VITAMIN DEFICIENCY AND THE PSYCHOSES.

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A STATE of vitamin deficiency arises (i) when inadequate amounts of a vitamin (or vitamins) are ingested, (ii) when absorption from the alimentary canal is defective or interfered with, (iii) when storage mechanisms are at fault, e.g. liver disease, and (iv) when the tissue cells themselves are unable to utilize the vitamin (1, 2). With war rationing the first factor is likely to be commoner than heretofore, especially in alcoholics (3), patients maintaining a strict "peptic ulcer diet" over long periods (4), diabetics (2), mothers sacrificing their rations for the family, food faddists, and in people living alone and doing their own cooking (5). Nowadays many exist on a "borderline" diet, in whom any stress such as pregnancy, infection, surgical procedure, fracture, hyperthyroidism, etc., will precipitate a deficiency state; moreover, in chronic gastro-intestinal disorders the available vitamins may be lost or destroyed (6–14).

Although there is evidence that vitamins A, C and E may be associated with some neurological disorders, in the present state of our knowledge the only vitamins proven to have a causal relationship with certain neuropsychiatric syndromes are to be found in the B complex. These are thiamin and nicotinic acid (15). Riboflavin, pyridoxine and biotin are possibly implicated, but their precise role is not yet established (16–18).

The exhibition of a specific vitamin may not relieve all the symptoms of a deficiency state, as several factors of the B complex are usually involved—in fact, a secondary deficiency state which had been latent may become activated (2, 7).

The acute encephalopathic syndromes (*vide infra*) are likely to be encountered amongst cases of confusion and delirium in the wards of a general hospital. Whilst they may occur infrequently, it is probable that an increasing number of psychotics will be recognized as having their mental pictures coloured or complicated by symptoms indicating B deficiency. Amongst the psychoneuroses a proportion of cases will in all probability be found to be suffering essentially from a subvitaminosis.

THIAMIN (Vitamin B_1 or Aneurin).

Thiamin plays an important part in the fundamental processes of oxidation in the living cell; it is active as a coenzyme in the oxidation of carbohydrate (19, 20). Its lack may produce reversible changes in neurones of the C.N.S.

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I. *A "Neurasthenic" Syndrome.*

This is probably the earliest and most frequent manifestation of thiamin deficiency. Symptomatology is varied, but anorexia, fatigue and insomnia are outstanding. Irritability, inability to concentrate, mild depression, headache, backache, constipation, flatulence, etc., are common (21–24). Williams and his co-workers (25, 26) induced B_1 deficiency in volunteers, producing similar symptoms. They state: ". . . At the end of the period of deprivation of thiamin the clinical picture in all our cases was that of anorexia nervosa, and this condition as one encounters it clinically is usually an end stage of more severe neurasthenia. . . ."

O'Shea *et al.* (27) induced a comparable deficiency syndrome, and noted that the subjects seemed confused and less able to reason and exhibit good judgment. They found that foresight and judgment, as measured by performance on the Porteous maze tests, were impaired, but that tests for general intelligence, reasoning ability and speed of hand-muscle co-ordination showed no impairment of these functions.

That every case of "neurasthenia" is due to vitamin deficiency is obviously absurd, but the probability remains that some cases are nutritional in origin.

II. *Wernicke's Encephalopathy.*

This syndrome, which often has an abrupt onset, is probably not uncommon. It is "traditionally associated with alcoholism," but it may occur as a terminal complication of other diseases, particularly chronic gastro-intestinal disorders (e.g. gastric carcinoma) (28, 29). The pathological changes are briefly: foci of vascular stasis and parenchymatous degeneration in the peri-aqueductal grey matter of the mid-brain and the floor of the fourth ventricle (24, 28, 30). The work of Alexander and his associates (31–33) has established that the lesions occurring in man and those produced by experimental thiamin deficiency in pigeons are identical in topographical distribution and histological characteristics.

Although the original clinical features described by Wernicke were clouding of consciousness, varying ophthalmoplegias and ataxia, a wider range of symptomatology is being recognized (34). Thus the mental picture may present clouding of consciousness of any degree from drowsiness or apathy to delirium and complete coma. The most characteristic focal neurological manifestation is paralysis of conjugate eye movement (although any type of internal or external ophthalmoplegia may be encountered). A disturbed respiratory rhythm is said to be of diagnostic value (28), and nystagmus may be present or may appear only after the ophthalmoplegia has cleared. Polyneuropathy in the lower limbs is frequent; according to Jolliffe (34) this invariably precedes or accompanies the ophthalmoplegia. Recently Wortis, Jolliffe *et al.* (3, 24) suggest that whilst the mental changes and the ophthalmoplegia are associated with B_1 deficiency, the syndrome as a whole is due to a multiple deficiency.

III. *Korsakov's Psychosis.*

Considerable doubt exists as to the role which thiamin plays in this psychosis (3, 15, 24, 35). The syndrome may be encountered following head injury, subarachnoid haemorrhage, etc.—conditions in which the pathogenesis is seemingly unrelated to dietary deficiency. Even where alcohol appears an aetiological factor many cases are known to recover without special therapy. Again, it is said (29, 34) that some patients with Wernicke's disease, treated by intensive thiamin, are left with a residual Korsakov's psychosis unaffected by continuation of therapy. Despite these criticisms, certain workers (36, 37) are convinced of the close relationship between the psychosis and B_1 lack. They explain the failures by postulating that in these cases irreversible structural changes have occurred already. We must record that in our experience, prolonged thiamin therapy has produced beneficial results on either the mental symptom-complex, or the polyneuropathy, or both.

IV. *Delirium Tremens.*

There is evidence of nutritional deficiency and a disturbed carbohydrate metabolism in delirium tremens but the problem is exceedingly intricate (29, 38). There appears to be little incontrovertible evidence that the B complex is related to its pathogenesis, despite many favourable reports of B therapy in the literature (15, 35). However, delirium tremens may be followed or complicated by an encephalopathic syndrome of the Wernicke or nicotinic acid deficiency type (24, 29). Whilst the treatment of the dehydration usually found in this condition is of paramount importance, the exhibition of large doses of thiamin at the same time in the experience of one of us (W. A. C.) apparently lowered the mortality-rate considerably.

V. *The Polyneuropathies and Related Disorders.*

A polyneuropathy (polyneuritis), occurring in any systemic or mental disorder, which is bilateral and symmetrical and which manifests itself primarily and most severely in the lower limbs, is likely to be due to thiamin deficiency. Polyneuropathies intimately associated with avitaminosis occur in beri-beri, pellagra, sprue, alcoholism, pernicious anaemia, pregnancy, diabetes, hyperthyroidism, and in the cachexias of new growth, senility and tuberculosis (2, 11, 14, 35, 39, 40). Single, unilateral or local neuritides are almost certainly not related to B_1 lack (2, 10).

Beri-beri.—Although a psychosis has not been described in beri-beri, the experimental work of Williams *et al.* (41) suggests that mental symptoms may accompany the well-known somatic changes.

Pernicious anaemia and subacute combined degeneration (2, 35, 42–45).—In the past few years we have encountered several patients suffering from pernicious anaemia, or subacute combined degeneration, who developed an acute psychosis of either a confusional character or a depression with persecutory delusional ideas. The psychosis has cleared up within a few weeks with parenteral crude liver extract. Until recently we presumed that the main aetiological factor concerned was that responsible for the anaemia. Now one

questions to what extent did B complex lack participate in the mental picture. It was noted that when using the crude extracts the mental state appeared to improve more rapidly than the blood picture.

Laboratory Aids in the Diagnosis of Thiamin Deficiency.

Several methods are available to assess the thiamin status. The thiamin content of the blood or of the urine can be measured by chemical means, e.g. the thiochrome method (46–48), or by microbiological methods, e.g. a yeast-fermentation test (46). By the latter the blood value has been found to average 5·4 μg., whilst values below 3 μg. are said to occur in cases of peripheral neuropathy or Wernicke's disease. Again, urinary excretion of thiamin is diminished in thiamin deficiency and a saturation test has been devised—said by some to be the most reliable (49). The blood cocarboxylase gives a good indication of thiamin saturation of the body (5). More recently the rise in the bisulphite-binding substances of the blood, particularly pyruvic acid, has been utilized (24, 50, 51). Thus, Williams and his co-workers (41) believe that abnormal changes in the pyruvic acid, lactic acid and dextrose of the blood following oral or intravenous dextrose furnish the most reliable test of the severity of metabolic defects in thiamin deficiency.

Treatment.

As in all vitamin deficiency states, treatment is twofold: (*a*) provision of a balanced highly nutritious diet of natural unrefined foods, and (*b*) the administration of the specific factor or factors.

In treating B_1 deficiencies, dosage must be large, particularly in the acute encephalopathies, where prompt and adequate treatment may be a life-saving measure, and it should be administered parenterally. Also, where there is reason to believe that the avitaminotic state is due to an absorption failure, the factor should be given parenterally. Jolliffe (15) suggests the following dosage, and in the treatment of over 3,000 cases claims that he never experienced toxic symptoms:

TABLE.—*Parenteral Thiamin Treatment* (*after Jolliffe*).

Disease or syndrome.	Amount in mgm.	Frequency.	Comment.
Neurasthenic	10–30	Daily	Trial of at least 3 weeks if less than 3 months' duration; if of longer duration trial of at least 3 months.
Polyneuropathy:			
Mild	10–30	,,	10–21 days.
Moderate	20–50	Twice daily	3–6 weeks.
Severe	20–100	,, ,,	3–6 weeks, then in smaller doses until well after improvement ceases.
Wernicke	50–100	Three times daily	2–7 days.

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Nicotinic Acid (Niacin, P–P Factor).

Nicotinic acid is chemically related to nicotine. In the body nicotinic acid amide combines with other compounds (adenine, phosphoric acid, etc.) to form a coenzyme essential for the transference of oxygen in the fundamental processes of the cell (19, 20). The body cannot synthesize nicotinic acid, and without it coenzyme formation is impossible (52). Although much is known of the manner in which this coenzyme acts, it is still obscure as to its relationship to pellagra.

Storage is better than with thiamine, and the tissues in a deficiency hold on to nicotinic acid, in the form of a coenzyme, tenaciously, so that with obvious pellagra the nicotinic acid content of the whole blood may not fall below that found in normal controls (53).

Pathology.

There are no specific changes in the C.N.S. in pellagra, but according to most writers the occurrence of primary irritation of large nerve cells such as the Betz and anterior horn cells, either alone or in combination with hyaline changes of the cerebral blood vessels, and degeneration of the posterior and lateral tracts in the spinal cord, are highly suggestive. The lesions in the spinal tracts are probably of a Wallerian type, and are not to be confused with subacute combined degeneration. In uncomplicated cases the spinal roots and peripheral nerves are not affected (1, 54).

Commenting in general on the selective affinity of the vitamins for certain parts of the C.N.S., Hsü remarks: ". . . The distribution and the order of frequency of the lesion in the one condition (beri-beri) are more or less the reverse of the other. In 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 disease progresses farther the process of degeneration extends centripetally in beri-beri and centrifugally in pellagra."

It has been found that in pellagra complicated by beri-beri the cerebral metabolism (as measured by the oxygen utilization, and the glucose and lactic acid levels of the arterial and venous blood) is decreased. Himwich, Spies *et al.* (55) state that such observations may afford a basis for the explanation of the mental changes.

1. *A Neurasthenic Syndrome.*

Spies and his collaborators (2, 23) found that a syndrome simulating or identical with "neurasthenia" frequently preceded the onset of pellagra. Many authorities now regard mild nicotinic acid deficiency as a definite clinical entity, with a symptomatology similar to that previously described for B_1 "neurasthenia"—a condition not necessarily developing into a fully blown pellagra. It may well be commoner in this country than is appreciated.

II. *Pellagra.*

It was estimated that in the U.S.A. in 1938 there were 100,000 pellagrins (56). Its rarity in Great Britain is possibly due to lack of recognition (57).

The diagnostic triad, "dermatitis, diarrhoea and dementia," is out of date (8). The signs and symptoms characteristic of the disease are: mental abnormality, weight loss, stomatitis, glossitis, dermatitis, porphyrinuria, diarrhoea, tachycardia, peripheral neuropathy and vomiting, in their relative order of frequency (15, 58, 59). All are not necessarily present in the same case. The mental symptoms may be mild, and "psychoneurotic" in type: a dislike of bright lights, of noise, of strong odours or tastes; fidgetiness; a feeling of being on edge; apprehension, and increased emotional excitability (60). "Pellagrins" describe their symptoms as being strange to themselves. They tire easily, perhaps suffer from insomnia, headache, nausea and vomiting. Glossitis is constantly present, but it is often mild and may be confined to the tongue margins. The characteristic symmetrical dermatitis may be preceded by diarrhoea of many months' duration. Probably in this country, dermatitis should not be regarded as a necessary diagnostic sign (pellagra sine pellagra). Stannus (45) has called the incomplete stage (stomatitis without other symptoms of pellagra) "pellagra fruste," others "larval pellagra." The polyneuropathy seen in some cases may be mild or severe; it has been shown to be due to thiamin deficiency and not to lack of nicotinic acid (2, 13, 62, 63). Of particular interest are those cases presenting severe psychotic disturbances in addition to the characteristic somatic signs. States of confusion are commonest, but manic-depressive, delirious and paranoid reactions have been described (23, 29). Spies and others (7, 13, 58, 64, 65) point out that severe mental disturbances indicate a very advanced stage of the disease, and that they are preceded by the milder symptoms enumerated above.

That pellagra is encountered relatively frequently in mental hospitals is well recognized (57, 66–68). What is not appreciated is that a number of chronic deteriorated patients may suffer from a concomitant chronic pellagra. Chronic pellagra is known to produce irreversible organic changes in the C.N.S. (2, 3). The deterioration in some long-standing schizophrenic patients may be associated with the pellagrinous changes. Sydenstricker (7) has pointed out that early diagnosis is important and treatment is often necessary over a prolonged period; treatment in the later stages of the disease may be disappointing and indeed useless (21, 29). Mindus (69) has examined a group of 60 female patients in a Swedish mental hospital, with "neurasthenica gastrogenica," in which the predominating symptoms were depression with or without paranoid trends, lassitude, anorexia, weight loss, anaemia, insomnia and hypochlorhydria. He treated half the group with a high calorie diet rich in vitamins. Those so treated fared "strikingly better" than the controls. Our observations at West Park lend support to the views expressed above. We have recently observed a number of cases of frank pellagra amongst the "chronic" patients, and we suspect that there are many more cases of pellagra sine pellagra. We consider that such symptoms as the following should lead one to suspect niacin deficiency: unexplained diarrhoea, particularly if long standing and intermittent; abnormalities of the tongue—undue redness, marginal indentation, atrophy of papillae (45); weight loss (sudden or gradual), especially when this cannot be accounted for by intercurrent disease or reduced dietary intake. In our series of pellagrins the initial lesion in two cases which

led to the subsequent diagnosis was an ulceration of the vulva and perineum, possibly secondary to chronic vaginitis. The following factors may be peculiarly favourable to the development of the disease in mental hospitals: faulty feeding habits, dysentery, and prolonged sedation (e.g. with barbiturates).

III. *Nicotinic Acid Deficiency Encephalopathy.*

In 1940, Jolliffe and his co-workers (70) reported 150 cases of an "encephalopathic syndrome" characterized by clouding of consciousness, cog-wheel rigidity of the extremities and uncontrollable grasping and sucking reflexes. They believed that this condition was essentially the same as that described by Bender and Schilder (71) under the name "encephalopathica alcoholica." In Jolliffe's opinion the syndrome does not occur exclusively in chronic alcoholics; it may be the only manifestation of a deficiency disease, or it may occur in association with pellagra, with the polyneuritis of B_1 deficiency, or with the ophthalmoplegia of Wernicke's disease (15, 29). The differential diagnosis from such conditions as delirium tremens, the deliria of infectious disease, intracranial tumour or cerebral arteriosclerosis, in which groping, grasping and sucking, etc., may occur also, can present considerable difficulties. Examining the past records of such cases it was found that the mortality-rate was high (90 per cent.). The usual treatment given in the past had been large quantities of saline. Jolliffe continued the intensive hydration treatment in his cases; he added B_1 alone to one group, and nearly all the patients died; when a high vitamin diet was given 50 per cent. of cases survived, whilst in a further group treated with nicotinic acid by mouth, and parenterally, the survival rate increased to about 85 per cent. In the light of these experiences, Jolliffe concluded that pellagra was a "partial nicotinic acid deficiency," whilst the encephalopathy was a complete one. The only similar case recorded and treated successfully in this country is that described by Slater (72), who rightly points out that a number of such cases may lie unrecognized in general hospitals.

IV. *Nicotinic Acid Deficiency States Associated with Atypical Psychosis* (2, 3, 73).

Recently Cleckley, Sydenstricker and Geeslin (73) reported upon 19 severely undernourished patients whose psychoses were of the pattern seen in pellagra, but in whom there was no overt, frank clinical evidence of the latter disease. Some degree of glossitis was present in 17 of the cases, 5 cases presented deafness as a symptom, 2 a mild non-specific vaginitis, 1 diarrhoea and 1 stomatitis. The mental picture varied from "hebetude to profound stupor." Most of the cases occurred in elderly individuals, 2 only were chronic alcoholics, and 1 suffered from cerebrospinal syphilis. Dramatic "cure" was reported following intravenous nicotinate in 15 cases. In the opinion of the authors such cases are often perfunctorily diagnosed as cerebral arteriosclerosis, and inadequately treated until death from bronchopneumonia supervenes. They were convinced that a therapeutic test with nicotinic acid is justified in all cases of unexplained hebetude or unconsciousness. Jolliffe, commenting on these cases, considered that a few fitted into his conception of an encephalopathic syndrome (*vide supra*). In a later paper Sydenstricker and Cleckley (74)

reported a further series of cases, and although many of these were confused, lethargic or even comatose on admission, some exhibited " manic excitement." In nearly all this group a red tongue was the only abnormal physical sign indicating deficiency, although the psychosis complicated or followed serious physical conditions, such as arteriosclerosis, hemiplegia, peptic ulcer, prostatectomy, fractured femur and pneumonia. The authors state that ordinarily " toxic psychosis " is the diagnosis.

Laboratory Aids in the Diagnosis of Nicotinic Acid Deficiency.

At the present time there seems to be no satisfactory chemical or biological test available (5, 7, 46, 53). Despite the contention of some authorities that porphyrinuria is an integral part of the disease, it is doubtful if it is an essential feature of pellagra and it does not aid in the diagnosis (53, 75). Nicotinic acid determined chemically has not significantly different values in the blood of pellagrins and in those of normal controls (76). " Tolerance curves " have not proved of value. One of the most promising tests is that for the bluish fluorescent substances F_1 and F_2 in the urine (5). F_1 is said to occur in high concentration in pellagra, whilst F_2, which is present in normal urines, is reduced in pellagra. Administration of nicotinic acid reduces the F_1 content and F_2 reappears in the pellagrin's urine (46). The urinary excretion of trigonelline may prove to be a useful measure of nicotinic acid deficiency (76, 77).

Treatment.

Pellagra is treated with an abundant high calorie diet and the specific vitamin (59, 78). In the early stages milk and meat juices may have to be the mainstay owing to the painful mouth lesions and the gastric disturbances. The dosage of nicotinic acid recommended is 500 to 1,000 mgm. each day in the early stages of treatment (2, 15, 59, 79). It should be given in ten divided doses of 50 mgm. or 100 mgm. each hour during the day. If nicotinic acid amide is given instead, the dosage recommended is 15–30 mgm. every hour for ten hours a day. The effect of this régime is little short of dramatic, the lesions of the mucous membranes often yielding to treatment within a day or two. Improvement in the mental state is usually evident within a few days, but the skin lesions may take a fortnight or longer to clear (7, 58).

The addition of brewer's yeast, 15–30 gm. daily, is advisable owing to the danger of precipitation of latent deficiencies in other B factors, e.g. thiamin or riboflavin (" concurrence of vitamin deficiency diseases "). If there are definite signs of thiamin deficiency before treatment this vitamin should be administered together with the nicotinic acid (2).

Later when the patient is apparently well a maintenance dose of 25–50 mgm. nicotinic acid three times a day should be given for a prolonged period in addition to the continued enriched diet (24).

The treatment of the " atypical psychoses " (Group IV above) and of the encephalopathic syndrome is very similar to that outlined above. It is very likely that in the early days tube-feeding will be necessary and dehydration will need combating by intravenous glucose saline. The specific therapy

should be given partly by parenteral means. Jolliffe (15) recommends 100–200 mgm. nicotinic acid amide parenterally each day, and 500–1,000 mgm. nicotinic acid by mouth if the patient is able to swallow. This dosage is sustained for 3–7 days and thereafter smaller amounts are given by mouth.

Recently Sydenstricker (5) has suggested that a combination of vitamins may be preferable to thiamin in the treatment of Wernicke's disease. He has used a mixture of 50 mgm. nicotinamide and 5 mgm. each of thiamin, riboflavin, pyridoxine and calcium pantothenate, given by injection six times daily.

In the neurasthenic syndrome Jolliffe (15) recommends daily doses of 100–300 mgm. nicotinamide by mouth in addition to an enriched diet. As with the thiamin deficiency neurasthenic state, therapy should be tried for three months, or longer. Ruffin (21) adds a word of caution, stating that his experiences in the treatment of patients suspected of a mild deficiency are disappointing, and that the improvement noted in some cases may be temporary and due to suggestion. He considers vitamin therapy to be dramatic and unequivocal; that a trial of longer than three or four weeks has no justification. However, Williams's experimental work argues in favour of a longer trial, as he found a slow disappearance of the induced signs and symptoms when the restriction of vitamins in his subjects had been moderate and prolonged.

The hypochromic anaemia associated with nicotinic acid or riboflavin deficiency or in multiple neuritis does not respond to yeast, but does so to iron (80).

Since nicotinic acid has been found so effective in elderly arteriosclerotic patients, some authorities have argued that it exerts its beneficial action by its vasodilator effect on the cerebral vessels. This seems unlikely since nicotinamide and nikethamide (coramine, a related compound) are as effective as nicotinic acid in treating the acute deficiencies, and these substances have little vasodilator action (5).

The toxic manifestations of nicotinic acid consist of burning and itching sensations in the skin, particularly over the face and ears, occurring shortly after administration and persisting up to 20 minutes (59). The peripheral vessels are dilated and the skin temperature increases—in fact the patient's aspect may simulate scarlatina. The blood pressure may fall and nausea and vomiting can occur. A reduction in dosage or a temporary cessation of treatment is then indicated. There is no evidence that nicotinic acid in the dosage mentioned is dangerous to life. Nicotinamide is much less toxic (81).

Riboflavin (Vitamin B_2), Pyridoxine (Vitamin B_6) and Pantothenic Acid.

There is no evidence at present that riboflavin is related directly to neuropsychiatric conditions (35). Nevertheless, together with nicotinic acid and thiamin it is a component of the coenzymes essential in the intermediate stages of carbohydrate metabolism (24). The physical signs of ariboflavinosis are, briefly: angular stomatitis (cheilosis), nasolabial seborrhoea—often involving the eyelids and ears also—"shark skin" appearance of cheeks and chin, a peculiar glossitis (flattened mushroom-shaped papillae) associated with a

magenta-coloured tongue, and eye changes from mild circumcorneal injection (which may only be detected with a slit-lamp) to corneal vascularization and opacities (16). Ariboflavinosis may be precipitated in pellagra when large amounts of nicotinic acid are administered to a patient who maintains an inadequate diet (7, 16).

Spies *et al.* (17) treated large numbers of undernourished persons with clinical evidence of pellagra and beri-beri with nicotinic acid, thiamin and riboflavin. The diet of a few of these patients remained the same since they did not regain strength enough to restart work and so earn sufficient to buy better food. The residual symptoms included "extreme nervousness, insomnia, irritability, abdominal pain, weakness and difficulty in walking." Intravenous synthetic vitamin B_6 produced dramatic relief within four hours of administration. Spies concludes that pyridoxine is an important factor in human nutrition, and claims that these observations support the hypothesis that clinical deficiency diseases occur as complexities and not as single entities.

Pyridoxine may mobilize riboflavin from storage, or dissociate it from some combination in which it is physiologically active. Pantothenic acid may have a similar action (16, 82). Pyridoxine has been used in progressive muscular atrophy and the dystrophies, sometimes in combination with α-tocopherol. The consensus of opinion is that its value is very doubtful and its use in cases of Parkinsonism is disappointing (35, 53, 55, 83).

Vitamins A, C and E.

Vitamin A deficiency in young animals is said to stop skeletal growth whilst the soft tissues, including the nervous system, continue to grow (84). The possible clinical implications in man have not been formulated (5, 46).

It seems likely that the depletion of ascorbic acid which occurs in certain illnesses associated with alcoholism (e.g. delirium tremens) is a predisposing factor in subdural haemorrhage following injury (33, 85). Bowman and Wortis (86) point out that the vitamin C values in the blood and C.S.F. of delirium tremens are low. They consider that even if the subvitaminosis is not directly related to the production of the delirium, therapy may prevent and combat intercurrent injection.

The role of vitamin C in the senile psychoses and in senility has been questioned recently. The skeletal changes in senility and in scurvy are said to be similar (19). Berkenau (87) suggests that the delay in saturation in his small group of psychotic patients may be significant. Rafsky and Newman (88) found high retention values in their subjects, whilst the clinical experiences of Stephenson, Penton and Korencheowsky (89) suggested that combined B and C therapy "prevented or improved certain features"—muscular, cardiovascular and mental deterioration: benefit was recorded in the perceptual, cognitive and emotional spheres. However, Moore (90) considers that small doses of thiamin and nicotinic acid counter certain adverse symptoms in aged patients. Wexburg (91) has described a syndrome consisting of acute or subacute mental disorder of the organic reaction type, usually associated with postero-lateral sclerosis, sometimes with polyneuritis, often with hypochromic or hyperchromic anaemia, and hypochlorhydria ("senile encephalomyelosis").

He recommends treatment with the B complex, and suggests that all cases of deliria and confusional states in the senium should be examined and treated from the hypovitaminotic point of view.

On the basis of the experimental production of nutritional myopathy and encephalomalacia in chicks, etc., lack of vitamin E has been incriminated in amyotrophic lateral sclerosis, the myopathies and in tabes dorsalis. The evidence of its therapeutic value is doubtful, and its relationship to disease of the nervous system in man is at present not clear (5, 53, 64, 83, 92–96). Vitamin E lack is known to produce degenerative changes in the germinal layers of the testes in rats and morphological changes in the anterior lobe of the hypophysis (19). It is possible that these and similar observations in experimental deficiency may prove to be of importance in the advance of psychiatric knowledge.

Conclusion.

That adequate nutrition is essential for the physical and mental well-being of the individual can be regarded as axiomatic. However, our knowledge of the relationship between inadequate nutrition and mental ill-health is depressingly meagre. The rapid flood of research on vitamins in the last few years has caught up the psychiatrist in its swirl. Although it behoves us to be cautious when all and sundry are vitamin-minded, recent work strongly suggests that some mental disease is produced by a lack of these accessory food factors. This paper is an attempt to reproduce recent views in a brief form, and the classification adopted must be regarded as purely arbitrary.

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