413 SCREENING CRITERIA FOR HYPOTHYROIDISM IN HOSPITALIZED PRETERM INFANTS (PTI)

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T4 and T3 are low in PTI compared to healthy term infants (TI) making screening results in PTI difficult to interpret. To determine the best age, the appropriate lower value of T4, and the value of free T4(FT4) for screening, 76 sick newborns (14 TI, 62 PTI) had serial T4, T3, TSH, and FT4 measured until discharge. TSH values were normal (NL) in all but one TI. Cumulative results showed T4, T3, and FT4 all significantly lower in PTI than sick TI. T3 values gradually rose in PTI over 5 weeks. None of the weekly FT4 values were significantly different:

	Week	1	2	3	4	≥5	cumulative*
TI	ng/ml	2.00	2.00	1.55	2.12	1.86	1.93
	SD(N)	.61(8)	.44(10)	.51(6)	.61(6)	.18(5)	.51(35)
PTI	ng/ml	1.66	1.72	1.64	1.44	1.55	1.62
	SD(N)	.56(30)	.43(27)	.51(25)	.38(24)	.32(20)	.47(119

T4 values are mean and standard deviation, N=patient weeks* $p < .01$

Female PTI were significantly higher than male PTI for cumulative values of T4, T3, FT4. The best lower limit for T4 was 45 ng/ml at all ages. This is the mean-1.65 SD (lower 5%) in TI at 1 to 3 wks, and the Maryland state lab after 3 wks. This value yielded 4/30, 2/27, 3/25, 3/21, and 0/19 abNL tests at wks 1 to 5, respectively. T3 and FT4 were not as specific. Of 11 PTI with abNL T4, only 2 died before values returned to NL. We conclude that screening (using 45 ng/ml T4) is possible at any age. Should consecutive T4's be abNL, T3 or FT4 may exclude hypothyroidism.

414 IDENTIFYING THE CHILD WHO MAY BENEFIT FROM GROWTH HORMONE (GH) THERAPY.

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Twelve dwarfed children (3-13 yrs. of age) with heights < 4 SDs below the mean, growth rate < 4 cm/yr. and retarded bone ages were investigated. They all had low Somatomedin-C (Sm-C < .25 U/ml) basal levels and standard GH provocative stimuli. Following a 10 day course of GH treatment at a dose of .168 U/kg^3/4, they were seen at 12 weeks for height measurements. Based on the endogenous GH levels, and the plasma Sm-C and growth increments, 3 separate groups could be identified. Predicted growth rate was calculated according to Rudman's protocol (JCEM 48,472, 1979).

Group	n	Plasma GH Range(ng/ml)	Sm-C(U/ml) Response to GH.Mean(range) Basal	Day 1	Day 5	Day 10	Predicted grth(cm/yr)
1	5	2-5	.17 (.1-.25)	.13 (.1-.27)	.54 (.46-.88)	1.10 (.4-1.3)	4-10
2	2	18-20	< .19	< .19	< .18	< .1	< 4
3	5	10-90	.18 (.1-.25)	.4 (.1-1.1)	1.22 (.4-2.6)	1.04 (.13-2.6)	5-14

Group 1 represents children with classical growth hormone deficient dwarfism all of whom responded to treatment with a rise in Sm-C and enhanced growth. Group 2 is a set of twins with Laron type dwarfism. Group 3 probably represents children with biologically inactive but immunoreactive GH.

In conclusion, the acute increase in Sm-C levels appears to predict best an adequate growth response to exogenous GH.

415 SERUM SOMATOMEDIN-C CONCENTRATIONS (SMC) IN PRETERM INFANTS.

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An animal model suggests that vitamin D deficiency causes linear growth retardation by decreasing SMC. To define normal SMC in preterm infants where low 25-hydroxyvitamin D levels (25-OHD) are associated with later growth retardation, SMC were measured by RIA in serial samples from 37 infants of gestation 30.0±1.9wks and birthweight 1183±182gms. 13 were on standard formula plus 400I.U. vitamin D (control); 12, a high calcium, high phosphorus formula (Ca-P); and 12, standard formula plus 1µg/kg 25-hydroxycholecalciferol (25-HCC). SMC remained low over the first 9wks of life but had increased ($p<.005$ by paired t-test) at 12wks. Although there were no significant differences among the 3 groups, the 25-HCC treated group had the lowest SMC and highest 25-OHD. SMC did not correlate with serum 25-OHD, gestational age, length, weight, or weight gain at any age. The delayed increase in SMC may be developmental since several other liver-made proteins (DBP, ceruloplasmin, albumin) follow a similar time course. In human prematures, SMC is not decreased by low but not rachetic 25-OHD. Indeed, supplemental 25-HCC may decrease SMC.

SOMATOMEDIN-C CONCENTRATIONS u/ml* WITH AGE

Age(N)	3w(18)	4w(22)	5w(14)	6w(21)	7w(15)	9w(11)	12w(11)
Total	.26±.23	.18±.17	.20±.14	.22±.14	.24±.24	.32±.19	.50±.35
Control	.29±.33	.16±.14	.21±.09	.24±.10	.17±.11	.38±.08	.57±.33
Ca-P	.23±.07	.29±.21	.23±.16	.29±.17	.41±.34	.41±.22	.50±.40
25-HCC	.24±.11	.14±.13	.13±.17	.15±.12	.13±.07	.12±.11	--

*nl adult .4-2.0u/ml, term cord 0.55±.22u/ml, ab provided by NPA.

• 416 SOMATOMEDIN BINDING PROTEIN IN GROWTH HORMONE DEFICIENCY.

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The somatomedin (SM) peptides are carried in plasma complexed to SM binding proteins (SMBP). The SM complexes have two major forms in plasma. The 150K dalton complex is made up of three subunits: an acid stable SMBP, SM peptide, and an acid labile component. The 40K complex is made up of a SMBP and SM peptide In addition, there is unsaturated SMBP found mainly in the 35-40K region. We have compared levels of unsaturated SMBP in 7 normal adults to 21 children with growth hormone deficiency before and during treatment with hGH 0.1U/Kg/day x 4 days. The SM-C/IGF-I content of each plasma was measured by RIA. There was a significant ($p<0.01$) difference in unsaturated SMBP between normal controls (17.8±0.8 %Bound/20ul) and untreated hypopituitary patients (27.8±2.2 %Bound/20ul). Thus a lower SM-C/IGF-I was associated with a higher unsaturated SMBP. Furthermore, there was a significant negative correlation between SM-C/IGF-I content and unsaturated SMBP in the untreated hypopituitary patients ($r=0.73$, $p<0.001$). Treatment with hGH normalized the mean unsaturated SMBP in the hypopituitary patients within two days. Full displacement curves and Scatchard analysis showed that the increased unsaturated SMBP in hypopituitary plasma was entirely due to an increased affinity ($8.4\pm0.9 \times 10^{-10}$M) when compared to normal ($2.3\pm0.2 \times 10^{-9}$M). We conclude that a higher affinity form of unsaturated SMBP is uniquely present in hypopituitarism which disappears with GH treatment. This change is in contrast to the low levels of acid stable SMBP which increase after GH.

417 EMPTY SELLA SYNDROME IN CHILDHOOD.

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Extension of the subarachnoid space through a defective diaphragma sella may cause progressive enlargement of the pituitary fossa, and may result in secondary endocrine disturbances, CSF rhinorrhea or visual field defects. Symptoms usually present in the fourth or fifth decade, and reports in children are very rare. A 13.4 year old male presented following minor trauma to the face, when symmetrical pituitary fossa enlargement was noted on skull x-ray. The sella volume was 3.2 times normal mean volume for age and there was some minimal calcification within the diaphragm. He was totally asymptomatic, and on physical examination his height, weight and sexual development were appropriate for age, his visual fields were intact and there were no focal CNS signs or thyroid enlargement. Endocrine evaluation showed normal basal plasma levels of T4 (7.7 µgm/dl), TSH (2.2 µU/ml), LH and FSH (2 and 5 mIU/ml) and prolactin (6.9 ng/ml). In response to intravenous insulin and thyrotropin releasing hormone, there were satisfactory increases in GH (Δ 12 ng/ml), cortisol (Δ 13.5 µgm/dl), TSH (Δ 10.6 µU/ml) and prolactin (Δ 11.1 ng/ml), and his responses to gonadotropin releasing hormone were appropriate for his degree of sexual development (Δ LH 26 mIU/ml; Δ FSH 2 mIU/ml). A CT scan performed after injection of matrizamide contrast into the lumbar subarachnoid space, confirmed that the sella was "empty", with a narrow rim of pituitary tissue visualized against the anterior wall. No pituitary hormones were detected in the CSF. Empty sella syndrome, in some patients, may therefore possibly have its origins in childhood.

• 418 PERIPHERAL RESISTANCE TO THYROID HORMONE IN AN INFANT.

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Peripheral resistance to thyroid hormone is a rare syndrome characterized by elevated serum total and free T_4 and T_3 concentrations, an absence of clinical manifestations of hyperthyroidism and abnormal TSH suppression. We studied a clinically euthyroid 6 month old infant, the youngest patient with this syndrome yet described, to determine the mechanism of thyroid hormone resistance. The degree of pituitary insensitivity to T_3 was investigated by measuring serum T_4 and TSH, and the TSH response to TRH infusion (100 µg) in response to increasing doses of T_3.

Day	µg/day T_3	T_4(µg/dl)	Basal TSH(µU/ml)	TSH 30min post TRH
1	---	22.1	7.6	47.4
8	10	14.3	2.8	37.6
15	20	16.1	4.7	32.6
22	40	11.2	3.8	18.6
29	80	7.4	1.6	3.2

Four times the replacement dose of T_3 (40 µg/day) was required to normalize the serum T_4 and the response to TRH. With 80 µg/day T_3 the TSH response to TRH was virtually abolished, as occurs in hyperthyroidism, but there were no clinical signs of thyroid hormone excess. Specific nuclear T_3 binding was compared in cultured skin fibroblasts from the patient and a normal infant. Binding was normal at low concentrations of unlabelled T_3, but at high concentrations there was evidence for a second low-affinity T_3 receptor. While resistance to thyroid hormone has been demonstrated in this infant, the cellular mechanisms are unclear.