

diol 1.0, androstanolone 1.7, 19-nortestosterone cyclopentylpropionate 9.5.

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Vitamin B₁₂ Serum Levels and Diabetic Retinopathy.* (21277)

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Methods for the determination of vit. B₁₂ activity in serum have been reported(1,2,3), although the measured activity may not be due to this vitamin *per se*. Recently, a modified procedure was described(4) which permits the estimation of as little as 10 micro-micrograms of activity of this crystalline vitamin. The availability of this method prompted us to compare the serum vit. B₁₂ levels of diabetics with or without retinal lesions. These findings which will be reported in this communication, should be of particular interest since we have shown earlier(5) that following an intramuscular test dose of vit. B₁₂, diabetic subjects with retinopathy excrete significantly more of the vitamin than non-diabetics; while diabetics without retinopathy excrete considerably less than non-diabetics.

Procedure. All patients used in this investigation suffered from diabetes mellitus of different degrees of severity. They were drawn from the Diabetic Clinic of The Wilmer Institute of Johns Hopkins Hospital. When the diagnosis of diabetes had been established and the absence or presence of retinopathy[†] recorded, venous blood specimens were drawn from all subjects and allowed to clot. Sera were separated by centrifugation and were kept frozen in a deep-freeze until assay. The procedure of assay will be published in detail. Samples were identified by code numbers at

Johns Hopkins Hospital and analyzed. Only after completion of the assay was the ophthalmoscopic diagnosis of the patients compared with the analytical results.

Results. Over a period of 6 months involving at least 10 different assays, blood specimens from 16 patients with retinopathy (5 males and 11 females) and from 18 patients (7 males and 11 females) were analyzed. The vit. B₁₂ activity in sera expressed as micro-micrograms per ml was plotted against age of the patients. It can be seen from the scatter-diagram (Fig. 1) that the B₁₂ levels of the 2 groups of diabetics are distinctly different. If a line were drawn parallel to the horizontal axis at the level of 200 mg/ml, it would divide the observations clearly into 2 groups, with only one exception in the non-retinopathic group and none in the retinopathic group. The mean values of serum B₁₂ levels with the standard errors of the mean are 162 ± 18 and 292 ± 24 $\mu\mu\text{g/ml}$ for the non-retinopathic and retinopathic groups, respectively. The difference in the serum levels is statistically significant with $P < 0.001$.

Although the role of vit. B₁₂ in metabolism

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[†] All diabetic patients were examined with a giant ophthalmoscope following mydriasis. Those cases were included in which the fundi could be well visualized and in which no ocular disease was present. Only the eyes with no evidence whatsoever of capillary aneurysms, exudates, or hemorrhages were classified as nonretinopathic.

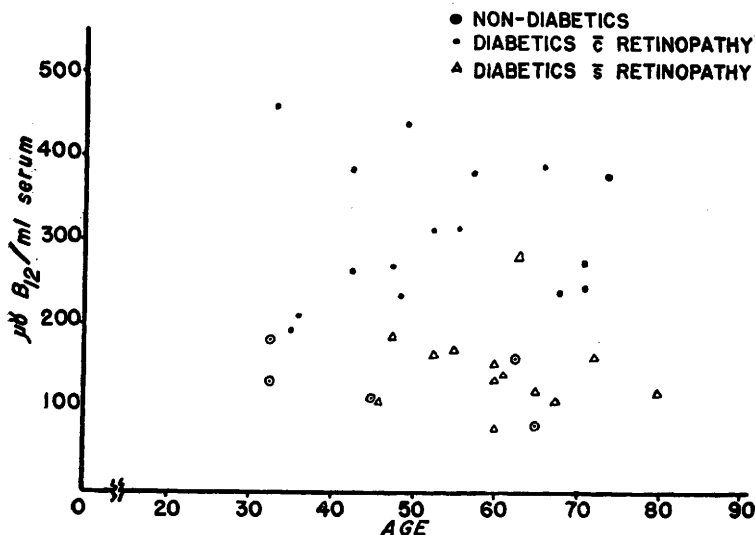


FIG. 1. Vitamin B₁₂ levels in sera of diabetics with and without retinopathy.

is still not fully understood, there is a steady increase in evidence to substantiate our original hypothesis that this micro-nutrient plays an important role, directly or indirectly in carbohydrate metabolism. The data presented in this paper, coupled with those previously reported(5), make it clear that diabetics who have developed retinopathy handle vit. B₁₂ somewhat differently from those who have not developed this complication. On the one hand, subjects with retinal lesions are unable to retain a normal portion of a parenteral test dose of vit. B₁₂, and on the other these same subjects have higher levels of this vitamin in the peripheral blood. The differences between these two groups of diabetics are so distinct that it is impossible to escape the conclusion that vit. B₁₂ is somehow fundamentally involved in the pathogenesis of the retinopathy.

The possible role of vit. B₁₂ in the correction of hyperglycemia is likewise indicated from the reports of Ling(6) in which it was found that the hyperglycemia produced following the administration of a load test of glucose to B₁₂ deficient animals can be corrected by the injection of vit. B₁₂. Preliminary data from our laboratory likewise indicated that the hyperglycemia and glycosuria induced in animals by the prolonged injection of either ACTH or cortisone, or in man by the administration of cortisone alone can be corrected by the parenteral administration of vit. B₁₂. These data

taken together with findings presented in this communication make it tempting to postulate that the administration of an admixture of vit. B₁₂ with insulin, cortisone, or ACTH might offer certain clinical advantages over the administration of these hormones alone. However, the complexity of this disease commonly treated with these hormones makes it extremely difficult to evaluate whether co-administration of vit. B₁₂ would have any effect on the prognosis.

Summary. Data are presented to demonstrate that the serum levels of vit. B₁₂ activity in diabetics with or without retinopathy are widely different. Those with the retinal lesions have a much higher activity (292 ± 24) than those without retinopathy (162 ± 18). This difference is statistically significant.

The possible implication of vit. B₁₂ in this disease is discussed.

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