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Effect of serum from children with isolated hGH deficiency (IGHD) and Laron type dwarfism (LTD) on skin fibroblasts.

Cultures were made of fibroblasts obtained from the skin of 9 patients with IGHD, 5 with LTD, 3 with acromegaly and of 17 normal controls. There was no difference in morphology and growth rate between the fibroblasts obtained from the patients and those from the controls. When fibroblasts from normal children were incubated with sera of children with IGHD or LTD, there was a significant reduction in their protein content and incorporation of ^3H -thymidine. When fibroblasts obtained from children with LTD were incubated with the patients's own serum or with serum taken from a child with IGHD, there was a significant reduction in protein content and ^3H -thymidine incorporation when compared to that of fibroblasts cultured in serum obtained from normal controls or acromegalic patients. It is concluded that in patients with IGHD or LTD fibroblasts are responsive to serum growth factors. It would also appear that human serum contains growth factors other than GH-dependent somatomedins.

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NSILA (nonsuppressible insulin-like activity): a fetal growth factor?

NSILA is a growth hormone dependent serum peptide closely related to the Somatomedins (SM), whose significance as growth hormones has not yet been clarified *in vivo*. Factors involved in fetal growth are plentiful, recent data suggesting a possible role of SM. Using a sensitive competitive protein binding assay we have determined NSILA in 23 pregnant women and in 28 paired maternal and cord sera. Mean \pm S.E.M. levels ($\mu\text{U}/\text{ml}$) during pregnancy (952 ± 56) were not significantly different from those in 8 non-pregnant women (821 ± 25) and did not change much in the course of pregnancy. NSILA in cord serum (597 ± 38) was significantly lower ($p < 0.001$) than in correspondent maternal serum (1039 ± 63). Preliminary data indicate a reverse behaviour of NSILA carrier protein. The finding of cord NSILA levels within the normal childhood range is compatible with a role in fetal growth. NSILA carrier protein possibly controls the rate of diaplacial transfer and/or the half-life of NSILA in the fetus.

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Nonsuppressible Insulin-Like Activity (NSILA) and Somatomedin (SM) in Laron's Syndrome.

In attempt to compare levels of NSILA and SM and study the sulfation activity of purified NSILA in a condition with low SM, NSILA was determined in a boy with high IR-HGH and low SM ($.28 \text{ U}/\text{ml}$ (norm.range for age $.91 \pm 15$)). NSILA in bioassay (fat pad) was below $25 \mu\text{U}/\text{ml}$ (norm.range 160 ± 37). In a specific carrierprotein binding assay NSILA was $23 \mu\text{U}/\text{ml}$ (norm.range 345 ± 65), (hypopit.range 183 ± 27). The preparation of NSILA was obtained by Sephadex G-50 chromatography of serum in 1M acetic acid. The activity of concentrations in range of $5-40 \mu\text{U}/\text{ml}$ in medium alone was very low, whereas a significant increased activity parallel to that of normal serum could be demonstrated in the presence of the patients serum. This was not limited by the concentration of serum as 10% and 20% serum gave identical curves. Analogy between NSILA and SM in this condition is thus demonstrated and furthermore that the low SM activity can be enhanced by addition of NSILA not excluding the presence of a growth hormone independent stimulating factor in serum.

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Report on a mass screening program (14,000 samples) for neonatal hypothyroidism using a filter paper T4 and TSH method. From January 1976 to April 1977, 14,000 newborns were screened in the district of Midi-Pyrenees. The screening program detected 4 cases of neonatal hypothyroidism (1/3500) with T4 $35 \text{ pg}/2$ spots and TSH $200 \text{ uU}/2$ spots. At 20 days of age T4 levels were under $2.8 \text{ ug}/\text{dl}$ and TSH reached more than $40 \text{ uU}/\text{ml}$. The T3 levels were low in 3 cases but normal in 1 case ($150 \text{ ng}/\text{dl}$). Thyroid scintigram (Tc 99 m) showed no gland for the four cases. On the fourth week, the neonatal symptoms of hypothyroidism were nearly absent, except mottlings in two cases, a large posterior fontanelle in two cases and a physiological jaundice in one case. A thyroid extracts treatment was started in the four cases since the 30th day. Now, in the oldest child, after 13 months of treatment, the mental development is normal (IQ : IIO).

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Detection of neonatal hypothyroidism in Switzerland by TSH determination using filter paper blood samples.

TSH radioimmunoassay has been adapted for the determination in dried blood spotted on filter paper (disc $\varnothing 6.5 \text{ mm} = 10 \mu\text{l}$ blood, sensitivity $12 \mu\text{U}/\text{ml}$, processing time 40 hours). This test has been introduced in our screening program for metabolic diseases on January 1, 1977. Since April 1977, 90% of all children born in Switzerland are included.

Of 18'800 infants tested routinely on their 5th day of life, seven cases with primary hypothyroidism were discovered owing to excessive blood TSH ($100 \mu\text{U}/\text{ml}$). The diagnosis was not recognized clinically although all 7 infants showed some symptoms. T4 therapy has been started within their second week of life. There were no false positive results. The incidence of 1 in 2700 newborns is higher than reported so far. It has to be shown whether this is due to genetic or geographic factors, to the occurrence of transitory forms, or to a more complete ascertainment by the TSH (versus T4) assay.

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Cord blood screening for congenital hypothyroidism.

A regionalised screening programme for neonatal hypothyroidism using umbilical cord blood has been developed. An initial serum thyroxine (T_4) was performed on all infants and supplementary thyrotropin (TSH) measurements were made only on those samples where T_4 was $< 10^{\text{th}} \%$ ile. Infants ($< 0.2\%$) with low T_4 but serum TSH $> 50 \mu\text{U}/\text{ml}$ were recalled. In 38,000 births 14 detected cases had thyroid dysfunction (TD) confirmed by thyroidal radiiodine uptake (RAI). Primary TD occurred in 13: - Athyrosis 4, Dys-hormonogenesis 3, Hypoplasia 3, Lingual thyroid 2, Iodide induced 1; and secondary in 1 case. Without the hypoplasia cases (where "subclinical hypothyroidism" was present on follow up: normal T_4 , abnormal RAI, and elevated TSH) and the secondary case, the incidence of significant primary hypothyroidism (SPH) was 1 in 4,000. Treatment with L-thyroxine $5.0 \mu\text{g}/\text{kg}/\text{day}$ was begun day of life 25-83 in the 10 SPH cases with 8 treated before 5 weeks and 5 before 4 weeks of age. A high incidence of congenital hypothyroidism has been documented, and the effectiveness of cord blood screening for its early detection and treatment demonstrated.