THE ROLE OF VITAMIN B_{12} IN INCREASING THE NUTRITIVE EFFECTIVENESS OF PARENTERALLY ADMINISTERED PROTEIN HYDROLYSATE IN SURGICAL TRAUMA

V. V. L'vova and Corresponding Member AMN SSR
Professor N. A. Federov

Laboratory of Pathophysiology (Head–Corresponding Member AMN SSR Professor N. A. Federov) Central Order of Lenin Institute of Hematology and Blood Transfusion, Ministry of Health SSSR (Director–Active Member AMN SSR A. A. Bagdasarov), Moscow
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 52, No. 12, pp. 23-28, December, 1961
Original article submitted December 31, 1960

A problem which is important both theoretically and practically is to increase the effectiveness of parenteral protein nutrition of patients suffering from surgical trauma. Numerous investigators [8, 11, 14, 17 and others] have attempted, without success, to achieve nitrogen balance during the post-operational period by increasing the caloric value and the nitrogen content of the food. There are a number of difficulties associated with increasing the nitrogen content of the solutions used for parenteral feeding. In clinical practice, we are therefore compelled to find other methods of increasing the effectiveness of parenteral protein nutrition under conditions of surgical trauma. For this purpose we have used vitamin B_{12}.

It has been shown that vitamin B_{12} increases animal growth, but it is still not clear what brings about this favorable effect. Some workers consider that vitamin B_{12} plays some part in the synthesis of proteins and of the nucleic acids. Charkey and co-workers [6] have shown that in chicks, vitamin B_{12} reduces the concentration of amino acids which are used in the formation of the proteins of various tissues. On the other hand, Meites [13], Rupp and others [15, 16] have produced evidence that the increased growth of animals fed with unrestricted amounts of food to which vitamin B_{12} has been added is a result of their increased appetite, and is not due to any change in the utilization or metabolism of the food. Certain authors [5, 7, 12] have shown that vitamin B_{12} influences protein metabolism only indirectly, by increasing carbohydrate and fat metabolism.

We have set ourselves the problem of studying experimentally, under conditions of surgical trauma, the action of vitamin B_{12} in increasing the assimilation of intravenously injected nitrogenous substances.

METHOD

The experiments were carried out on dogs on which a partial resection of the gastric fundus had been performed. Before operation, the animals were kept for 7-9 days on a protein-free diet, in order to bring the protein metabolism to a certain definite level. During this period, each dog received daily 150 g of sugar, 50 g of plum oil, 145 g of starch, vitamins A, B_1, B_2, C, D, and nicotinic acid, 1 g of brewers' yeast, and 5 g of a saline mixture, containing all the necessary cations and anions. From the first day after operation onwards, and for the next 7-13 days, the animals were maintained almost exclusively by parenteral feeding with a protein hydrolysate prepared by the Central Order of Lenin Institute of Hematology and Blood Transfusion, to which 120 ml of a 40% solution of glucose containing vitamins B_1 and C had been added directly before administration. Each dog received daily 400-500 ml of the hydrolysate, which corresponded to 0.2-0.3 g of nitrogen (1.25-1.80 g protein) per kg weight. During this period, each dog received by mouth nothing but 100 g of glucose, water, and vitamins A, B_1, B_2, C, D, and nicotinic acid; this diet ensured the necessary minimal supply of vitamins, and the constancy of the calorie intake. At the end of the period of parenteral protein nutrition, the animals were once more put back on a protein-free diet. Unoperated animals kept under the same conditions were used as controls. Altogether, we performed 13 experiments on 13 dogs.

In each experiment we studied protein metabolism in terms of the following quantities: nitrogen balance, the nitrogen fractions (nitrogen of urea, ammonium, and amino acids) of the daily urine, and the changes in the concentration and total of circulating serum proteins, the volume of the circulating plasma, the hemoglobin index, and the weight of the animals. The total nitrogen in the urine was determined by the micro-method of Kjeldahl and Conway, and the nitrogen present as urea and ammonium was determined by Krebs' method, by use of the enzyme urease; the concentration of serum proteins was determined by an immersion reflectometer, and the total circulating plasma was measured by Evans' dye method (dye T-18-24).

RESULTS

In the post-operational period, when the dogs received the protein hydrolysate parenterally, for 7 days we not only failed to attain a positive nitrogen balance, but could not even avoid a nitrogen loss, on average, of 2.6-3 g per day. In these experiments, the great increase in the total amount of nitrogen excreted with the urine should be noted; it was three times greater then the amount before operation (Fig. 1, see table, experiments Nos. 1 and 2).

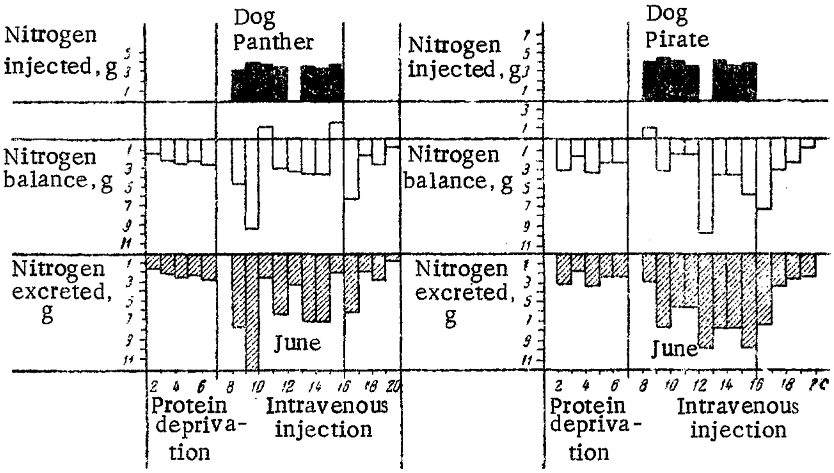

Fig. 1. Parenteral feedings of dogs, after operation, with hydrolysate. Abscissa—days of the experiment, ordinate—amount of nitrogen (in g). Lowermost columns—amount of nitrogen (in g) excreted per 24 hours in the urine; uppermost black columns—amount of nitrogen given daily; middle columns, running down from the abscissa—negative nitrogen balance, columns running upwards—positive nitrogen balance (in g). Vertical lines separate the pre-operational period, the period of parenteral nutrition, and the subsequent period.

In control animals, which were kept under the same conditions, but on which no operation was performed, from the first day of injection of the hydrolysate and until the last day, there was no nitrogen loss, and there might be even a small positive nitrogen balance (experiments Nos. 3 and 4, Fig. 2, dog Damka). Therefore, the increased excretion of nitrogen with the urine and the large negative nitrogen balance in the post-operational period, during which parenteral feeding with protein hydrolysate was carried out, are directly due to the specific influence of surgical trauma on protein metabolism.

To increase the effectiveness of the parenteral feeding with protein hydrolysate during the post-operational period, we gave each dog a daily intramuscular injection of 20 μg of vitamin B_{12} for the whole period of parenteral feeding. Then, in contrast to the previous experiments the extent of the nitrogen balance was greatly reduced, equilibrium was nearly attained, and on some days there was a net gain of nitrogen (Fig. 3). On average, in these animals, the nitrogen balance was only $-0.5 + 0.02$ g per day, instead of -2.6-3 g of nitrogen in dogs which had not received vitamin B_{12} (experiments Nos. 5-9).

The dog Milka did not receive a vitamin B_{12} injection every day; on days when it was injected, the negative nitrogen balance was appreciably reduced, and thereby this balance over the period as a whole was also lowered (Fig. 4).

These experiments demonstrate convincingly the positive role of vitamin B_{12} in increasing the assimilation of intravenously injected protein hydrolysate.

We have demonstrated the effectiveness of vitamin B_{12} only during the period of altered protein metabolism following surgical operation; in the control experiments (without operation) vitamin B_{12} had caused no appreciable increase in the nitrogen balance. Therefore, vitamin B_{12} reduces disturbed protein metabolism, but under normal conditions it has no appreciable effect (experiments Nos. 3, 4, 10, and 11; see Fig. 2, dog Malysh). There are also

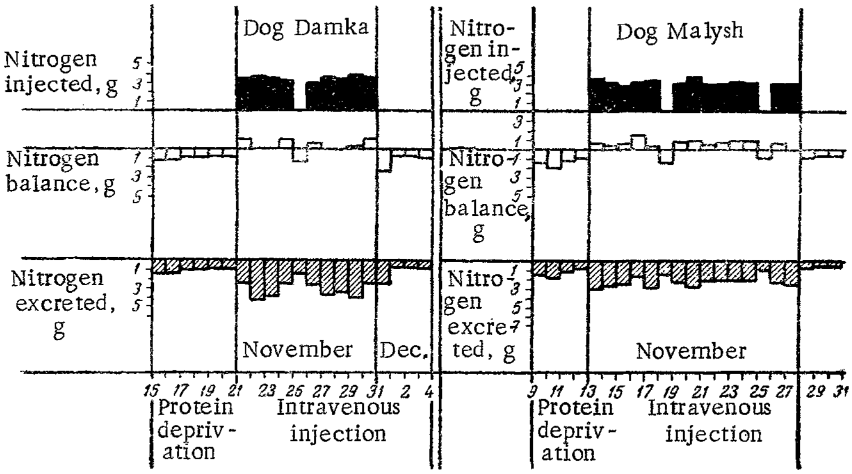

Fig. 2. Parenteral feeding of unoperated dogs. No food taken by mouth. Indications as in Fig. 1, except that the vertical line separates the period of protein starvation from the next in which feeding by mouth was stopped, and intravenous injection of hydrolysate started.

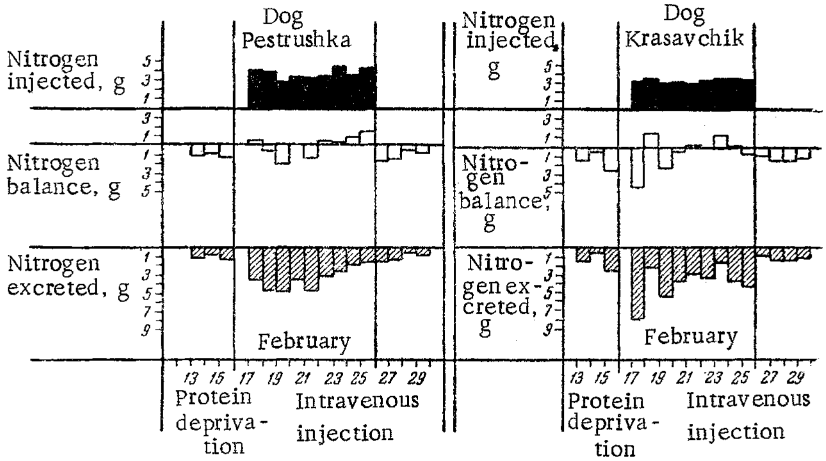

Fig. 3. The influence of vitamin B_{12} on nitrogen balance in dogs during parenteral feeding with hydrolysate. Indications as in Fig. 1.

reports [15, 16] on the specific effect of vitamin B_{12}, particularly in reducing the nitrogen loss caused by thyrotoxin, though it does not reduce the nitrogen loss induced by cortisone.

We must now inquire into the mechanism of the increased assimilation of the protein hydrolysate under the influence of B_{12} during the post-operational period. The first possibility is that vitamin B_{12} eliminates the conditions which in the operated animals bring about a breakdown of the animals' own proteins. To test this hypothesis, we carried out experiments in which vitamin B_{12} was injected after operation into dogs together with a physiological glucose solution, i. e. when there was no parenteral protein administration. The results showed that under these conditions, vitamin B_{12} did not reduce the extent of the nitrogen balance (see table, experiments Nos. 12 and 13). Therefore, vitamin B_{12} increases the uptake of injected protein hydrolysate given when protein metabolism is disturbed, but does not reduce the breakdown of tissue proteins.

Influence of Vitamin B_{12} on the Increased Effectiveness of Parenteral Protein Nutrition Given to Dogs After Operation

No. Expt.	Name of dog	Preparation	Per day				Per kg weight				Note
			nitrogen excreted (in g)		nitrogen injected	nitrogen balance	nitrogen excreted (in g)		nitrogen injected	nitrogen balance	
			before p.f.*	during period of p.f.	(in g)		before p.f.	during p.f.	(in g)		
1	Panther	Hydrolysate	2.315	6.687	3.595	-3.092	0.114	0.375	0.203	-0.172	After operation
2	Pirate	The same	2.485	6.695	4.12	-2.574	0.122	0.358	0.221	-0.137	The same
3	Damka	The same	1.160	3.322	3.713	+0.391	0.071	0.212	0.237	+0.025	No operation
4	Ruslan	The same	2.175	3.980	3.608	-0.372	0.148	0.284	0.257	-0.027	The same
5	Milka	Hydrolysate+B_{12}	4.624	3.970	2.973	-0.997	0.265	0.228	0.171	-0.057	After operation, B_{12} not given every day
6	Al'va	The same	1.493	4.034	3.435	-0.599	0.111	0.323	0.275	-0.048	After operation
7	Krasavchik	The same	1.567	3.931	3.409	-0.522	0.105	0.296	0.257	-0.039	The same
8	Pestrushka	The same	1.099	3.372	3.391	+0.020	0.087	0.294	0.296	+0.002	The same
9	Krasotka	The same	2.763	3.553	3.021	-0.532	0.176	0.268	0.228	-0.040	The same
10	Malysh	The same	1.468	2.601	3.414	+0.813	0.113	0.215	0.282	+0.067	No operation
11	Tobik	The same	2.656	3.984	3.595	-0.389	0.155	0.247	0.223	-0.024	The same
12	Seryi	Physiological saline + B_{12}	2.045	2.534	-	-2.534	0.115	0.153	-	-0.153	After operation
13	Druzhok	The same	2.590	2.942	-	-2.942	0.102	0.125	-	-0.125	The same

*p. f. = parenteral feeding

A possible mechanism whereby the assimilation of the nitrogenous ingredients of the protein hydrolysate might be increased is through the action of B_{12} in synthesizing methyl groups.

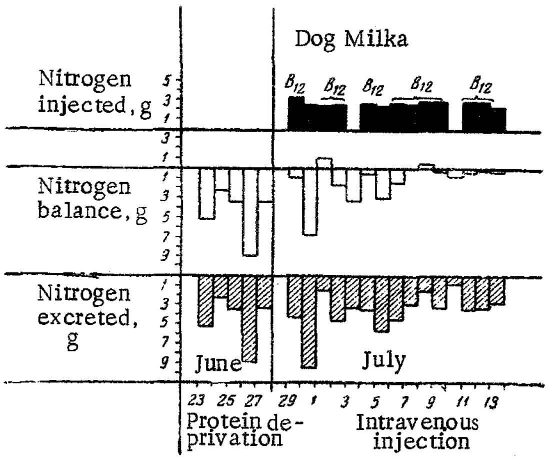

Fig. 4. Influence of vitamin B_{12} on the nitrogen balance in the dog Milka after operation, during parenteral nutrition with hydrolysate and the injection of vitamin B_{12} on certain days (not every day). Indications as in Fig. 1.

SUMMARY

Increased breakdown of tissue proteins was observed to follow an operation on the gastrointestinal tract. It was not eliminated by parenteral feeding with protein hydrolysates. A daily intramuscular injection of 20 μg of vitamin B_{12} into dogs, under these conditions, restored the nitrogen balance, and on some days there was a net gain of nitrogen assimilated. The increased effectiveness of parenteral protein hydrolysate caused by vitamin B_{12} was connected with the increased assimilation of the protein ingredients administered, and not with any reduction of protein breakdown.

LITERATURE CITED

1. V. V. L'vova and N. A. Fedorov, Abstracts of Reports of the 37th Plenum of the Academic Council of the Central Institute of Hematology and Blood Transfusion [in Russian] (Moscow, 1958) p. 20.
2. N. A. Fedorov and V. V. L'vova, Arkh. pat., No. 3 (1954) p. 54.
3. N. A. Federov and V. V. L'vova, In book: Modern Problems of Hematology and Blood Transfusion [in Russian], Vol. 34 (Moscow, 1959) p. 59.
4. N. A. Federov and V. V. L'vova, Abstracts of Reports of the 39th Plenum of the Academic Council of the Central Institute of Hematology and Blood Transfusion [in Russian] (Moscow, 1960) p. 5.
5. A. Black and J. W. Brutzler, J. Nutr., Vol. 47 (1952) p. 159.
6. L. W. Charkey, H. S. Wilgus, A. R. Patton et al., Proc. Soc. Exp. Biol., Vol. 73 (N. Y., 1950) p. 21.
7. B. F. Chow and L. Barrows, Fed. Proc., Vol. 9 (1950) p. 354.
8. R. Elman, J. Am. Diet. Ass., Vol. 32 (1956) p. 524.
9. A. M. Hartman, L. P. Dryden and C. A. Cary, Arch. Biochem., Vol. 23 (1949) p. 165.
10. E. L. Hove and J. O. Hardin, Proc. Soc. Exp. Biol., Vol. 77 (N. Y., 1951) p. 502.
11. T. B. Van Itallie , F. D. Moore, R. P. Geyer et al., Surgery, Vol. 36 (1954) p. 720.
12. L. K. Knoebel and A. Black, J. Nutr., Vol. 48 (1952) p. 477.
13. J. Meites, Proc. Soc. Exp. Biol., Vol. 75 (1950) p. 195.
14. C. O. Rice and J. H. Strickler, Med. Tms. Vol. 81 (London, 1953) p. 307.
15. J. Rupp, K. E. Paschkis and A. Cantarow, Proc. Soc. Exp. Biol., Vol. 76 (1951) p. 432.
16. J. Rupp and K. E. Paschkis, Ibid., Vol. 82 (1953) p. 65.
17. S. C. Werner, D. V. Habif, H. T. Randall, et al., Ann. Surg., Vol. 130 (1949) p. 688.