INTRAVENOUS *TREATMENT OF PERNICIOUS ANEMIA WITH* VITAMIN B_{12}

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NUMEROUS observers have reported successful hematologic and clinical remissions in pernicious anemia in relapse following intramuscular injections of vitamin B_{12}, and the oral administration of this vitamin alone, or with normal gastric juice, extracts of hog duodenal mucosa, or folic acid. The only report bearing on intravenous therapy is by Gardner *et al.*[1] who administered beef muscle extract showing vitamin B_{12} activity (equivalent to 0.35 to 9.0 μg.) intravenously for 10 days and noted a hematologic effect which was less than that observed after the daily intramuscular injection of 1.0 μg. of crystalline vitamin B_{12}.

The present study was undertaken to study the effect of daily intravenous injections of crystalline vitamin B_{12} to 5 patients with pernicious anemia in relapse. Four of them received 1.0 μg. daily for 13 to 33 days. Two of the patients were subsequently treated with 7.0 μg. intravenously, weekly, for 28 to 63 days. The fifth case was treated with 0.5 μg. daily for 26 days. Prior to treatment each of the patients showed hyperchromic macrocytic anemia, histamine-fast achlorhydria, and megaloblastic bone marrow. Roentgen examinations of the gastrointestinal tract, urinalyses, and blood chemistry determinations disclosed no abnormalities. Hemoglobin and erythrocyte determinations were made three times a week, leukocyte counts once a week, and reticulocyte counts daily. Maximal reticulocyte peaks and anticipated red blood cell levels at 15 days were calculated from the formulae of Isaacs and Friedman[2] and Ungley,[3] respectively. None of the patients showed evidence of chronic pulmonary or heart disease.

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RESULTS

All of the patients showed a satisfactory clinical response as evidenced by increase in appetite, sense of well-being, and strength. No untoward reactions were experienced following injections. In case A. S., bronchopneumonia developed during the second week of therapy, for which he was treated with penicillin intramuscularly. This episode may account for the suboptimal reticulocyte peak and slightly lower erythrocyte level at 15 days. More patients will have to be treated with 0.5 μg of vitamin B_{12} intravenously, daily, to compare the results with those obtained with the larger dose. In the group receiving 1.0 μg. daily, the reticulocyte response was suboptimal in 2 cases and reached anticipated levels in the other instances. Erythrocyte counts at the end of 15 days in all patients were higher than expected. In cases treated for 41 and 87 days, polycythemic levels of 5.80 and 5.91 million per cu. mm., respectively, were attained. Hemoglobin levels, although elevated, were slightly hypochromic, probably reflecting the rapid red blood cell regeneration.

TABLE I.

Hematologic Data on Patients with Pernicious Anemia in Relapse Treated with 1 μg. of Vitamin B_{12} Intravenously Daily

Patient	Dose B_{12}	Time	Initial Hb.	Final Hb.	Initial RBC $\times 10^6$	Final RBC $\times 10^6$	Retics. peak/day	Antic. peak retic.	Predicted RBC: Observed RBC $\times 10^6$ at 15 days	Predicted RBC: Days of observation
	μg.		Gm.	Gm.			%	%		
A. S.	0.5/day	26 days	6.0	9.0	1.38	2.65	19.7/8	30.5	2.43/2.20	26
W. S.	1.0/day	33 days	5.0	11.5	1.16	4.06	33.3/8	42.0	2.50/3.50	33
I. C.	1.0/day	33 days	7.0	14.2	1.70	4.65	27.6/6	29.0	2.99/3.38	33
J. H.	1.0/day 7.0/week	13 days 4 weeks	9.5	16.5	2.50	5.80	6.9/6	15.0	3.74/4.35	41
M. G.	1.0/day 7.0/week	24 days 9 weeks	6.2	16.0	1.46	5.91	28.6/6	28.7	2.76/5.03	87

No neurologic changes were observed prior to or following vitamin B_{12} therapy.

Discussion

Erythremic levels in pernicious anemia following treatment are rare.[4] Personal experience of one of us (LMM) with more than 300 cases of pernicious anemia treated with various agents disclosed only one instance in which the erythrocytes rose above 5.8 million per cu. mm. This patient was treated with animal protein factor and vitamin B_{12}. Previous observations demonstrated that daily intramuscular injections of 1.0 μg. of vitamin B_{12} to patients with pernicious anemia in relapse was followed by suboptimal reticulocytosis and unsatisfactory hematologic levels after 2 months of treatment.[5] In contradistinction, the present group treated with 1.0 μg of vitamin B_{12} intravenously, daily, showed a better than anticipated increase of red blood cells in all 4 cases. The failure to achieve optimal reticulocyte levels has been repeatedly observed where hematologic remissions were otherwise satisfactory.[6,7] Whether the immediate availability of vitamin B_{12} in the bloodstream results in the production of more "serum hematopoietic factor" to antagonize folinic acid inhibitor,[8] or the presence of the cobalt radical of the vitamin B_{12} induces greater erythropoiesis than by intramuscular or oral routes, is open to speculation. The mechanisms whereby cobalt increases red cell production by interference with the transport of oxygen in the erythroid cells of the bone marrow have been variously ascribed to binding of sulfhydryl groups[9] or alterations in the catalase molecule in which the cobalt atom replaces an iron atom, making the latter available for additional hemoglobin synthesis.[10] Berk and coworkers demonstrated an erythropoietic effect in patients with and without anemia following oral administration of cobalt.[11] No case of pernicious anemia in relapse was included in their series.

Conclusions

Daily intravenous administration of 0.5 or 1.0 μg. of vitamin B_{12} to 5 patients with pernicious anemia in relapse induced a satisfactory clinical remission.

Erythrocyte regeneration was satisfactory in 1 case (receiving 0.5 μg. per day) and greater than anticipated in 4 cases (receiving 1.0 μg. per day).

Erythremic levels were attained in 2 patients treated for 41 and 87 days with 1.0 μg. of vitamin B_{12} daily.

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RESUMEN

Tratamiento endovenoso de la anemia perniciosa con Vitamina B_{12}

La administración endovenosa de 0,5 u 1,0 microgramo por día de vitamina B_{12} a 5 pacientes con anemia perniciosa recidiva logró una remisión clínica satisfactoria.

La regeneración de los eritrocitos fué satisfactoria en un caso (recibiendo 0,5 microgramo por día) y mayor de lo que se había anticipado en 4 casos (recibiendo 1,0 microgramo por día).

Los niveles eritrémicos se consiguieron en 2 pacientes tratados durante períodos de 41 y 87 días con 1,0 microgramo por día de vitamina B_{12}.