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Development of TRH and TRH degrading activity (TRH-DA) in the hypothalamus and plasma of rats.

It has been shown that adult hypothalamus and plasma contain an enzymatic system which inactivates TRH. Developmental pattern of both TRH and TRH-DA has been studied in young rats. Wistar rats 0-33 days were decapited. Hypothalamus (HT) were dissected out, extracted in appropriate buffers for both TRH-DA and TRH measurements. TRH-DA was evaluated in parallel in plasma (P). TRH content was measured by RIA and TRH-DA by incubation with (H^3)TRH. Amount of intact (H^3)TRH remaining after 60 min. incubation period is taken as an index of enzymatic activity.

	D 2	D 5	D 18	D 20	D 33	Adult
TRH content (ng per HT)	2.8	3.0	3.5	3.8	5.2	5.14
TRH-DA(HT) % remaining	23	23	26	30	45	42
TRH-DA (P) % remaining	100	95	63	56	40	22.5
n =	14	12	7	5	6	10

HT TRH content reachs adult values at the end of the first month of life. On the contrary TRH-DA is high in the neonate and decreases thereafter. As shown in human, neonatal plasma has a low TRH-DA. Adult values are not reached at day 33.

In conclusion - In rats TRH HT content and TRH-DA is not mature at birth. Role of the age-related dissociation between plasma and HT TRH-DA is still unknown.

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Plasma TRH degrading activity (TRH-DA) in human neonatal plasma.

In vitro degradation of TRH by human plasma has been demonstrated in adults. This study concerns plasma TRH-DA during the neonatal period. (H^3)TRH is incubated in 50ul of plasma, extracted and intact (H^3)TRH quantitated by high pressure liquid chromatography after one hour incubation period. (H^3)TRH after 0 minute incubation is the reference value and results are expressed in % TRH remaining after one hour. Paired mother and newborn (arterial cord plasma) n=7 and neonates from day 1 to 5 (n=5 each day) are studied.

	Mother	Cord	D 1-2	D 3	D 4	D 5
TRH-DA % remaining	45.6	95.6	99	75	64.5	40.1
± S.D.	± 6.3	± 1.8	± 0.25	±10.1	± 3	± 2.0
T3 ng/ml	1.7	0.6	2	2.2	2.2	3.0
± S.D.	± 0.1	± 0.2	± 0.15	± 0.17		± 0.5

Maternal values TRH-DA are not significantly different from adult euthyroid control (37.5±5). Plasma of neonate have a very low TRH-DA. Activity appears at day 3 and reachs maternal values at day 5. The known increase of plasma T3 level in newborn occurs 2 days before appearance of any degrading activity.

In conclusion - Plasma of newborns have no TRH-DA until day 3. This metabolic immaturity may play a role in the neonatal thyroid hyperactivity. T3 induction of this enzymatic process demonstrated in rats as to be considered in human.

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Effect of prolonged illumination (phototherapy) on the concentration of TSH and T_4 in human neonates.

Phototherapy (Ph) used as a therapeutic tool in the newborn, may constitute a model of functional pinealectomy. With this assumption we have been searching for changes in pituitary function in newborns undergoing Ph. We have found that Ph in the newborn alters LH (Science 199:1229, 1978) and FSH levels (ESPE 1978) while prolactin is not significantly affected. In this report we present our findings on serum TSH and T_4 values in newborns receiving Ph and in controls (C).

Mean T4 (mcg/dl) and TSH (ng/ml) values

	Before Ph		During Ph		Post-Ph			
					3-6 days		9-12 days	
	Ph	C	Ph	C	Ph	C	Ph	C
T4	10.8	10.	8.1	10.7	8.1	10.3	8.4	10.5
TSH	1.1	1.1	0.67	0.9	0.97	0.8	0.71	0.65

T_4 is significantly lower in Ph newborns than in C during Ph and up to the 12th day post-phototherapy ($p<0.02$). TSH values do not increase in response to the decrease in T_4 concentration, possibly indicating a central effect of Ph. However other mechanisms may also be responsible for these hormonal alterations.

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Glucose induced changes of thyroxine (T_4) and triiodothyronine (T_3) plasma levels in obese children before and after hypocaloric diet and fasting.

To clarify the influence of a glucose load (Gl) on the thermogenetic effective thyroid hormones T_4 and T_3 plasma levels of obese children were studied after oral and intravenous glucose load during the postprandial period. T_4-values decreased by 31% in a group of 14 obese children (overweight 17-100%) 60 min. after oral Gl. This change was associated with an increase of T_3/T_4-quotient to 50-60% 60 min. after i.v. Gl T_4-values also were reduced 15,5% in normal weight (5) and 14% in 40 obese children. After feeding a diet of 600-1000 Kcal/die (30% protein, 45% carbohydrate, 25% fat) for a period of 21 days in 14 obese children T_3-values decreased after oral Gl. T_3/T_4 quotient was diminished to 69,4% after 60 min. After a 5-7 days fasting period T_4 increased significantly (p 0,001) in 15 obese children. In a group of patients with an overweight of 40-60% also a significant T_4-increase was found after i.v. Gl, but not in a group with an overweight of 21-40%. It is concluded that glucose stimulates and fasting and a hypocaloric diet reduce the peripheral T_4/T_3 conversion in obese children.

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Blood polyamines in fetal and postnatal growth and HGH effects on their levels.

Studies in vitro and in animals have demonstrated that tissue levels of polyamines (spermidine, spermine putrescine) are augmented during embrional and cellular growth. Moreover a number of hormones have been shown to stimulate polyamines biosynthesis in target organs. These data prompt us to determine fluorymetrically, after TLC separation, dansyl-polyamines in blood during pregnancy, in umbilical cord, in normal subjects of various pediatric ages and in hypopituitary patients after HGH i.m. The obtained results can be summarized as follows: I) during pregnancy polyamines are higher than in non pregnant women; two peaks are demonstrable at 10th and 36th weeks. 2) in umbilical cord values are higher than in pregnancy. 3) in children they are higher than in adults, maximal values are found in infancy. 4) after HGH an increment was evident in 3 out of 4 patients at start of therapy and in 4 out of 5 patients under continuous therapy. These results suggest a parallelism between blood levels of polyamines and period of maximal fetal and postnatal growth and a possible relationship between GH and polyamines biosynthesis as in animals.

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Longitudinal study of plasma testosterone in male pseudohermaphrodites during early infancy.

Plasma testosterone was longitudinally studied during the first months of life in 7 XY infants with male pseudohermaphroditism. In all, the 2 testes were palpable in normal or inguinal position. In 1 case the defect of masculinization was complete and associated with a salt loss syndrome. The 6 others had ambiguous genitalia with perineal hypospadias and micropenis. In 2, the physiological rise of testosterone was absent or blunted, and a combined adrenal and testicular enzymatic defect was demonstrated (3 β hydroxysteroid dehydrogenase and 20-22 desmolase deficiencies). In 5, a normal postnatal testosterone rise with peak values ranging between 3.4 and 6.4 ng/ml suggested an abnormal peripheral responsiveness to androgens.

The longitudinal study of plasma testosterone in the first months of life may be useful to distinguish secretory defects from peripheral responsiveness abnormalities, thus improving the early choice of gender sex in infants with male pseudohermaphroditism.