Radioimmunological determination of somatomedin B  
in healthy children and  
in children with growth disturbances

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Abstract. Serum somatomedin B levels were determined by radioimmunoassay in 209 healthy boys and girls from one month to 16 years of age. Low values were found up to the second year life. In the first year the mean level was 13.8 mg/l in girls and 11.5 mg/l in boys. In older children the values increased to levels between 13 and 22 mg/l in boys and between 13 and 18.5 mg/l in girls. They were independent of the stage of pubertal development.

Somatomedin B levels were normal in 71 children with constitutional growth delay, primordial dwarfism, familial dwarfism and other forms of growth disturbance. The mean levels were between 12.1 and 14.4 mg/l. Values below 6 mg/l were present only in children with hGH deficiency. In these patients we could find an increase of the mean level from 4.3 mg/l without therapy to 9.4 mg/l under treatment. Thus the determination of somatomedin B seems to be useful for the diagnosis of hGH deficiency.

Somatomedin B is a hGH dependent acid peptide with a molecular weight of 5000 Dalton. It is a unique protein with four disulfide cross-links and N-terminal aspartic acid. The primary structure has been determined and shows a close relationship to small trypsin inhibitors and phospholipases (Fryklund & Sievertsson 1978). It is characterized by its property to stimulate DNA synthesis in human glia-like cells by increasing thymidine uptake (Uthne 1973). There seems to be no growth stimulating effect on cartilage tissue (Bomboy & Salmon 1975; Fryklund et al. 1978). Because of these properties and since it has been found to be inactive in cartilage sulphate assays, somatomedin B is no longer classified as a somatomedin. Nevertheless, there can be no doubt that somatomedin B is a hGH dependent protein (Fryklund & Sievertsson 1978; Underwood & van Wyk 1979).

In 1975 a radioimmunoassay for somatomedin B was developed by Yalow et al. (1975). Before that somatomedin was determined by bioassay or radio-receptor assay (Takano 1975; Van den Brande & du Caju 1974). Except for the study of Hall et al. (1981) and Underwood (1981) there are only few studies about immunoreactive somatomedin. It was shown, that somatomedin B was significantly elevated in patients with acromegaly (Evermann et al. 1977; Yalow et al. 1975) and depressed in patients with hGH deficiency compared to normal levels (Evermann et al. 1979; Hizuka et al. 1978; Yalow et al. 1975).

In this study serum somatomedin B levels were determined by radioimmunoassay in normal children of various age groups and in children with various growth disturbances in order to explore whether this method is useful in the diagnosis of growth disturbances.

Materials and Methods

Patients

Somatomedin B levels were determined in 102 boys and 107 girls with normal height and weight according to the somatogram by Kunze & Murken (1974).
Forty-three girls and 41 boys aged 11 to 16 years were classified according to the pubic hair stages by Tanner.

In addition, somatomedin B levels were determined in children with the following growth disturbances: hGH deficiency (n = 10), familial dwarfism (n = 7), constitutional growth delay (n = 46), primordial dwarfism (n = 9), Turner's syndrome (n = 10), and children with various osteochondrodysplasias (n = 9).

Methods
Somatomedin B was determined with the radioimmunoassay of Kabi Diagnostica, Stockholm, Sweden. The lactoperoxidase-method (LPO) was used for labelling. The procedure was slightly modified by using 2.0 mCi \(^{125}\text{I}\) instead of 0.5 mCi. LPO and \(\text{H}_2\text{O}_2\) were raised from 4 respectively 2 \(\mu\)l to 10 respectively 6 \(\mu\)l. The reaction-time was prolonged from 50 to 100—120 s. The labelled somatomedin B was diluted 1:16. Thus we could enlarge the yield of labelled somatomedin B from 18.3 to 33%.

Before centrifugation, after incubation, 500 \(\mu\)l dilution buffer with 10% polyethyleneglycol was added in order to improve the tube attachment of the sediment. The sera were diluted 1:10000. In 17 tests the intra-assay coefficient of variability was 12.7% and the inter-assay coefficient of variability was 11.1%. Sensitivity (\(\varepsilon\)) was ascertained according to the formula \(\varepsilon = B_0 - 3\sqrt{B_o}\). The mean level was 2.2 mg/l with a range from 1.0 to 3.3 mg/l. Presuming a normal distribution, after performing the F-test, Student's \(t\)-test was used for calculation of significance.

Results
I. Somatomedin B levels in normal children
The results are illustrated in Fig. 1. Low levels were found in the first 2 years of life with a mean of 11.5 mg/l in boys and 13.8 mg/l in girls. In older children the levels increased to mean values of 20 mg/l ranging between 13 and 22 mg/l in boys and between 13 and 18.5 mg/l in girls. If boys and girls were subdivided into 3 age groups, somatomedin B levels were not different in girls (Fig. 2). In boys there was a significant difference between the first and second and the second and third group (\(P < 0.001\)), but none between the first and third group.

II. Children in puberty
During puberty, sex or stage of pubertal development had no influence on the somatomedin B levels. The values ranged between 13.7 and 16.1 mg/ml in girls and between 12.3 and 15.3 mg/l in boys (Fig. 3).

III. Growth disturbances
Somatomedin B levels were determined in 91 children with various forms of growth deficiency.

![Fig. 1. Somatomedin B levels in sera from healthy boys and girls in dependence of age. None of the normal subjects beyond the first 2 years had a level below 6 mg/l. In Figs. 1 and 3 means with 95% confidence limits as well as medians are given. With few exceptions both values are corresponding well (■ means, – medians).](image-url)
Somatomedin B values in sera from healthy children in various age groups (G 1–3). (Mean and 95% confidence limits).

Except in children with hGH deficiency the levels were normal (Fig. 4).

The girls with Turner's syndrome, aged from 9 to 16 years, had a mean level of 10 mg/l while on treatment with oxandrolone. In the other groups the mean levels were between 12.1 and 14.4 mg/l.

Patients with a hGH deficiency had a mean value of 4.3 mg/l. None of them reached the lower normal limit of 6 mg/l. Treatment with hGH raised the values to a mean of 9.4 mg/l ($P < 0.001$). These results are depicted in Fig. 5.

**Discussion**

At present comparable studies about somatomedin B are not available. Before developing the radio-
Somatomedin B levels in children with various growth disturbances. Except in the children with hGH deficiency with values below 6 mg/l the levels were normal.

Immunoassays for the hGH dependent somatomedins A, B and C, somatomedin or sulphation factor was determined by bioassays and later by radioreceptor assays. In the last years few similar studies with somatomedin A and somatomedin C have been published. In the following these results are regarded to point out the comparable properties of the somatomedins.

Somatomedin levels are lower in newborns than in older children. Radioimmunologically determined somatomedin B mean levels have been reported to be 7.1 mg/l (Furlanetto et al. 1977; Gluckmann & Brinsmead 1976; Rosenfeld et al. 1979). Hall et al. (1981) found newborn somatomedin A levels that were only 50% of adult values at birth. Adult levels were reached at 10 years of age. In contrast to our findings with somatomedin B, immunoreactive somatomedin A showed a marked pubertal rise. In boys the increase occurred when the testes reached a size of 5 ml (Hall et al. 1981). Similar results were reported for somatomedin C (Broughton & Jones 1981; Underwood 1981). In our study there was no relationship between somatomedin B and pubertal stages.

Radioimmunological somatomedin B was normal in children with constitutional growth delay, primordial dwarfism, familial dwarfism and in other forms of growth deficiency.
In accordance with other reports (Evermann et al. 1977; Yalow et al. 1975) we found significantly low somatomedin B levels in patients with hGH deficiency. Somatomedin A and C are depressed as well (Furlanetto et al. 1977; Hall et al. 1981; Schwalbe et al. 1977). With hGH therapy they rise to normal levels (Hall 1972; Hizuka et al. 1978).

The diagnosis of hGH deficiency still depends on inconvenient stimulation methods. All of them can produce false negative results. A screening method would be desirable, in which a hGH deficiency could be excluded by only one venipuncture.

Since in none of our patients with hGH deficiency the somatomedin B levels were within the normal range, a single value of 6 mg/l or less suggests that diagnosis.

Thus the determination of somatomedin B, even though it is regarded not to be a genuine somatomedin, seems as somatomedin C, which is performed in the meantime by Nichols Institute (Broughton & Jones 1981), to be a reliable screening method for hGH deficiency. It seems to be justified to perform more inconvenient hGH stimulation methods only in patients with somatomedin B levels below 6 mg/l.

References


Uthne K (1973): Human somatomedins: purification and some studies on their biological actions. AB Kabi, Stockholm.


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