A NOTE ON THE EFFECTIVENESS OF VITAMIN B₁₂ IN THE TREATMENT OF TROPICAL SPRUE IN RELAPSE

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A SHORT time ago, vitamin B₁₂ was isolated⁴⁻⁶ and shown to have a profound effect on blood regeneration in persons with pernicious anemia, nutritional macrocytic anemia, tropical sprue and nontropical sprue.⁶⁻⁹ It also was found to be beneficial in relieving the acute and subacute combined degeneration of the spinal cord which so often is associated with pernicious anemia.¹⁰⁻¹³ However, until very recently the amounts of vitamin B₁₂ available have been so small that investigators have not had sufficient amounts to treat patients fully. We decided to use part of our small supply of this material to make an intensive study of 3 patients with tropical sprue and to treat them over a considerable period of time, the thought being that it would probably take much larger amounts of vitamin B₁₂ to produce full remission than might be apparent from the dramatic hemopoietic response produced by minute doses. These 3 patients, studied in the hospital under controlled conditions, indicate that such is the case. The three following case histories of these patients illustrate their clinical and hemopoietic response to vitamin B₁₂ administered at fairly frequent intervals over a period of from 138 to 160 days.

These patients were selected for study by the following criteria: (1) The patient must have macrocytic anemia as determined by Wintrobe indices. (2) The bone marrow must show the typical megaloblastic type of maturation arrest seen in macrocytic deficiency anemias. (3) The erythrocyte counts must be below 2.5 million. (4) The patient must be untreated, or must not have been treated recently enough to interfere in any way with the evaluation of vitamin B₁₂ as a therapeutic agent. (5) He must have persistently low reticulocyte counts during the preliminary period of observation. (6) He must have alimentary tract symptoms consistent with the diagnosis of tropical sprue.

Pipets certified by the United States Bureau of Standards were used for the red cell counts. The hemoglobin content was determined by means of the Photovolt photoelectric hemoglobinometer, calibrated so that 14.5 grams was equivalent to 100 per cent. The reticulocytes were counted in dry preparations of brilliant cresyl blue counterstained with Wright’s stain. Platelets were enumerated in the counting chamber used for red blood cells by means of a fresh solution of sodium citrate.

Sternal bone marrow was obtained by aspiration prior to treatment and again near the peak of reticulocytosis.

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Gastric analyses were performed in each case.

On admission the patients were given the "preliminary" sprue diet previously described and were maintained on this diet throughout the period of study. After the baseline studies were completed, the three patients selected were treated with vitamin B12 at intervals of from 138 to 160 days.

Case 1. D.G., a 28 year old Puerto Rican woman was admitted to the hospital in May 1948, complaining of loss of appetite, soreness of the tongue and diarrhea characterized by frequent, light-colored, foamy stools.

Family history and past history: Irrelevant.

Present illness: The patient was in good health until after the birth of a normal child, four years prior to her admission. At this time she lost her appetite, had occasional nausea and vomiting and developed diarrhea consisting of from six to eight soft, bulky, foamy, foul-smelling, light yellow stools daily. During the following eight months she grew progressively weaker and lost 17 pounds in weight. At the end of this time she came to the Out-Patient Department of the hospital where a diagnosis of tropical sprue was made. She was given 8 cc. of crude liver extract three times a week. Following this therapy she improved only slightly and then, very slowly. She became discouraged and stopped coming for treatment. By April 1948 she again developed loss of appetite, soreness of the tongue and severe foamy diarrhea. Within a month she was so weak she came to the hospital and was admitted for treatment.

Physical examination showed a poorly-developed, undernourished young woman who was obviously and chronically ill. The mucous membranes were very pale. The tongue was smooth and red, especially at the tip and edges.

Gastric analysis showed free hydrochloric acid in the gastric contents. The initial blood values were:

- red blood cells 2.41 million; hemoglobin 7.6 grams (48 per cent); reticulocytes 1.0 per cent as can be seen in figure 1. She was given a total of 210 micrograms of vitamin B12 in nine injections in a period of 147 days. Fifteen days after the last injection her blood values were: red blood cells 4.12 million; hemoglobin 10.1 grams (71 per cent); reticulocytes 0.8 per cent. The details of the hematologic response are shown in figure 1.

- There was gradual clinical improvement. The soreness of the tongue and the diarrhea disappeared. When she was discharged after 166 days in the hospital she had gained 17½ pounds in weight and felt able to work.

Case 2. E.R., a 54 year old Puerto Rican woman was admitted to the hospital in May 1948, complaining of progressive weakness, burning and soreness of the tongue and numbness of the extremities.

Family history and past history: Irrelevant.

Present illness: Four years prior to this admission to the hospital, her illness began insidiously with general debility and difficulty in walking. One and a half years later she developed soreness of the tongue and diarrhea consisting of liquid, foamy stools, light yellow in color. Following treatment with liver extract the diarrhea improved, the burning of her tongue disappeared and she gained in strength. She continued liver therapy for six months, then, for economic reasons, discontinued it. A few months later she again developed general debility and numbness of the legs, but no diarrhea. She was admitted to the hospital where a diagnosis of sprue was made. Following treatment with liver extract she improved clinically and hematologically and was discharged from the hospital forty-five days after admission. She failed to return for further treatment and one year later she was admitted to the hospital again, complaining of progressive weakness, soreness of the tongue and numbness of the lower extremities, but no diarrhea.

Physical examination showed a pale woman in no acute distress but obviously weak and chronically ill. The skin and mucous membranes were pale. The sclera had a slight icteric tint. The tongue was red at the tip and edges. The vibratory sense was intact.

Gastric analyses showed free hydrochloric acid in the gastric juice. Her initial blood values were:

- red blood cells 1.59 million; hemoglobin 5.0 grams (32 per cent); reticulocytes 0.2 per cent, as can be seen in figure 2. She was given a total of 205 micrograms of vitamin B12 in nine injections in a period of 160 days. Twelve days after the last injection her blood values were: red blood cells 4.11 million; hemoglobin...
FIG. 1.—Hemopoietic response of D. G., a patient with tropical sprue, to vitamin B$_{12}$.
Fig. 1.—Hemopoietic response of E. R., a patient with tropical sprue, to vitamin B₁₂.
Fig. 3.—Hemopoietic response of J. G., a patient with tropical sprue, to vitamin B$_{12}$
11.1 grams (71 per cent); reticulocytes 1.8 per cent. The details of her hematologic response can be seen in figure 2.

She had a striking clinical improvement and was discharged from the hospital 185 days after admission. Since then, she has been seen several times and is doing her work and has remained well. Some numbness of both legs persists. The vibratory sense remained intact.

Case 3. J.G., a 73 year old Puerto Rican woman was admitted to the hospital in June 1948, complaining of foamy diarrhea, burning of the tongue and general weakness.

Family history: One sister died, probably of sprue or pernicious anemia. Past history: Irrelevant.

Present illness: She was well until six months prior to her admission when she lost her appetite, developed foamy diarrhea and soreness of the tongue. She rapidly lost strength and during the six months she was ill, lost 68 pounds in weight.

Physical examination showed a very ill pale woman. She had atrophic glossitis. The abdomen was flatulent and distended.

Gastric analysis showed free hydrochloric acid in the gastric juice. Her initial blood values were: red blood cells 1.49 million; hemoglobin 3.5 grams (35 per cent); reticulocytes 0.2 per cent, as can be seen in figure 3. She was given a total of 200 micrograms of vitamin B12 in eight injections in a period of 138 days. There was definite improvement in her stools. Twenty-four days after the last injection her blood values were: red blood cells 3.89 million; hemoglobin 5.6 grams (75 per cent); reticulocytes 1.1 per cent. The details of her hematologic response can be seen in figure 3.

COMMENT

The three patients with tropical sprue reported were repeatedly given injections of crystalline vitamin B12 intramuscularly. Case 1 was given a total of 210 micrograms in nine injections ranging in amounts from 10 to 25 micrograms in a period of 147 days. Case 2 received a total of 205 micrograms in nine injections ranging in amounts from 10 to 25 micrograms in a period of 160 days. Case 3 was given a total of 200 micrograms in eight 25 microgram injections in a period of 138 days. In each case there was little or no detectable change for the first three or four days; then, when the reticulocytes began to rise in the peripheral blood on the fourth or fifth day, the patients began to feel better. Following the reticulocyte peak which occurred from the sixth to the ninth day the red blood cells and hemoglobin gradually increased. In each case there was gradual gain in strength, and in patients 1 and 2 who had diarrhea there was some improvement in their alimentary tract function although the stools did not become entirely normal.

No final conclusions as to dosage and intervals between injections can yet be made but no therapeutic agent thus far used in the treatment of tropical sprue has been so effective per unit of weight as vitamin B12.

SUMMARY

Three cases of tropical sprue were treated with repeated injections of vitamin B12 and showed dramatic and sustained therapeutic responses.

REFERENCES

VITAMIN B12 IN TREATMENT OF TROPICAL SPRUE IN RELAPSE

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