Intravenous Treatment of Pernicious Anemia with Citrovorum Factor (Leucovorum).*† (18994)

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There is ample evidence that the intramuscular administration of citrovorum factor (CF) will induce hematologic and clinical remissions in patients with pernicious anemia, nutritional macrocytic anemia and sprue(1-4). The present study was undertaken to determine whether the intravenous injection of this vitamin would induce similar results. Two patients with typical Addisonian pernicious anemia in relapse were treated with 3.0 mg of CF intravenously, daily, for 41 and 78 days, respectively. Each case showed hyperchromic macrocytic anemia, histamine-fast achlorhydria, and megaloblastic bone marrow. Roentgen examinations of the gastro-intestinal tract, urinalyses and blood chemistry determinations disclosed no abnormalities. Hemoglobin and red blood cell determinations were made 3 times a week, leukocyte counts once a week, and reticulocyte estimations daily.

G. F., white male, age 63, was admitted to the hospital with the chief complaints of progressive weakness, anorexia, pallor, parasthesias of arms and legs, dyspnea and precordial pain on exertion of three months' duration. The positive findings on physical examination were: evidence of recent weight loss, yellowish pallor of skin and mucous membranes, smooth tongue, apical systolic murmur, spleen palpable one cm below the left costal border and enlargement of prostate gland. Neurologic status was entirely normal. The initial hemoglobin and red blood cell values were 8.0 g per 100 ml and 2.14 million per cmm, respectively. He was given 3.0 mg of CF intravenously, daily, for 41 days. Improvement in sense of well being, appetite and strength were observed on the seventh day and continued upward during the course of treatment. A submaximal reticulocyte peak of 9.6% was noted on the ninth day of treatment. At the end of this period of observation it was found that the hemoglobin and erythrocytes had reached stationary levels of 12.0 g per 100 ml and 3.86 million per cmm, respectively. Accordingly, the route of administration was changed to the intramuscular one. This resulted in a rise of blood values to normal levels in 6 weeks (Fig. 1). The patient appeared clinically well and returned to work. No nervous system changes were observed.

I. R., white female, age 74, was a known case of pernicious anemia of four years' duration who was successfully treated with the parenteral administration of liver extract. For the past year the patient failed to attend the clinic and received no specific therapy. At the time of the present admission her symptoms were mild and were mainly those of weakness and fatiguability. Physical examination was entirely negative. Neurologic survey revealed hyperactive deep tendon reflexes and positive Babinski reaction on the right side. The initial hemoglobin and red blood cell values were 11.5 g per 100 ml and 2.84 million per cmm, respectively. She received 3.0 mg of CF intravenously, daily, for 78 days. Clinical improvement started on the eighth day with an increase in appetite and sense of well being and continued during the entire period of observation. No reticulo-

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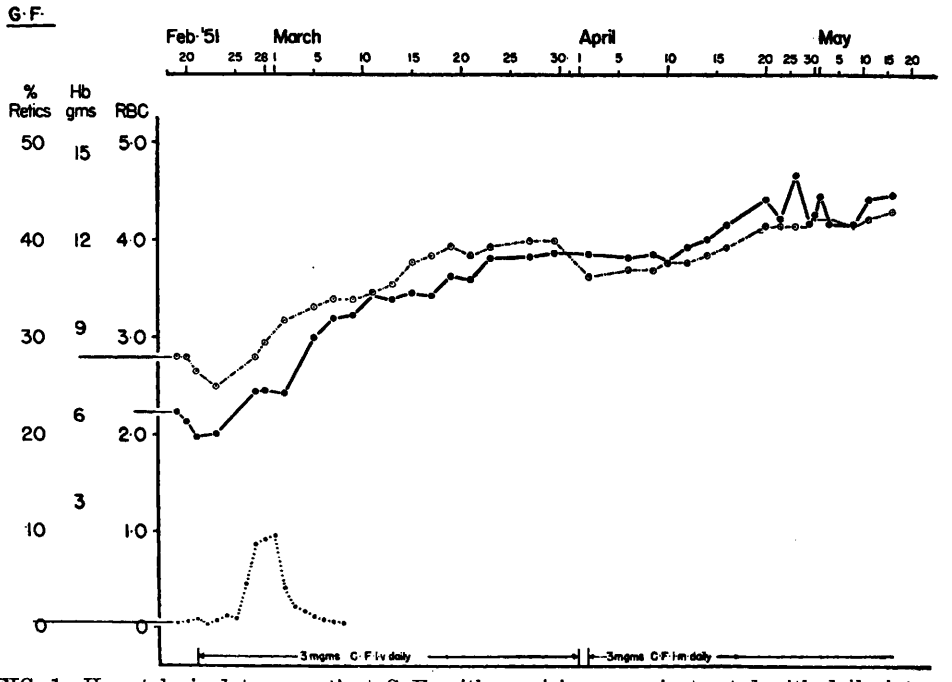

FIG. 1. Hematologic data on patient G. F. with pernicious anemia treated with daily intrav. inj. of 3 mg of CF. Reticulocyte response was submaximal and blood levels were suboptimal. Administration of same dose intramuscularly induced a normal blood count.

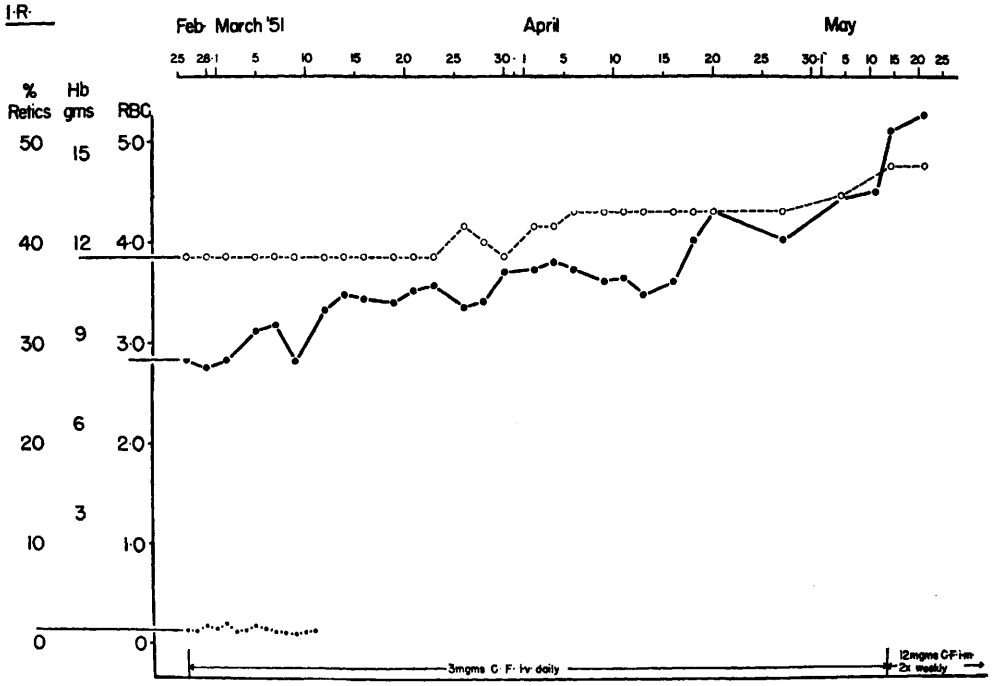

FIG. 2. Hematologic data on patient I. R. with pernicious anemia treated with daily intrav. inj. of 3 mg of CF. No reticulocyte response was observed. The hemoglobin and erythrocytes rose to normal levels in 68 days.

cyte response was noted. The blood values reached normal levels on the 68th day. Ten days later the patient was placed on 12 mg of CF intramuscularly, twice weekly. At the end of 117 days she appeared entirely well (Fig. 2). No alteration in neurologic status was noted.

Discussion. From the foregoing data it is clear that intravenously administered CF in doses of 3.0 mg a day induced clinical remissions and a moderately good to a complete hematologic response in two patients with pernicious anemia in relapse. It would appear that in one case (I. R.) the excretion rate surpassed the utilization rate because when the route of administration was changed to the intramuscular one the hemoglobin and erythrocytes rose to normal levels. There was no instance of development or progression of nervous system changes in either patient after 3 to 4 months although one of them (I. R.) showed evidence of spinal cord disease before treatment was begun. Recently we have observed rapidly developing alterations in the central nervous system after 3 months of oral treatment of a patient with pernicious anemia using 6.0 mg of CF daily(5). The present hematologic results also differ from our earlier report in that in this group normal blood counts were attained(2). The reticulocyte response was absent or submaximal in the 2 cases presented and this confirmed the observations made when patients were treated by the intramuscular route(2).

Summary. The daily intravenous administration of 3.0 mg of CF to two patients with pernicious anemia in relapse was followed by a satisfactory clinical remission, poor reticulocyte response, suboptimal hemoglobin and red blood cell levels in one case and a normal blood count in the other. The subsequent intramuscular injection of the same dose to the first patient resulted in a good hematologic remission.

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Effect of Intravenous Aureomycin on the Intestinal Flora of Dog and Man.* (18995)

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With increasing experience it is becoming evident that the toxic effects of aureomycin on the gastrointestinal tract may occur when the drug is given intravenously as well as orally(1,2). Since this may be due to excretion of the drug into the gastrointestinal tract, its administration parenterally may exert an antibacterial effect on intestinal flora. This report deals with a study of effects of intravenous aureomycin on the normal intestinal flora of dog and man.

Effect of aureomycin on intestinal flora of dogs. Method. Sixteen healthy mongrel dogs† received aureomycin intravenously daily for a period of 10 days. Four of them were given 1000 mg, six 600 mg, and six 400 mg, in 2 equal doses each day. The bacterial flora of the stools in all dogs was examined(3) before treatment was started, daily during the course of treatment, and for a few days thereafter.

Results. (a) 1000 mg/day. This dose proved to be toxic, as previously reported(4). Two of 4 dogs died in 3 days without any

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