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MATURATION OF GONADOTROPHIC FUNCTION IN THE PREMATURE NEONATE.

In order to study gonadotropin secretion in the second half of pregnancy LH and FSH plasma levels were estimated in cord sera from 28 premature and 19 mature neonates as well as serially at weekly intervals in 45 prematures postnatally (p.n.)(22 ♂,23 ♀; gestational age (g.a.) 26-34 wks). Results: LH and FSH cord levels were higher in the premature group for both girls ($P<0.05$) and boys ($P<0.01$) compared to mature neonates. There was no sex difference. Prematures were divided in 3 groups according to g.a.: a:26-28 wks, b:29-30 wks, c:31-33 wks. P.n. from week 2 onwards a strong FSH increase was present only in the premature girls with a trend towards longer FSH elevation in the infants with a shorter g.a. FSH was higher when g.a. was shorter ($P<0.05$).In premature boys FSH was low and showed no p.n. rise. LH levels declined the first week p.n. in girls and boys. In girls a transient increase was seen from week 2 onwards. This increase was stronger and longer in duration when g.a. was shorter. From wk 7-10 LH was higher in gr.a than in gr.c ($P<0.01$). Conclusions: gonadotropin cord levels decrease with progression of gestational age without sex difference. Postnatally the sex difference (low gonadotropin levels in boys and high levels in girls) may be explained either by a more developed central inhibition of gonadotropin secretion, the so-called 'intrinsic restraint', or by a stronger activity of negative feedback by gonadal products in boys than in girls

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FETAL GROWTH IN DIABETIC RAT PREGNANCY - IN VIVO AND IN VITRO STUDIES

Macrosomic infants of diabetic mothers are the result of an early growth delay and an augmented growth towards term. Early growth delay appears to be associated with the increased malformations of these infants. In rat pregnancy diabetes produces with no exception small fetuses. The response of fetal cells to different growth factors has been poorly defined. Therefore 48 h post conception 65 mg/kg streptozotocin i.v. were injected and on day 20 5µCi 3-H thymidine i.p.. On day 21 after a 14 h fast fetuses were delivered and blood glucose (mg/dl), body weight (g), length (cm) and thymidine incorporation (cpm/mg rib cartilage) were determined: M ± SEM; (n).

	BG	weight	length	thym.
Normal (5)	57 ± 7	5.73 ± 0.13	5.1 ± 0.04	317 ± 52
Hyperglyc. (6)	282 ± 18	4.61 ± 0.12	4.89± 0.06	125 ± 21
p	<0.001	<0.001	<0.05	<0.02

Colony formation from isolated chondrocytes of hyperglycemic fetuses in response to pro-/insulin (62.5-250 ng/ml) or IGF I / IGF II (6.25-25 ng/ml) was significantly less (<0.05-0.001) compared to normal fetuses. This demonstrates a defect at the cellular level. Possibly, early growth delay in human diabetes may be explained by a similar mechanism.

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ACUTE EFFECTS OF MATERNAL STRESS ON THE FETAL NEUROENDOCRINE SYSTEM IN RATS AND THEIR PARTIAL PREVENTION BY TYROSINE ADMINISTRATION

Investigating the effects on fetuses during acute maternal stress (immobilization for 2 h) at day 20 or 22 of gestation, respectively, a decreased catecholamine- and ß-endorphin (ß-EP)- as well as an increased LH-RH- and GRF content of the hypothalamus, a diminished ß-EP content of the pituitary, an elevated plasma level of catecholamines as well as of corticosterone were found in fetuses of both sexes. Plasma LH and testosterone were lowered in male fetuses, whereas androstendione was raised in female fetuses. Administration of tyrosine to mother animals 30 min before starting stress prevented partly the effects of stress, mainly on the CNS level.
Conclusion: Prenatal stress changed the fetal neurotransmitter metabolism and the hypothalamic secretion of neurohormones (LH-RH, GRF, CRF) and of opioids as well as sex hormone blood levels which may contribute to long-lasting behavioural changes (i.e. heterotypical sexual behaviour in the male or defeminized playfighting in the female offspring). Tyrosine can prevent - at least in part - these effects.

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SERUM THYROGLOBULIN CONCENTRATIONS IN INFANTS OF VARIOUS MATURITY.

A few studies have suggested that s-thyroglobulin (Tg) in cord blood is higher in premature (PT) than in fullterm (FT) babies. S-Tg was determined by RIA in 33 routinely sampled blood from 33 infants. S-Tg ranged from 2.5-148 ug/l, median 33 ug/l, signficantly higher than in adults ($p< 0.001$). Subsequently, detailed informations on s-Tg, T4, T3, TSH, and thyroid hormone-binding proteins TBG, TBPA, and albumin were conducted in 14 FT, in 6 small-for-date (SGA) infants born at term (chron.age 1-303 days, weight 2400-9000 g) and in 12 PT babies (gest.age 33-36 weeks, chron.age 50-970 days, weight 2930-11800 g).
Results: 1) Wide range values of s-Tg were seen, 21-108 ug/l, median 42 ug/l, in FT, SGA and PT-infants, with no significant differences between the groups, but higher levels than in adults. 2) S-Tg did not change significantly with chronologocal age or body-weight ($R = -0.41$, $p> 0.1$) in the material as a whole, but in FT-infants s-Tg was correlated to s-T4 ($R = 0.48$, $p=0.05$). Individual data showed a decrease of s-Tg with age and increase with s-T3. 3) No correlation was found between s-Tg and s-TSH or thyroid hormone-binding proteins ($p> 0.1$).
Conclusion: S-Tg is increased in FT, SGA and PT-infants compared to adults, but do not correlate to maturity. These findings have to be considered at the neonatal thyroid screening programmes.

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PROBLEMS AND STRATEGIES IN NEONATAL SCREENING FOR CONGENITAL HYPOTHYROIDISM IN A DEVELOPING COUNTRY. (INTRODUCED BY R.ILLIG)

Neonatal screening in India poses more of organizational and socio-economic rather than medical challenges. Based on our data on hypothyroid infants and pilot study of 450 cord sera, the plan for screening considered cord TSH <30 µu/ml as normal, 30 to 80 as borderline, with recall by letters and >80 as suggestive, with recall by home visits. Of the 17240 live births only 12407 cord sera were collected. Envisaging follow up difficulties, T4 was assayed in cord sera when TSH was >30 µu/ml. 2.81% (350) babies needed recall. Only 30% of 302 (2.43%) babies with cord TSH 30 to 80 responded to recall letters and were normal; availability of both cord TSH and T4 helped in excluding hypothyroidism in majority of nonrespondents. 48 (0.38%) newborns had TSH >80 µu/ml; 80% of this group and 100% with TSH >100 were traced by home visits. Hypothyroidism was confirmed in 5/48, biochemically and by thyroid scan. All 5 hypothyroids had cord TSH >300. The incidence in this nonendemic region of India was 1:2481. Thus false elevation of cord TSH 80 to 300 µu/ml was noted in 0.34% with a chance of detecting a hypothyroid 1 in 10 when TSH >80. Maternal TSH of these newborns were normal. The approximate cost of screening per newborn was Rs.9.14. Screening strategies in a developing country besides other requirements must ensure meticulous clerical assistance, co-operation and education of nurses and parents, precise and cost effective technics and facilities for continued surveillance of detected hypothyroids.

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IMPROVED EFFICIENCY OF A TSH SCREENING PROGRAM BY INTRODUCTION OF A TIME RESOLVED FLUOROIMMUNOASSAY (DELFIA®)

A new immunofluorometric assay (FIA) using an Europium labelled ß-hTSH antibody was modified by TORRESANI for TSH determinations in dried blood specimens in 1985 [1]. In order to improve our TSH-Screening program done by radioimmunoassay (RIA), we further modified the assay procedure of FIA and compared both methods(FIA vs RIA) during a three-months-period covering 4100 newborns. Increasing the incubation period from 4 (I) to 16 hours (II) and the size of the sample from 3 mm(I)to 5 mm Ø (II)the following assay parameters improved:

	n	Intraassay CV	Interassay CV	Recovery	Sensitivity µU/ml
RIA	10	9.25 %	14.17%	112 %	7.5
FIA I	10	9.84 %	14.04%	110 %	3.2
FIA II	10	6.35 %	9.85%	102 %	1.5

Regression analysis revealed a low correlation between both methods for TSH< 20 µU/ml ($r= 0.52$) and a good ($r=0.99$) for TSH ≥20 µU/ml. Recall rate (TSH≥ 20 µU/ml) was significantly lower (0.7 vs 1.7 %) and falsely elevated values occurred less frequently (0.2 vs 0.59 %). 3 cases of hypothyroidism were reliably detected by both methods. Conclusions:The handling of microtitration plates in FIA is more time consuming compared to common RIA procedures and asks for further automatization. However, a substantially lower recall rate improves the practicability and cost/benefit ratio of the TSH screening program.
[1]Clinical Chemistry, 1986, in press.