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PREVALENCE OF ALLERGY IN RELATION TO NUTRITIONAL ALLERGEN CHALLENGE, GASTROINTESTINAL AND RESPIRATORY TRACT INFECTIONS (RTI) IN AT RISK INFANTS

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Aim: Development of allergy was studied in relation to nutritional allergen challenge and infectious diseases during the first 16 months of life.
Methods: 240 infants were allocated either to breast-milk feeding during first 5 months, followed by a hypoallergenic diet (**BM**), or hypoallergenic whey formula feeding (Nidina HA, Nestlé: **HA**).
Results: In a high risk group of infants (positive family history **and** cord blood IgE > 0.5 kU/L) prevalence of atopic disease was similarly frequent in both nutritional groups (BM 12 %, HA 11 % at age 4 months; 32 %, 39 % at age 16 months resp.). While **upper RTI** equally frequent occurred in both nutritional groups, the HA group showed a significantly higher prevalence of **lower RTI** (BM 12 %; HA 36 %; $p < 0.05$), associated with a more frequent development of respiratory allergy (29 % with lower RTI; 2 % without lower RTI; $p < 0.005$) Other atopic diseases (skin and gastrointestinal symptoms) occurred in 19 % of infants with lower RTI and 22 % without lower RTI (n.s.). Prevalence of atopic disease was also significantly different in relation to gastrointestinal infections (41 % with vs. 25 % without), although gastrointestinal intolerance was similar in both groups (38 % vs. 40 %).
Conclusion: While there was a similar allergy prevalence in Nidina HA fed and breast-milk fed infants at risk, a particular group of infants exposed to gastrointestinal or lower RT infections showed a higher allergy prevalence in association with Nidina HA feeding and should therefore favorably be nourished by breast-milk.

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ANTENATAL GLUCOCORTICOID ADMINISTRATION IN A NATIONWIDE COHORT OF VERY PRETERM AND VERY LOW BIRTHWEIGHT INFANTS: FOLLOW-UP AT 5 YEARS OF AGE

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The relationship between antenatally administered glucocorticoids and overall outcome at 5 years of age, applying stepwise logistic regression analyses with 14 confounding factors, was studied. Data were collected on 1338 liveborn infants (gestational age <32 wks and/or birthweight <1500 g) born in 1983 in the Netherlands. Data were analyzed in a subset of 671 infants (gest. age ≥26 and <32 wks) of whom 642 had been assessed at 5 years of age (loss to follow-up 4.3%). Overall outcome expressed as impairment, disability or handicap (WHO, 1980) was based on: congenital malformation, neuromotor function, mental development, hearing, visual function, language and speech development, musculoskeletal system, respiratory tract. There was no higher risk of impairment at 5 years of age in children of treated mothers versus non-treated mothers. With disability or handicap as outcome variables there was a significant interaction of glucocorticoid treatment and tocolysis. In the presence of tocolysis (>24 hours) there was no higher risk on disability or handicap at 5 years of age. In 13 children whose mothers received no tocolysis or only <24 hours, the antenatal administration of glucocorticoids was associated with a significantly higher risk on disability or handicap, probably a result of confounding by indication of the treatment.

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LONG-TERM NEUROLOGICAL AND COGNITIVE OUTCOME OF CHILDREN WHO WERE PRENATALLY EXPOSED TO COUMARINS, A PILOT STUDY.

Van der Veer E[1], Olthof E[1], De Vries TW[3], Heijmans HSA[2], Smrkovsky M[2], Geven-Boere LM[4], & Touwen BCL[2]. Univ. Hospital[1] & State Univ.[2] Groningen; Med. Center Leeuwarden[3]; Dutch Fed. Thrombosis Centers[4], s'Gravenhage, the Netherlands. Perinatal studies have shown that intra-uterine exposure to coumarins may influence the development of bone and neural tissues. To study the late effects of prenatal exposure to coumarins, physical, neurological, and mental development were assessed. In a pilot study 21 index (I) children and 17 controls (C) were examined at the age 8-10 years. **Results:**

number of children	IQ-score I	IQ-score C	Reading I	Reading C
no participation	-	2	-	2
high	2	1	2	-
average	15	14	13	14
low	3	-	4	1
unable to score	1	-	2	-
mean score:	99	103	4.7	5.1

Neur.exam (n; NOS) I	Neur.exam (n; NOS) C	Paed.exam (n) I	Paed.exam (n) C	
18 (55-62)	14 (54-61)	14	11	normal
2 (42-48)	3 (55-58)	6	6	minor
1 (19)	- -	1	-	abnormal

Conclusions: No statistical significant differences were found between the index and control group in this small study. Nevertheless, an indication seemed to be present for a possible effect of prenatal exposure to coumarins. Five children showed minor neurological dysfunction (MND); the two children with the more serious variant (NOS = neurological optimality score 42-48) had both been exposed to coumarins. The distribution of the IQ-scores corresponded with the distribution of the scores in the Dutch standardization sample. There were 3 children with an IQ < 80. All three had been exposed to oral anticoagulants during pregnancy in the 2nd and 3rd (n = 2), or in the 3rd trimester only. One child with severe abnormalities, namely hypoplasia of both optic nerves, cerebral palsy and retardation, had been exposed during the 2nd and 3rd trimester of pregnancy. Paediatric exam directly post partum revealed no abnormalities. In view of these results a large follow-up study is required.

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ANTIOXIDANT ADMINISTRATION TO THE MOTHER PREVENTS OXIDATIVE STRESS ASSOCIATED WITH BIRTH IN THE NEONATAL RAT.

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With birth circulatory and respiratory changes ensue leading to fetal oxidative stress evidenced by changes in the glutathione status. Pregnant rats receiving NAC during gestation were sacrificed at 21±1d. Fetuses delivered by c-section and immediately sacrificed and newborns at 24h age. Livers were processed(1) and GSH and GSSG determined. Results were as follows:

	Fetuses Controls	Fetuses +NAC	Neonates Controls	Neonates +NAC	Pregnant rats Controls	Pregnant rats +NAC
GSH (µmol/g)	3.1±.4 (6)	3.9±.2** (5)	3.4±.7 (10)	3.7±.3 (5)	5.7±.9 (9)	5.7±1.2&& (4)
GSSG (nmol/g)	1.0±.2 (5)	5.0±2** (5)	12±5## (11)	9±4 (5)	30±10& (4)	52±3&& (4)
GSH/GSSG	3100	981	283	471	172	112

**p<0.01, *p<0.05:NAC/Controls; ##p<0.01, #p<0.5:Neonates/Fetuses; &&p<0.01, &p<0.05: Pregnant rats/Neonates.

We conclude that oxidative stress associated with birth in rat fetuses might be partially prevented by NAC given to the mother during gestation.

(1) Viña J et al; *Biochem J* 170; 627-630 (1978)

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ONSET MORTALITY IN INSULIN DEPENDENT DIABETES MELLITUS

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From data of the second nationwide incidence study in 1988-1990 on Insulin Dependent Diabetes Mellitus (IDDM) in children aged 0-19 years and of the population based register of mortality data the **onset mortality** in various age groups was calculated (table). Compared to the previous nationwide study in 1978-1980, the incidence of IDDM had increased, especially in the age group 4-19 years, but the onset mortality risk was significantly lower, although not yet zero. It is important to continue to monitor the mortality of IDDM cases for trends and to get clues for prevention of such deaths.

	1978-1980			1988-1990		
age group	deaths	new IDDM patients	mortality risk % (95% CI)	deaths	new IDDM patients	mortality risk % (95% CI)
0-4	3	183	1.64(0.33-4.79)	1	178	0.56(0.01-3.13)
5-9	1	363	0.28(0.01-1.53)	-	331	-
10-14	2	527	0.38(0.05-1.37)	1	496	0.20(0.01-1.12)
15-19	5	391	1.28(0.42-2.98)	1	522	0.19(0.01-1.07)
0-19	11	1464	0.75(0.38-1.34)	3	1527	0.20(0.04-0.57)

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CALCIUM METABOLISM IN CHILDREN WITH PRECOCIOUS PUBERTY TREATED WITH GnRH AGONIST

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In order to evaluate the effects of slow-release gonadotropin-releasing hormone analogues on calcium metabolism, we studied 10 (7 female, 3 male) children with central precocious puberty, treated with GnRH agonist D-Trp6-GnRH (Decapeptyl, Ipsen), their mean ± SD age was 5.5 ± 3.1 years. The patients were studied before the beginning (t0) and after 6 months of treatment (t1). Twelve sex and age-matched healthy children were also studied. We evaluated Bone Mineral Content (BMC) and serum levels of calcium, phosphorus, magnesium, PTH (M 44-68), CT, 25-OH-vitamin D

	t0	t1	Controls
BMC (g/cm2)	0.51 ± 0.12**	0.42 ± 0.11*	0.39 ± 009
Ca (mg/dl)	9.3 ± 1.1	9.2 ± 1.0	9.2 ± 0.9
P (mg/dl)	3.8 ± 1.1	3.9 ± 1.0	3.9 ± 1.1
Mg (mg/dl)	2.2 ± 0.4	2.1 ± 0.6	2.2 ± 0.6
25-OH-D (ng/ml)	23.11 ± 4.87	22.67 ± 4.64	23.5 ± 5.80
PTH (ng/dl)	6.02 ± 5.11	5.33 ± 4.25	6.23 ± 5.38
CT (pg/ml)	37.41 ± 16.1	35.99 ± 14.79	36.75 ± 15.34

t0 vs controls: * p< 0.01, ** p< 0.001

At t0, the 24 hour excretion of calcium, phosphorus and magnesium were similar to control group and did not changed at t1. Our study shows that children with precocious puberty have an increased BMC and that gonadotropin-releasing hormone analogues modify bone density, with a consequent its reduction; this reduction seems not related to calcium metabolism.