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Somatomedin and transferrin in celiac disease (CD).

Sulfation activity (Sm) and transferrin (Tf) were measured in 90 plasma samples from 39 children with CD classified 5 to 1 by intestinal biopsy performed at time of sampling : 10 before, 58 during gluten-free diet (GF), 22 after gluten reintroduction (GR). Sm was 0.32 ± 0.04 U/ml before GF, increased with GF from stages 5 to 1, to reach 1.23 ± 0.15, decreased at GR to 0.38 ± 0.06. Sm correlated to GF duration (r = 0.781). Correlation of Sm with growth velocity (V) was lacking at stages 5 to 2, and appeared at stage 1 (r = 0.778). Tf decreased from a high value of 3.62 ± 0.15 g/l at stage 5 to 2.97 ± 0.14 after GF at stage 1, rising to 3.35 ± 0.10 at GR. Tf correlated negatively with GF duration (r = -0.720) and positively to V on GF (r = 0.492) and GR (r = 0.601). Longitudinal studies from GF to GR and again GF confirmed the inverse trend of Sm and Tf variations. These data show that early catch-up growth in CD treated with GF does not relate to sulfation activity and may involve other factors, such as Tf.

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Plasma Somatomedin-C as a screening test for growth hormone deficiency in children and adolescents.

Random plasma somatomedin-C levels were measured in 101 children aged 7 months to 18 years with growth at or below the 5th percentile. 87 of 101 had short stature due to constitutional delay or genetic predisposition and 14 were growth hormone deficient. In the short normal group mean somatomedin-C levels were: 0-2 years: 0.22± 0.02U/ml; 2-5 years: 0.28±0.06U/ml; 5-12 years: 0.78±0.1U/ml; 12-18 years: 1.22±0.16U/ml; compared with 0.23±0.04U/ml in the growth hormone deficient children. 55 of 101 had somatomedin-C levels of 0.5U/ml, and had one or more growth hormone stimulation tests. All 14 growth hormone deficient patients fell into this group (range: 0.09-0.47U/ml). The 41 normal patients in this group (growth hormone 6ng/ml) were distibuted among the entire 87 normals as follows: 0-2 years: 10/10; 2-5 years: 19/23; 5-12 years: 11/30; 12-18 years: 1/24. There was considerable overlap of values among growth hormone deficient and short normal children under 12 years of age, but a clear separation above 12 years. In 5 of 6 patients in whom 2 measurements were made, there were major differences in these levels. 1) Random somatomedin-C levels lack specificity in screening for growth hormone deficiency under the age of 12 years. 2) The variation of levels in individual patients necessitates further study to identify a possible diurnal or pulsatile secretory pattern. 3) A standardized time of sampling should be considered.

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Effects of fasting and refeeding on growth hormone receptors in rat liver membranes.

The mechanism of the growth defect often associated with poor nutrition is not clear. We have studied the specific binding of growth hormone (GH) to liver membranes of 3 groups of rats which were (F) fasted for 4 days, (R) refed for 3 days after fasting, and (controls) allowed free access to food. The specific binding of ^{125}I-BGH (bovine GH) was low in microsomal membranes of (F) rats : 57 % that of controls. The number of somatotropic sites rather than the affinity of the binding was affected. The lactogenic sites as judged on the binding of ^{125}I-HGH (human GH) were not significantly reduced in membranes of (F) rats. The number of insulin receptors was elevated in microsomal membranes of (F) rats : 185 % that of controls ; this modification was associated with a decreased insulinemia in (F) rats. But no change of the plasma GH was found in (F) and (R) rats when compared to controls ; other factor(s) than the hormone level must regulate the somatotropic sites in this model. Refeeding led to a correction of the binding of ^{125}I-BGH and of ^{125}I-Insulin to microsomal membranes. Decreased plasma somatomedin bioactivity was associated with the low number of somatotropic receptors in the liver membranes of fasted rats ; it suggests a role of the GH liver receptors in the regulation of the plasma somatomedin activity.

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The effects of anti-leukaemic drugs on somatomedin production and cartilage responsiveness to somatomedin in vitro.

Drugs commonly used to treat children with acute lymphoblastic leukaemia were investigated in vitro to determine cartilage responsiveness to somatomedin using the uptake of radioactive sulphate and thymidine by porcine cartilage. Prednisolone and doxorubicin profoundly depress cartilage responsiveness at doses within therapeutic ranges and vincristine and cytosine arabinoside produce lesser but significant inhibition. Using rat liver perfusionsit was possible to demonstrate that growth-hormone stimulated liver production of somatomedin activity is profoundly depressed by vincristine and 6-mercaptopurine, is lowered by cyclophosphamide and cytosine arabinoside but is unaffected by prednisolone and doxorubicin.

The poor growth of children with ALL during treatment may be mediated by a drug-induced combination of diminished somatomedin production and cartilage response to somatomedin.

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Acute and chronic somatomedin-C response to growth hormone: evaluation of correlation with age and growth rate.

The correlation between acute and chronic SM-C responses to hGH treatment of hypopituitary dwarfism, and their value in predicting growth rates were studied in 20 GH-deficient children. SM-C by RIA and RRA was measured prior to hGH, 12 hours after 4 daily injections of hGH, 0.1 U/kg, and after 6 months of hGH 0.1 U/kg t.i.w.

	Day 1 (Baseline)	D2	D3	D4	D5	6 month
RRA	0.38±0.05 (mean ±SEM)	0.63	0.96	1.13	1.18	0.95±0.12
RIA	0.19±0.03	0.42	0.68	0.81	0.82	0.79±0.11

The correlation between SM-C by RRA and RIA was highly significant (r=0.92 on Day 1 and at 6 months, p < 0.001). The acute SM-C response to hGH was predictive of chronic SM-C levels (Day 5 vs. 6 month SM-C, r=0.80, p <0.001). However, individual SM-C responses were variable, with 7 children achieving SM-C levels >1 U/ml by Day 5, while 3 maintained levels < 0.10 U/ml. Although the annual growth rate increased from 3.6 ± 0.1 to 6.7 ± 0.6 cm/yr, no correlation was observed between growth rate and baseline, acute or chronic SM-C levels. Children under 10 years of age had the smallest increment in SM-C, but the best growth rate. However, even when subdivided by age, no correlation was observed between 6 month SM-C and growth rates (r=0.10, p >0.75). We conclude that (1) the acute SM-C response to hGH predicts chronic SM-C levels, (2) SM-C and growth response to hGH are age-dependent and (3) the level of SM-C elevation with hGH cannot predict growth response.

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The binding of ^{125}I somatomedin B (SMB) to proteins in serum from normal and growth hormone deficient (GHD) children.

A report[1] suggests that SMB may inhibit proteases with trypsin-like activity. These proteases could be concerned with the release of biologically active growth factors (IGF) from their specific carrier proteins. The objectives of this study were to (a) examine if decreased binding of ^{125}I SMB occurs in serum from GHD children thus reflecting an increased pool of unbound SMB. (b) To explore the binding characteristics of SMB. Purified SMB was labelled to a mean specific activity of 209 µCi/µg. Dilution curves of serum from GHD children (N = 15, 2 1/2 - 18y) and age matched controls were studied. After incubation (4°C, 2h), free from bound label was separated with ammonium sulphate. The mean percentage of label bound to diluted sera (12.5 - 50µl in the assay) from GHD children was lower than for controls (P <0.001). The characteristics of the specific binding protein were that of a low capacity (160 pmol/l) low K_a (4.37 x 10^6 l/m) binding protein. Globulins of high capacity with immunoelectrophoretic properties of α_2 macroglobulin and α_1 globulins were also demonstrated. It was concluded that the specific binding of ^{125}I SMB is low, that total binding is weak and that in consequence unbound SMB may be elevated in some GHD patients' sera.

(1) Fryklund, L. et al. In: Somatomedins and growth. Academic Press, London and New York. 1979, p 7-16.