid, mainly after the third day of cultivation, whilst anaerobic caecal organisms destroyed two-thirds of the nicotinic acid present in the original medium. It is suggested that in the normal caecum an equilibrium is to be found between organisms producing and those destroying nicotinic acid. An upset in this equilibrium may play an important part in the causation of deficiency diseases.

This balance may be upset by such conditions as vomiting, chronic diarrhoea, dysentery, sprue, coeliac disease, tuberculous enteritis, neoplasm of the gut, etc., and probably explains the frequency of deficiency states found in such conditions. Again, the increasing use of sulphaguanidine and succinyl sulphathiazole for the " sterilization " of the bowel may precipitate a further number of deficiency cases in the future.

Some of the liver diseases have been shown to result in vitamin deficiencies by interfering with their storage.

It might be appropriate at this stage to point out that alcohol as a factor in deficiency states is concerned in (1) diminished ingestion, owing to the alcoholic's failure to eat adequately, in (2) failure of absorption due to gastritis, vomiting, etc., and in (3) failure of storage due to liver damage. In our experience, other drug addictions, such as with the barbiturates, bromide, morphia, etc., may produce deficiency states; whether by interfering with absorption or by liver damage, is at the present not clear.

In recent years many people have existed on a borderline diet adequate for their needs when their lives run smoothly; in such persons any stress, such as pregnancy infection, surgical procedure, fracture, etc., may precipitate a deficiency state.

Our experience has shown that in the treatment of acute deficiency syndromes it is essential to give the factors parenterally, and only when the acute phase has passed is it advisable to treat by mouth. Again, the findings that anaerobic organisms destroy nicotinamide may account for those not infrequent cases which fail to respond to treatment when given by mouth. Most deficiency conditions are of a mixed nature; for this reason it is better to treat patients by a combination of the B complex factors, the relative dosage of each depending upon which " factor defect " syndrome is most evident. According to some authorities the exhibition of one factor alone may be dangerous, in that it may light up an overt deficiency state of another factor. Cases of Wernicke's encephalopathy treated by thiamine alone may leave them with a residual Korsakow's psychosis unaffected by a continuation of therapy. It is usual after the deficiency state has cleared up to continue treatment with whole yeast, although it is fully appreciated that the balanced and relatively more plentiful diet of hospital is probably more than adequate for the patient's vitamin maintenance.

In conclusion, whilst our knowledge of inadequate nutrition and its relationship to physical and mental ill-health is still meagre, I think that the importance

https://doi.org/10.1192/bjp.92.387.305 Published online by Cambridge University Press

of vitamin B complex in the maintenance of well-being is being increasingly established.

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