STUDIES IN VITAMIN B DEFICIENCY WITH SPECIAL REFERENCE TO MENTAL AND ORAL MANIFESTATIONS

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(WITH PHOTOGRAVURE PLATE)

Clinical descriptions of the results of a deficiency of members of the vitamin B complex are common in American published work but scanty in the medical literature of this country. Cheilosis due to riboflavin (vitamin B₂, lactoflavin) deficiency has been described in England by Wilson (1942) and Duckworth (1942); and Deeny (1942) has reported on 16 cases of pellagra in Northern Ireland, where, he says, mild forms of the disease are relatively common and usually pass unrecognized, the patient being diagnosed as suffering from neurasthenia, dyspepsia, or eczema. Studies of pellagra in England between 1934 and 1939 were made by Davies and McGregor (1939), who reviewed 16 cases. Since submitting this paper for publication Hardwick (1943) has described pellagra associated with chronic psychosis in 10 patients in an English mental hospital. Egaña *et al.* (1942) and Johnson *et al.* (1942) have described the effects on human volunteers of experimental diets deficient in the vitamin B complex. These include easy fatigue, loss of ambition and efficiency, poor appetite, insomnia, constipation, muscle pains, and slight anaemia in persons in sedentary occupations. The literature on the clinical manifestations resulting from a deficiency of the B group of vitamins has been reviewed by Bicknell and Prescott (1942).

Psychoneurosis and Dietary Deficiency

We have recently seen 17 cases of vitamin B complex deficiency in patients treated primarily for nervous disorders. This represents 2% of the patients seen by us in the outpatient department of the West End Hospital for Nervous Diseases. Originally they were mostly classified as suffering from functional nervous disorder, and with one exception were women. The parallelism between the manifestations of a deficiency of the vitamin B complex and those of psychoneurosis is seen from the following list. All are likely to be met with in the psychoneurotic; those in italics may result from a deficiency of the vitamin B complex.

General: *Fatigue, anorexia, indigestion, constipation, diarrhoea, dizziness*

Circulatory: *Tachycardia, palpitation, shortness of breath*

Vasomotor: *Pallor, blushing, sweating*

Nervous system: *Headache, backache, insomnia, photophobia, hyperacusis, noises in the head, vertigo, hyperaesthesia, paraesthesia*

Mental symptoms: *Inability to concentrate, self-consciousness, depression, phobias, anxieties*

So close is the parallelism that early cases of pellagra—which is a multiple deficiency disease—are often diagnosed as “functional” by those unacquainted with the early manifestations.

A patient may suffer from a general dietary deficiency and exhibit only the manifestations of a deficiency of the vitamin B complex in the early stages. This is partly because these manifestations are the first to show. The results of a deficiency in vitamin A, C, D, or K are not so obvious clinically: special laboratory tests must be employed for their detection unless gross deficiency is present. The B vitamins, being water-soluble, are not stored in the body to any extent, and diets poor in these vitamins give rise to deficiency symptoms in three months or less (Vedder, 1940). Although it is convenient to split up the B vitamins for purposes of classification, an uncomplicated deficiency of one of them does not exist clinically, because they occur together in Nature and no selected combination of foods is entirely lacking in any one of them. There is no such thing as pure vitamin B₁ deficiency, unless induced experimentally, because if the diet is deficient in vitamin B₁, it will also be deficient in the other B vitamins, such as riboflavin, nicotinic acid, pyridoxine, pantothenic acid, etc.

In our cases certain features were common to all. All the patients gave a history of a poor diet, or lack of appetite due to mental or physical causes, or a condition necessitating dieting (peptic ulcer, hypertension) or interfering with absorption (vomiting, typhoid). Many of the patients lived alone, or had grown-up families out at work all day, so that they did not prepare proper meals. Others had no appetite and subsisted on occasional snacks, which consisted largely of refined carbohydrate foods. A vicious circle was thus created because these foods contain little of the vitamin B complex, and an increased consumption of carbohydrate increases the need for B vitamins and lack of the latter produces further loss of appetite. Many of the patients did not eat meat, and few included adequate milk or cheese—all rich in the vitamin B complex—in their diet. A general preference was expressed for white bread, which is a poor source of the vitamin B complex, much of the vitamin B₁ and riboflavin being removed in the milling.

All the patients showed some of the signs and symptoms of functional nervous disorder—most commonly depression, headache, insomnia, and loss of appetite. Other symptoms were lack of energy, fatigue on slight exertion, breathlessness, inability to concentrate, and nervous dyspepsia. There was only one case of psychosis in the series, probably because such cases more commonly go to observation wards in the London area.

All our cases showed a marked improvement in their “psychoneurotic” symptoms, and the majority a complete disappearance of these symptoms, after treatment with the vitamin B complex. Except in the one case admitted, the environment was unchanged. We think that in most of these cases the condition was determined to some extent by the wartime marginal diet but actually precipitated only when mental or

physical factors led to loss of appetite or impaired absorption. Case I, which was treated as an acute emergency, illustrates the need for a mental ward in general hospitals. Two cases at a later stage reported from a mental hospital by Parfitt (1936) failed to make a complete recovery on treatment with the B vitamins, although their improvement was dramatic.

Oral Lesions

All the patients showed signs and symptoms of nicotinic acid deficiency (glossitis, and depression or other mental symptoms), and nearly all showed one of the signs originally considered specific for riboflavin deficiency (angular stomatitis or cheilosis). The value of cheilosis as a specific sign of riboflavin deficiency has, however, recently been questioned, and it appears that this may occur independently of a nutritional deficiency. It may result from other causes, such as poorly fitting dentures, which result in malocclusion (Ellenberg and Pollack, 1942), and even from sensitivity to lipstick or chewing-gum (Miller, 1941; Hecht *et al.*, 1939). We have also observed cheilosis in a patient with post-encephalitic parkinsonism, in which the condition was presumably due to the dribbling of saliva and not to a nutritional deficiency: the diet was adequate and there were no other manifestations of nutritional disease. A number of cases of cheilosis described in America failed to respond to riboflavin, but did to other members of the vitamin B complex, such as nicotinic acid, pyridoxine, or yeast (Machella, 1942; Machella and McDonald, 1943). Some, however, failed to yield to vitamin therapy of any type. The cheilosis in two of our cases did not respond to treatment with riboflavin and the vitamin B complex.

Signs and symptoms of peripheral neuritis, which are generally considered to be the result of vitamin B₁ deficiency, were present in only four cases.

Treatment

The patients were treated with supplements of vitamin B₁ 3 to 9 mg. daily, riboflavin 3 to 9 mg. daily, and nicotinic acid 100 to 500 mg. daily. The patients were also instructed to take as much meat, milk, cheese, and whole grain in their diet as possible and to take proprietary wheat-germ or yeast preparations when obtainable. American workers (Sydenstricker, 1941) have pointed out that intensive treatment with one factor of the vitamin B complex may provoke symptoms of deficiency in another factor. It is therefore advisable when giving intensive therapy with one factor to give supplements of wheat germ or yeast. All the patients except two responded to treatment. One suffered from mental retardation due to depression, and it was difficult to obtain co-operation. Three of the patients relapsed after periods of from two to five months without treatment and presumably on return to their deficient diet. Two of these responded to further treatment.

Seven selected case records are given below. They were chosen for their severity or long duration. The average age of the patients was 53, the youngest being 28. Most of them were women over 50. Photographs before and after treatment were taken of five patients, but on account of lack of space only two sets are reproduced on the Plate.

Case I

Female aged 63. Psychosis, polyneuritis, glossitis, microcytic anaemia. On March 30, 1942, she complained of depression, gradually increasing during the past four months, and for the past week had shown marked psychomotor retardation, with delusions of guilt, disease, and poverty, and impairment of memory, especially for recent events. Tongue red and dry, with flattening of papillae along lateral margins. Knee- and ankle-jerks, and vibration sense in legs, absent. Incontinence of urine on admission. Heart slightly enlarged. B.P. 170/110. Hb 64%; R.B.C. 3,500,000, and slightly microcytic. Relative lymphocytosis (37%). Blood urea and kidney function were normal.

Nicotinic acid up to 300 mg. daily, vitamin B₁ 10 mg. daily, vitamin C 50 mg. daily, and ferrous sulphate 3 gr. b.d., were given with dramatic improvement in her mental condition in the first 48 hours. While in hospital she developed mild diarrhoea (no pathogenic organisms found), which was probably due to increased bowel motility after administration of nicotinic acid and vitamin B₁. Later she developed tonsillitis, submaxillary adenitis, and an erysipeloid condition of the face. Treatment with sulphanilamide was successful.

On April 22, 1942, she was discharged feeling very well. When seen three months later she had no symptoms. There was a partial return of one knee-jerk, but ankle-jerks were still absent. Hb 80%, R.B.C. 4,750,000.

Comment.—This case presented the symptoms of an acute depression together with acute organic mental symptoms and peripheral neuritis. The history obtained from the patient and her sister revealed that she had had two previous attacks of depression, five years and one year previously. Her diet for nine months before admission did not include meat. She ate white bread. Her sister, on the same diet, remained well. It is likely that the condition was precipitated in this patient on a borderline diet by a cyclothymic depression with loss of appetite. A vicious circle was set up, the poor appetite leading to diminished intake of food and hence of the B vitamins, lack of which resulted in the onset of the deficiency symptoms—glossitis, polyneuritis, acute psychosis, and possibly anaemia.

Case II

Female aged 73 (Plate, Figs. 1 and 2). In 1936 she was treated for rheumatoid arthritis, obesity and hypertension, and varicose veins. B.P. 180/80. Breathlessness on exertion. She was given potassium bromide and iodide and sodium salicylate, and told to omit meat from her diet on account of hypertension. Her main article of food was bread-and-butter (margarine?). She had had no meat for three years. She also dieted for her obesity. Brachial neuritis was present early in 1942.

We saw her on June 15, 1942. There was then severe angular stomatitis with considerable crusting at corners of mouth. The tongue was sore, particularly on eating and swallowing, and felt as if scalded. On examination the tongue was very red and fissured (Fig. 1), the skin of the arms and neck was pigmented and coarse, and there was an erythematous rash with denudation and pruritus of the skin around the vulva and on the skin from the vulva to the knees. She was given 9 mg. of riboflavin daily.

In one week the lesions at the corners of the mouth were considerably improved and within a fortnight they had healed, but the pigmentation of the skin and the glossitis were unchanged. In addition to riboflavin 10 mg. daily, 400 mg. of nicotinic acid in divided doses and 6 mg. of vitamin B₁ were now given, and the patient was instructed to eat a full diet, including yeast and wheat-germ preparations. Within a fortnight the pigmentation over the neck, arms, vulva, and legs had almost disappeared, and the tongue no longer felt hot and as if scalded. The dosage of nicotinic acid was reduced to 250 mg. daily. After five weeks all the lesions had healed and the patient looked and felt much better. She no longer complained of breathlessness, sore tongue, or pruritus. After ten weeks' treatment the tongue was more normal in colour and many of the fissures had healed (Fig. 2). The patient was kept under observation for a total period of three months. Improvement was maintained, and at the end of this time she was discharged.

Comment.—In this case the lesions of the lips healed with riboflavin, which had no effect on the glossitis. This responded only to nicotinic acid. One very noticeable result of the treatment was the improvement in mood.

Case III

Female aged 70 (Figs. 3 to 6). Presenting complaints: depression, insomnia, memory impairment, glossitis, irritation, and rash on neck and lower extremities. Noted for six months. Before being seen by us she had been treated unsuccessfully for eczema for six months. Examination showed B.P. 185/95, a red smooth tongue, and shiny red, cracked lips. There was a scaly pigmented dermatitis on the exposed situations, particularly the neck, face, elbows, vulva, arms, thighs, and flexures (Figs. 3 and 5), with a seborrhoeic dermatitis of scalp and ears. The face was oedematous and pigmented, particularly around the eyes. The heart was enlarged, with a mitral systolic murmur; pulse 56; frequent extrasystoles, photophobia, and lacrimation. The patient had a very poor dietary history: she lived alone and had no appetite.

Sept. 16, 1942.—Treated with 400 to 500 mg. nicotinic acid, 9 mg. vitamin B₁, and 3 mg. riboflavin daily, and a yeast concentrate. Much improvement within a week. Marked improvement after 14 days.

Sept. 30.—Patient more active and less depressed. Swelling of face and eyes reduced. Pigmentation and dermatitis around neck, face, and elbows disappearing. Tongue not so red and sore. No photophobia or lacrimation.

Oct. 14.—Tongue no longer sore, and dermatitis almost disappeared, except on scalp and behind ears (Figs. 4 and 6). This was of the seborrhoeic type and unlike that on the face, neck, and arms.

Oct. 28.—Appetite better; considerable subjective improvement. Vitamin C and thyroid 1/2 gr. daily included in treatment. No dermatitis or glossitis, patient no longer depressed. Improvement maintained for a further two months with vitamin treatment, but seborrhoeic dermatitis of scalp and behind ears still persisted, although it responded later to local treatment.

Comment.—This case, which we consider to be one of mild pellagra (dermatitis, depression), was complicated by a dermatitis of seborrhoeic type, on the scalp and ears, which, unlike the dermatitis elsewhere, failed to respond to treatment with the vitamin B complex, but did so to local applications.

Case IV

Female aged 56. Presenting symptoms: insomnia, fatigue, headaches, forgetfulness, inability to settle down, and angular stomatitis. Poor appetite. Diet consisted of much bread and potatoes, no meat or cheese, and a little milk with tea. History of typhoid fever. Diagnosed in 1931 as psychasthenic. Stomatitis treated unsuccessfully for eleven years with local applications. Nervous symptoms treated with phenobarbitone, and bromide and strychnine.

Oct. 14, 1942.—First seen by us. Crusted lesions at corner of mouth (angular stomatitis). Feeling of grit in the eyes and some degree of photophobia. Coarse, greasy, seborrhoeic skin of face, particularly over nose, naso-labial folds, and chin. Sore tongue, with peppery feeling when eating or sucking. Denudation of skin of lower lip. Tongue very red, clean, raw, and swollen. Mild degree of anaemia (Hb 88%, R.B.C. 4,790,000). Treated with riboflavin 3 mg. t.d.s., nicotinic acid 300 to 400 mg. daily, vitamin B₁ 3 mg. t.d.s., and wheat germ.

Oct. 28.—Mouth lesions and sore tongue considerably improved. Photophobia and gritty feeling in eyes gone. Diet improved.

Nov. 11.—Improvement maintained; eating well, facial skin not so greasy and coarse. Angular stomatitis gone. Dosage of vitamins reduced to riboflavin 2 mg. t.d.s., nicotinic acid 300 mg. daily, and vitamin B₁ 3 mg. b.d.

Dec. 9.—Tongue no longer sore. Appetite good. Much improved mentally. Sleeping well. Tiredness and headaches gone.

Comment.—The “psychoneurotic” symptoms, seborrhoea, glossitis, and angular stomatitis had been present for 11 years and resisted general treatment. After two months’ treatment with vitamin B complex and improvement of the diet local and mental symptoms disappeared.

Case V

Female aged 63. In 1938 diagnosis of glossitis, psychoneurosis, and hypertension made. Poor appetite, indigestion, pallor, dry skin, scanty hair, oedema of feet. B.P. 230/115. Once a patient in a mental hospital. Treated with bromide, valerian, and thyroid. The glossitis subsequently treated with chromic acid, zinc sulphate lotion, and finally vaseline, without success. Diagnosis of chronic streptococcal tongue made by clinician of another hospital.

Seen by us on Nov. 2, 1942. Angular stomatitis present. Tongue very red, raw, and atrophic. Lips smooth, very red, and denuded of epithelium. Scaly pellagroid dermatitis on face. Questioning revealed poor dietary history. The patient ate only little meat and milk. Did not cook for herself. R.B.C. 5,000,000; Hb 78%. Treatment with riboflavin 5 mg. t.d.s., vitamin B₁ 3 mg. t.d.s., and nicotinic acid 400 mg. daily; advised to improve diet. A week later the tongue and lips were not sore and inflamed. After another 14 days the facial dermatitis had gone and the angular stomatitis had almost disappeared. Although the tongue had improved subjectively, it was still red and fissured. Dosage of vitamins reduced. On Dec. 9 there were no signs of angular stomatitis, and the mouth and tongue were no longer sore and dry. The tongue was less fissured and more normal in colour.

By June 7, 1943, after five months without treatment owing to inability to attend the hospital, the patient had relapsed and her symptoms were as bad as ever. On June 21, after 14 days’ treatment as described above, her condition had improved considerably.

Comment.—This was the first improvement in the mouth and lips for four years. The patient had also improved mentally; she was less tired and more cheerful. On stopping treatment with the vitamin B complex for five months the soreness of the tongue and mouth returned. This responded to treatment again.

Case VI

Female aged 70, seen by us on Dec. 30, 1942. She was anxious and depressed, had had pins-and-needles in hands and feet for five months, and dyspepsia. B.P. 165/85. Examination showed a flat, smooth, swollen, very red tongue denuded of papillae, cracks at corners of mouth with crusting, vertical fissuring of lips, and

pale mucous membranes. Noted for six months. No meat, eggs, cheese, and only a little milk in diet. Much bread and potatoes. R.B.C. 3,760,000; Hb 78%.

Treated with ferrous sulphate, riboflavin 6 mg. daily, nicotinic acid 200 mg. daily, and vitamin B₁ 9 mg. daily, with instructions to eat a full mixed diet, including wheat germ and yeast. Angular stomatitis healed in two weeks, and tongue nearly normal in colour. No dyspepsia; eating better, and no depression. After a month’s treatment anxiety had gone; the patient was eating much better and looking better. Mouth and tongue lesions had disappeared, although the tongue still appeared smooth and flat. Papillae of tongue reappeared after five months’ treatment. Paraesthesiae disappeared. Relapsed after two months without treatment. Admitted as an in-patient to a general hospital suffering from psychotic depression and delusions. Discharged well after four weeks’ treatment.

Case VII

Female aged 56, nurse from a South Coast hospital, seen May 6, 1943. Complained of sore fissured tongue with peppery feeling of one year’s duration, depression, dry cough, dyspnoea on exertion, difficulty in maintaining balance. Not previously “nervous”; went through air raids as night sister. Very poor dietary history—denatured cereals, white bread, and no meat. On examination tongue very red and deeply fissured; upper lip cracked at mucocutaneous margins; no Rombergism, but marked diminution of vibration sense in both legs. B.P. 150/100; moist sounds on inspiration at bases of both lungs; hypochromic anaemia. No dermatitis, subcutaneous oedema, or demonstrable cardiac abnormality. Unwilling to enter hospital or to co-operate in further investigations. Treatment as in former cases with riboflavin, nicotinic acid, vitamin B₁, and in addition ferrous sulphate for anaemia. On May 20 she was much less depressed, the tongue was a dull red and no longer sore, and there was no ataxia. By July 1 objective signs had disappeared except for residual fissures on the tongue. The patient remained at work during treatment.

Summary

Seventeen cases of a deficiency of the vitamin B complex, associated with oral lesions and mental symptoms, are reported. One was an acute psychosis, and a few had polyneuritis.

Although in most of these cases the condition appears to have been determined to some extent by the wartime marginal diet, it was actually precipitated only when mental or physical factors led to loss of appetite or impaired absorption. These factors included adherence to special diets (e.g., for peptic ulcer, obesity, and hypertension) and conditions interfering with the absorption of food (vomiting and gastro-intestinal diseases).

The striking features were the regular occurrence of the oral lesions, which were attributed to nicotinic acid and riboflavin deficiency, and the invariable presence of symptoms usually regarded as psychoneurotic, but which cleared up with vitamin B therapy without alteration of the environment or special psychological treatment.

A parallelism is drawn between some of the manifestations of the psychoneurotic syndromes and those of a deficiency of the factors of the vitamin B complex.

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B. Rao and C. V. Natarajan (*Ind. med. Gaz.*, 1943, **78**, 297) record an outbreak of smallpox in the Kolar Gold Fields in the late autumn and winter of 1942. The case mortality was high, being 33%. All the patients were given sulphanilamide by mouth without any effect on the course of the disease or the mortality.

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FIG. 1.—Case II, before treatment. Showing angular stomatitis and red, sore, fissured tongue.

FIG. 3.—Case III, before treatment. Showing scaly pellagroid dermatitis of back of neck.

FIG. 4.—Case III, after several weeks' treatment with vitamin B complex. Dermatitis and roughening of skin largely disappeared.

FIG. 2.—Case II, after treatment with vitamin B complex. The angular stomatitis disappeared in 14 days and the glossitis after 28 days.

FIG. 5.—Case III, before treatment. Showing oedema and pigmentation of tissues around eyes, scaly reddish-brown dermatitis on face and neck, and red sore lips. Patient crying and very depressed.

FIG. 6.—Case III, after several weeks' treatment with vitamin B complex. Dermatitis has disappeared from face and neck. Swelling round eyes has gone. Great improvement in mood: no longer anxious and depressed.