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SERUM VITAMIN B_{12} CONCENTRATIONS IN CHILDREN*

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Low serum vitamin B_{12} levels are generally considered to be an indication of a depressed body reserve of this vitamin and are usually found with megaloblastic changes[1]. However in patients with megaloblastic anemia due to inherited transcobalamin II deficiency, serum vitamin B_{12} levels are within normal range[2-4]. Low levels of this vitamin were also described in two brothers with transcobalamin I deficiency, but without hematological manifestations except for mild hypersegmentation of the neutrophils in one of them[5].

Although low serum vitamin B_{12} levels may be observed in dietary deficiency of this vitamin with or without clinical and hematological findings, they always present in patients with pernicious anemia, intestinal malabsorption and in the "blind loop syndrome"[6-7].

Age-related variations in cobalamin levels have been reported, but reference studies have generally been carried out on adults[8]. For this reason we would like to report serum vitamin B_{12} levels in children.

Material and Methods

Three to five ml blood specimens were obtained from 40 healthy children, with hemoglobin values of over 10 g/dl and an age range of six months to 18 years; these were the controls.

Blood specimens were also obtained from 98 children with various hematologic and other disorders who were of the same age range and socioeconomic condition as the controls. Of these the majority (78 in all) had been under

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observation in the Hematology Unit for leukemia (16 patients), blood coagulation disorders (16 patients), thrombocytopenic purpura (10 patients), hemolytic anemia (8 patients), glucose-6-phosphate dehydrogenase deficiency (7 patients), iron deficiency anemia (5 patients), inherited disorders of platelet function (3 patients), megaloblastic anemia (2 patients with vitamin B_{12} deficiency and 1 with folic acid deficiency), aplastic anemia in remission (2 patients), Schönlein-Henoch purpura (2 patients), infectious mononucleosis (2 patients), myeloid metaplasia (2 patients), congenital hypoplastic anemia (1 patient), Wiskott-Aldrich syndrome (1 patient). The rest of the patients were being followed up in the department of pediatrics on account of various infectious diseases, motor and mental retardation, hepatosplenomegaly, enuresis, chronic hepatitis, sinusitis and mucopolysaccharidosis.

Special care was taken to avoid hemolysis, bacterial contamination and excessive exposure to light during blood collection. After the clot was separated with a clean glass rod, tubes were centrifuged at room temperature for 10-15 minutes at about 1500 g to remove sera; they were then stored in a deep freeze at −20 °C till vitamin B_{12} contents could be assayed by means of the "radioimmunoassay kit" obtained from Amersham (England)[9-10]. Student's *t* test was used for statistical evaluation.

Results

For the entire control group the serum vitamin B_{12} levels ranged from between 200 and 1250 pg/ml with a mean of 558.8 ± 268 pg/ml. The level was higher than 800 pg/ml in four cases only. Although there was no difference in the serum vitamin B_{12} levels between boys and girls, the levels did seem to decrease with age (Figure 1).

The serum vitamin B_{12} levels of the majority of the 78 patients with different hematological disorders ranged from between 140 to 800 pg/ml; but in eight patients it was between 800 and 1250 pg/ml and in five patients (three with chronic myeloid leukemia (CML), one with preleukemia and one with hemophilia A) it was between 2000 pg/ml and 2350 pg/ml. However in the other 12 leukemic patients (nine with acute lymphoblastic leukemia on maintenance chemotherapy, three with acute myeloblastic leukemia (AML) on induction therapy) the vitamin B_{12} levels were within the range of the controls ($p>0.05$).

The vitamin B_{12} levels of different groups with hematological disorders, such as coagulopathy, thrombocytopenic purpura, hemolytic anemia and glucose-6-phosphate dehydrogenase deficiency did not differ significantly from those of the controls ($p>0.05$ for each group).

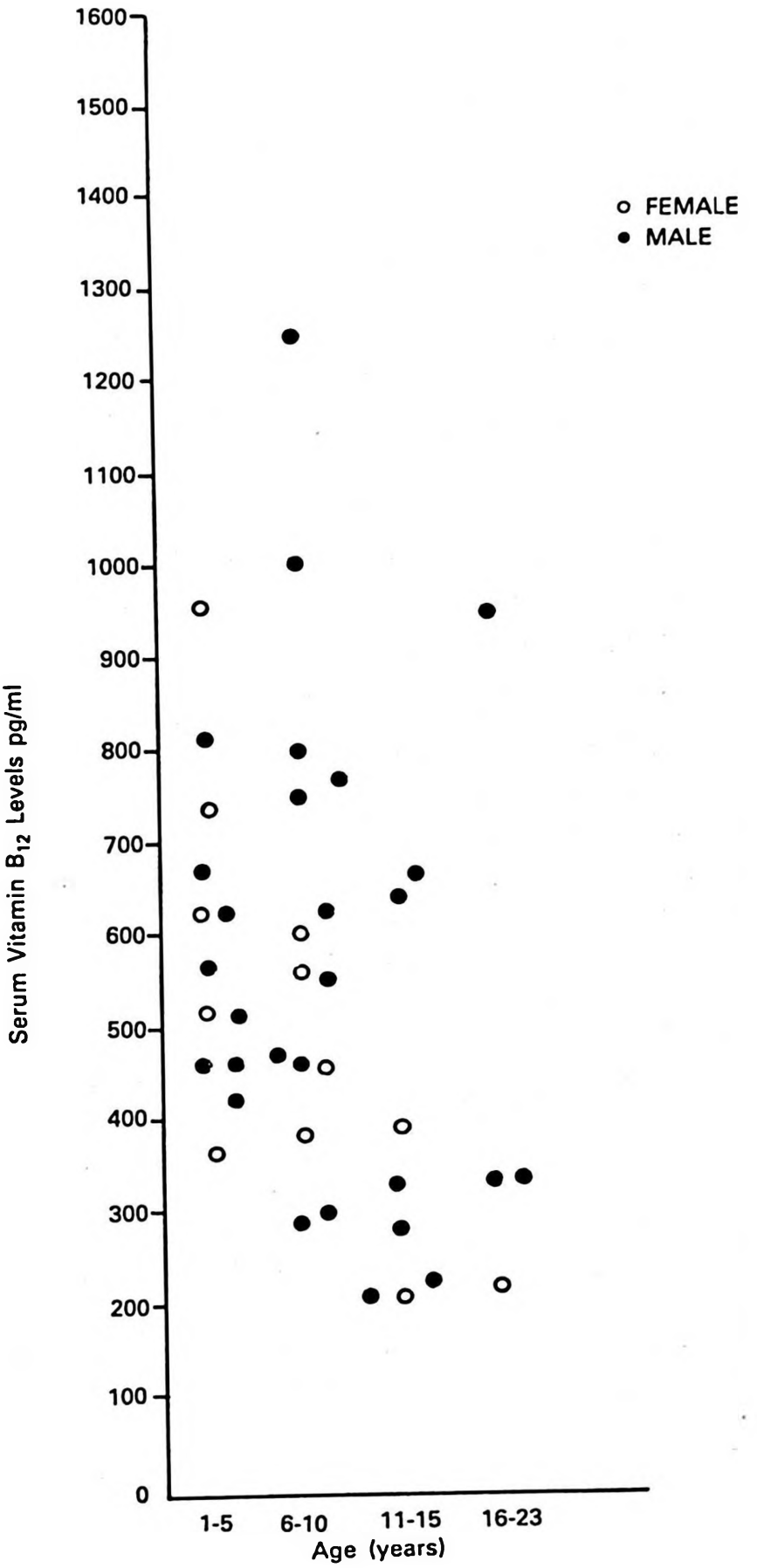

Figure 1

Distribution of serum vitamin B_{12} concentration in controls according to age and sex.

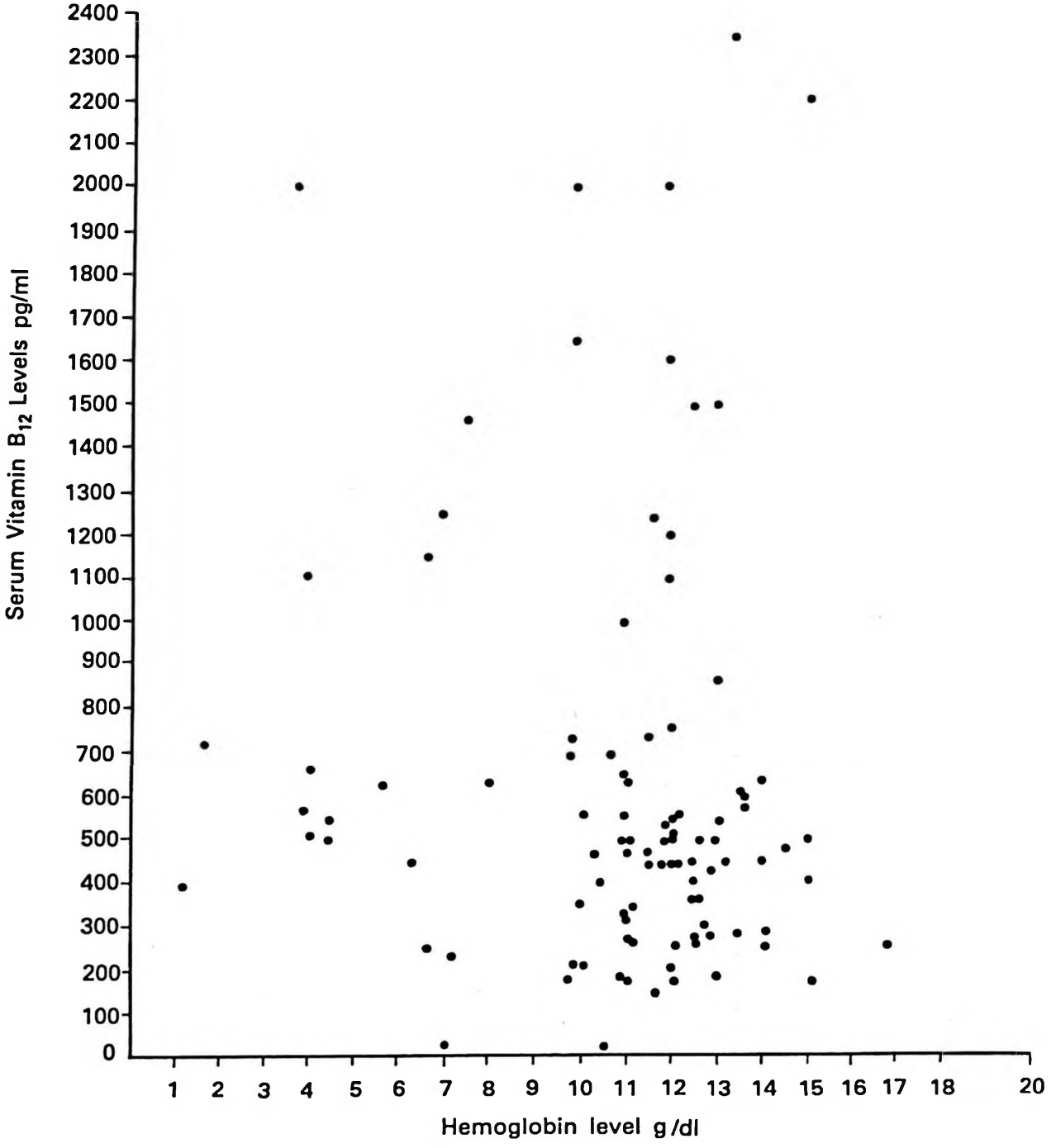

Figure 2

Vitamin B_{12} and hemoglobin levels of our patients.

High values of serum vitamin B_{12} were obtained in only one of five patients with iron deficiency anemia and in a single case of mucopolysaccharidosis. In children with acute or chronic hepatitis, vitamin B_{12} values were found to be within normal limits.

Markedly decreased (20 and 30 pg/ml) serum vitamin B_{12} levels were found in two patients with megaloblastic anemia due to vitamin B_{12} deficiency but the level was normal (500 pg/ml) in the case with folic acid deficiency.

In one of two cases of myeloid metaplasia the vitamin B_{12} level was found to be somewhat low (140 pg/ml) but there was no evidence of megaloblastosis.

Discussion

The distribution of serum vitamin B_{12} levels of the 40 control children was very close to the results of Liu and Sullivan[9], obtained among adults, using the same kit and basically a similar method to ours. They found that the vitamin B_{12} levels ranged from 104 to 1364 pg/ml with a mean of 453 pg/ml in a group of 85 volunteers and patients without anemia[9]. Further there was no significant difference between these results and those of Herbert et al[10] who used hemoglobin coated charcoal assay. So the range of vitamin B_{12} values from between 200 pg/ml and 1250 pg/ml in the 40 normal control children may be accepted as the upper and lower limits for our laboratory.

The very high vitamin B_{12} levels ($\geqslant$ 2000 pg/ml) in our study were found in children with CML; this has also been reported in adults with this disorder[5-7,11]. We thought it interesting that a very high vitamin B_{12} level returned to a normal range in a girl with CML, following blastic transformation (from 2200 to 600 pg/ml). It was also interesting to record a high serum vitamin B_{12} level – more than 2000 pg/ml – in a three-year-old boy with preleukemia. Eight months later he developed acute myeloblastic leukemia, at which time his vitamin B_{12} level was found to be normal. If this finding is confirmed in other patients, it could be used as a diagnostic criteria for preleukemia.

In a case of hemophilia A, the vitamin B_{12} level was found to be very high (2000 pg/ml) during a massive bleeding. High levels were also found in a case of mucopolysaccharidosis and in one of five patients with iron deficiency anemia.

Although high vitamin B_{12} levels have been reported in adults with acute and chronic liver diseases[12] we did not verify this among children with acute or chronic hepatitis.

Very low vitamin B_{12} levels were found in two cases of megaloblastic anemia, one of them had the Immerslund-Gräsbeck syndrome with generalized malabsorption, and this was completely corrected with the exception of proteinuria, following parenteral vitamin B_{12} administration[13].

Herbert[14] reported elevated vitamin B_{12} levels in eight patients with myeloid metaplasia. In one of our two cases of myeloid metaplasia the vitamin B_{12} level was found to be low. This was perhaps because the vitamin B_{12} deficiency was in its early stages before megaloblastosis had developed.

Summary

Vitamin B_{12} levels of 40 healthy children were determined by using the "radioimmunoassay kit" method. They were found to range from 200 to 1250 pg/ml with a mean of 558.8 ± 268 pg/ml.

It was found markedly low (< 100 pg/ml) in two patients only, and these had megaloblastic anemia of vitamin B_{12} deficiency.

Very high vitamin B_{12} levels (> 2000 pg/ml) were found in three patients with chronic myeloid leukemia and in a case of preleukemia. A very high level (> 2000 pg/ml) was also found in a case of hemophilia during massive bleeding in the hip joint, but not in the other hemophilic cases.

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