



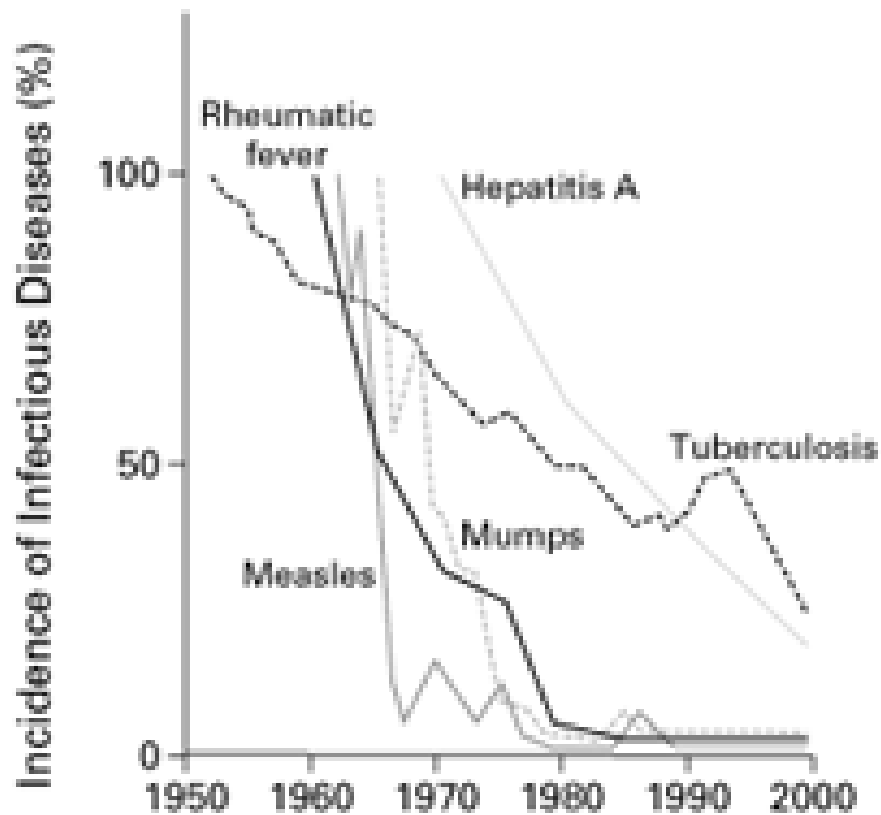
Stress during Pregnancy: Maternal Endocrine-Immune Imbalances and Fetal Health

Petra Arck, MD

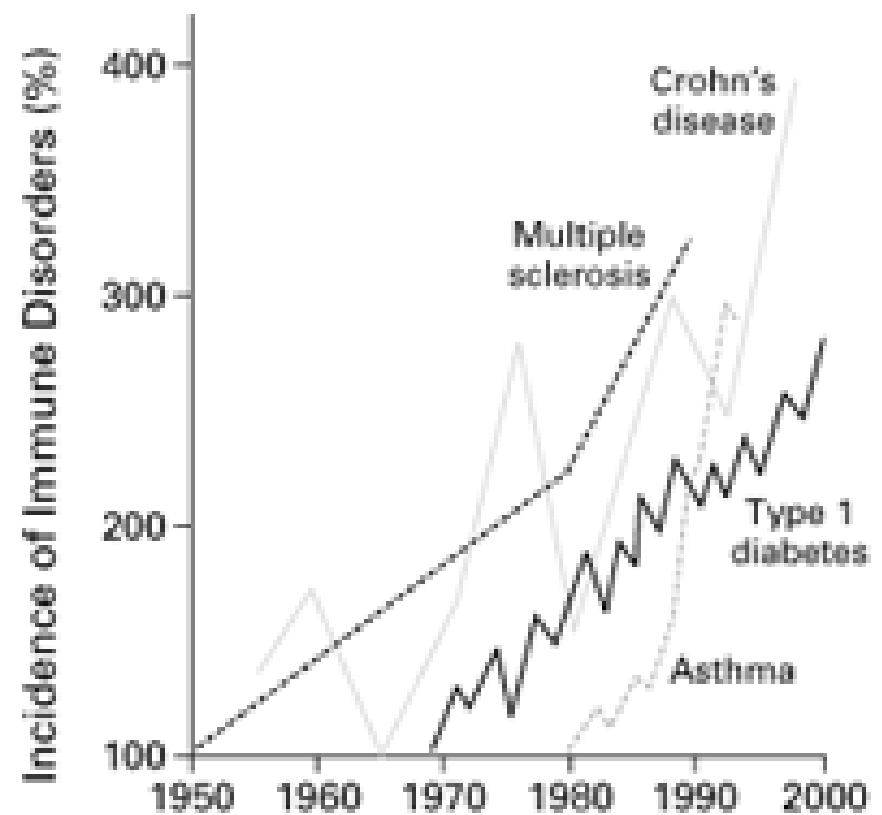


Incidence of Infectious Diseases and Immune Disorders

A



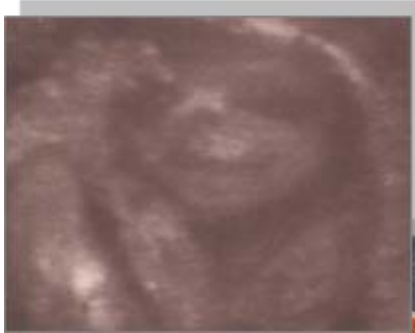
B



Environmental Factors



Developmental Milestones In Life



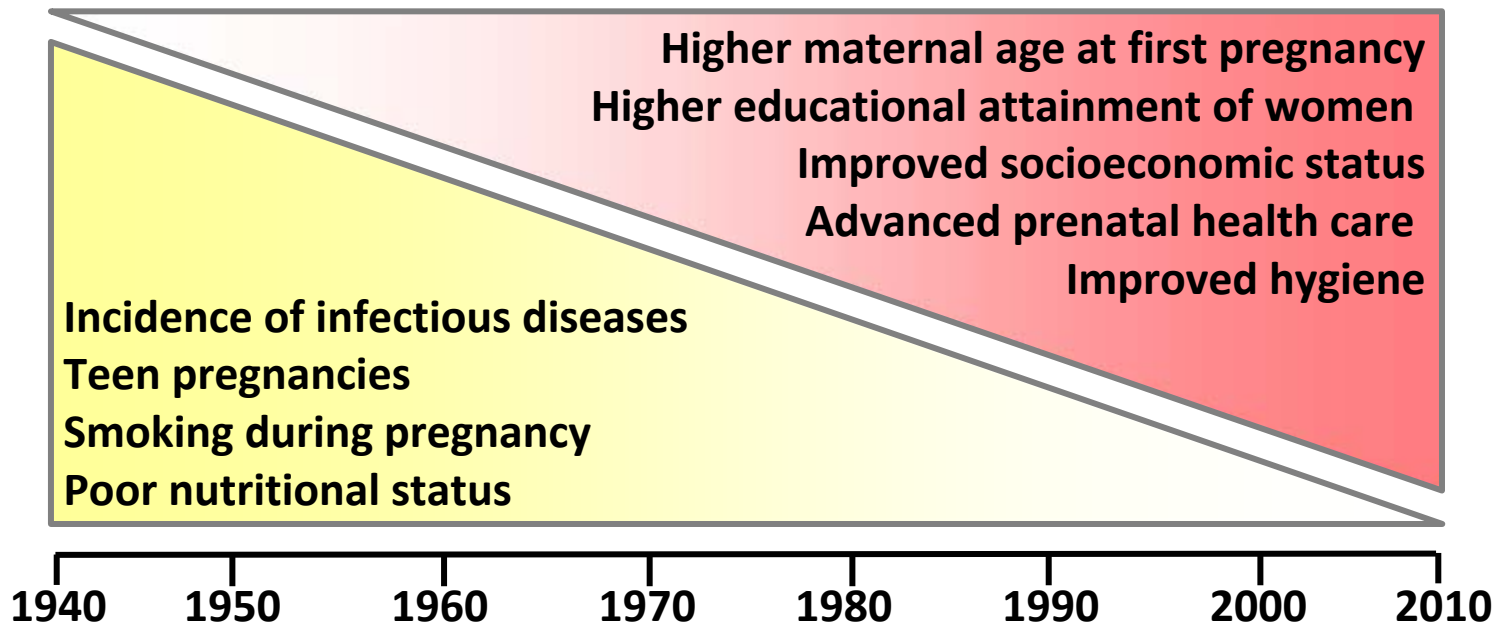
- *in utero*
- perinatal
- neonatal
- first years

Concept of the Fetal Programming Hypothesis

Environmental factors during pregnancy affect fetal development and trigger or aggravate the onset of disease in later life of the child



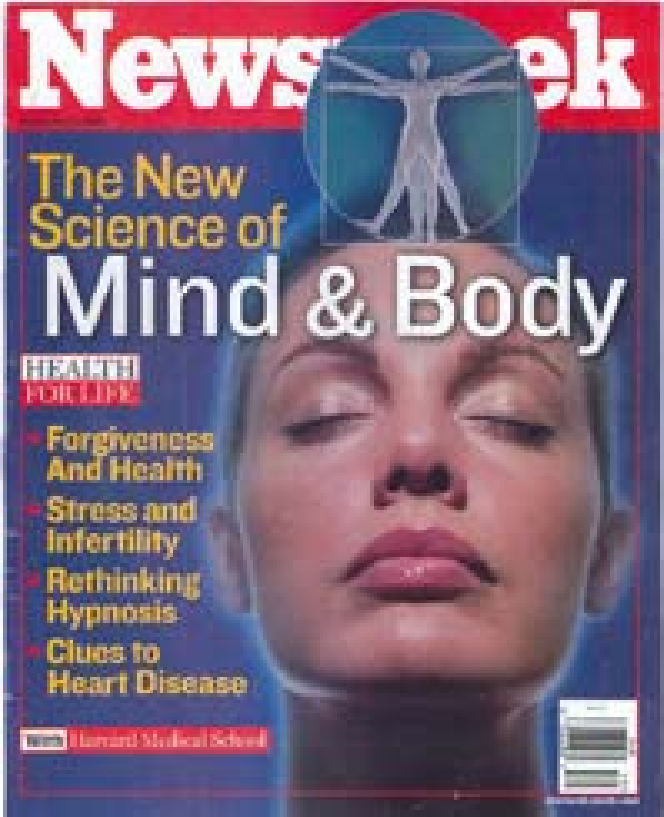
Plasticity of 'Women's Environment' over the past Decades



Plasticity of Environmental Challenges over the past Decades



Epidemiological Data Indicate Strong Link between Stress and Pregnancy Complications



High Social Rank Female Primates Have Higher Incidence of Miscarriages



Reproductive constraints on aggressive competition in female baboons

Craig Packer*, D. A. Collins†, A. Sindimwo‡
& J. Goodall‡

* Department EEB, University of Minnesota,
1987 Upper Buford Circle, St Paul, Minnesota 55108, USA

† ICAPB, Ashworth Laboratory, University of Edinburgh,
Edinburgh EH9 3JT, UK

‡ Gombe Stream Research Centre, Box 185, Kigoma, Tanzania

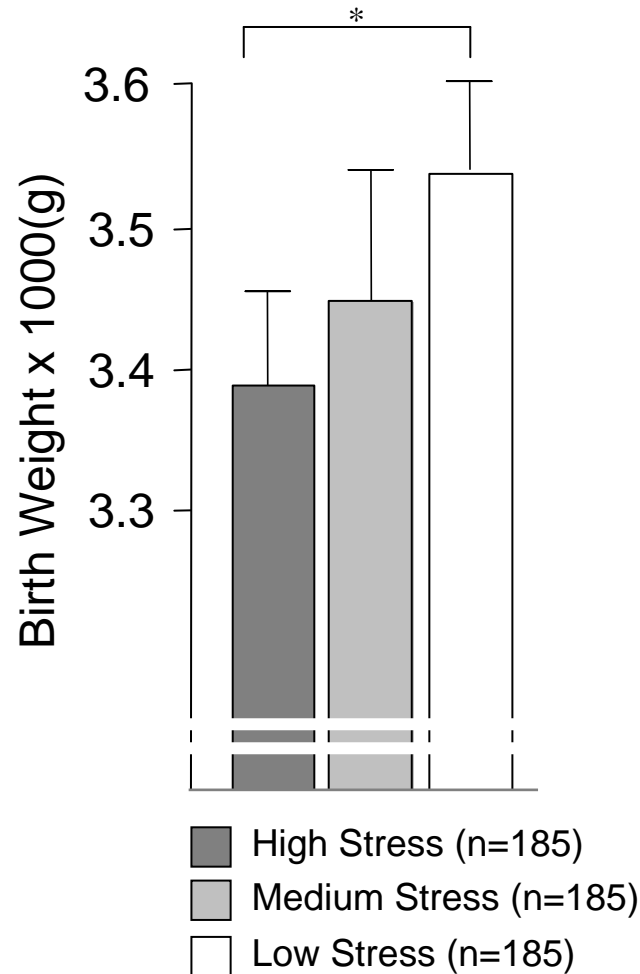
COMPETITIVE interaction between females of the same social group is characteristic of most primate species¹⁻³. In Old World monkeys, females of high social rank maintain priority of access to scarce resources and harass low-ranking companions¹⁻⁶. But different field studies have found differing correlations between female dominance and reproductive success: several populations show an advantage of rank whereas others do not^{1,3,5,7}. Although such variation may reflect divergent levels of predation, food availability or social stress in different environments, female competitive ability may also be balanced by significant reproductive costs and thus be subject to strong stabilizing selection. We report here that high-ranking female baboons (*Papio cynocephalus anubis*) at Gombe National Park, Tanzania, enjoy shorter interbirth intervals, improved infant survival, and accelerated maturation of their daughters. These advantages, however, are countered by a significantly higher probability of miscarriage, and a proportion of high-ranking females suffer from reduced fertility.

Increased Risk for Spontaneous Miscarriage In Humans

<i>Parameter</i>	<i>Normally progressing pregnancy</i>	<i>Subsequent spontaneous abortion</i>
Age, median (years)	29.6 (297)	31.2 (38)
BMI, median (kg/m ²)	22.1 ^a (288)	20.6 ^a (37)
Progesterone, median (ng/ml)	14.7 ^b (298)	12.7 ^b (37)
QoL-SF12, median (PCS)	52.0 (286)	51.7 (38)
Previous miscarriage (%)	25.3 (150)	20.8 (24)
Living with partner (%)	97.6 (292)	97.4 (38)
University degree (%)	32.4 (296)	44.7 (38)
ADS (score)	10.0 (290)	9.2 (38)
Social support (score)	4.73 (295)	4.73 (38)
PSQ (score)	28.8 (292)	31.7 (37)
PSQ demands (score)	33.3 ^c (295)	40.0 ^c (37)
Chronic disease ^d (%)	9.4 (298)	15.8 (38)
Medication ^e (%)	10.1 (298)	5.3 (38)
Employed (%)	83.4 (296)	73.7 (38)

Values in parentheses are the number of study participants for whom data were available. Values not in parentheses are median values, unless otherwise stated. Values with the same superscript letter are significantly different: ^a*P* = 0.024, ^b*P* = 0.037, ^c*P* = 0.024.

High Stress Perception is Associated with Lower Birth Weight *



* Gestational age at time of delivery \geq 37 weeks

Low Social Support, High Stress Perception, Smoking and Birth Weight

	Group	Low Support	High Support	<i>P</i>[†]
Child body weight (in g) *	Non-smoker	3418 ± 384	3542 ± 503	0.001
	Smoker	3175 ± 453	3571 ± 409	0.078

*presented as mean ± standard deviation

Mothers' Stress and Anxiety during Pregnancy is Associated with Increased Risk for Asthma in the Children

OR (95% CI) for asthma at 7½ y

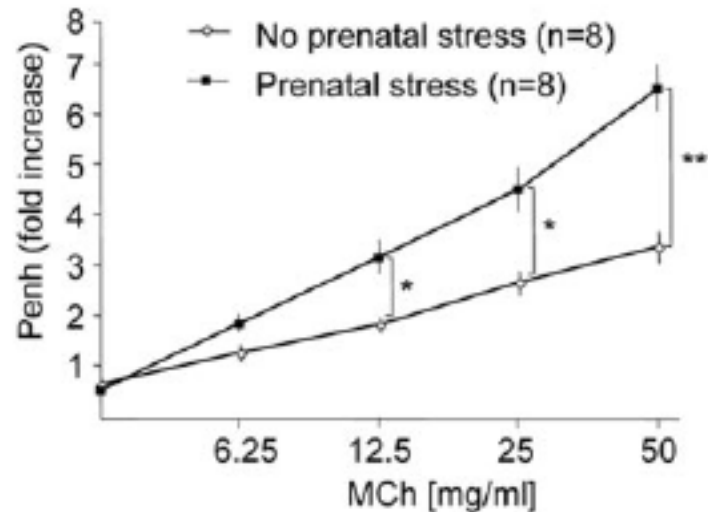
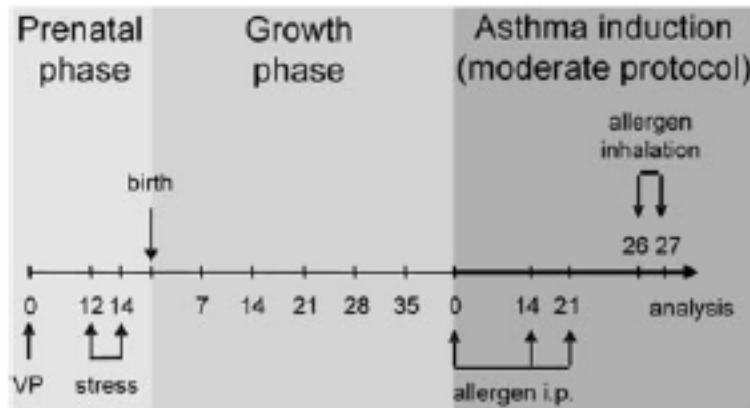
	N asthma/no asthma (% with asthma)	Crude	Adjusted*
Maternal anxiety at 18 wk			
1st quartile (0-2)	198/1734 (10.2%)	1 (reference)	1 (reference)
2nd quartile (3-4)	174/1176 (12.9%)	1.30 (1.04-1.61)	1.24 (1.00-1.55)
3rd quartile (5-7)	200/1295 (13.4%)	1.35 (1.10-1.67)	1.32 (1.07-1.63)
4th quartile (8-16)	163/870 (15.8%)	1.64 (1.31-2.05)	1.53 (1.22-1.93)
<i>P</i> (trend)		<.001	<.001
Maternal anxiety at 32 wk			
1st quartile (0-2)	168/1582 (9.6%)	1 (reference)	1 (reference)
2nd quartile (3-4)	185/1232 (13.1%)	1.41 (1.13-1.77)	1.36 (1.09-1.71)
3rd quartile (5-7)	204/1308 (13.5%)	1.47 (1.18-1.82)	1.42 (1.14-1.77)
4th quartile 8-16)	178/953 (15.7%)	1.76 (1.40-2.20)	1.65 (1.30-2.08)
<i>P</i> (trend)		<.001	<.001



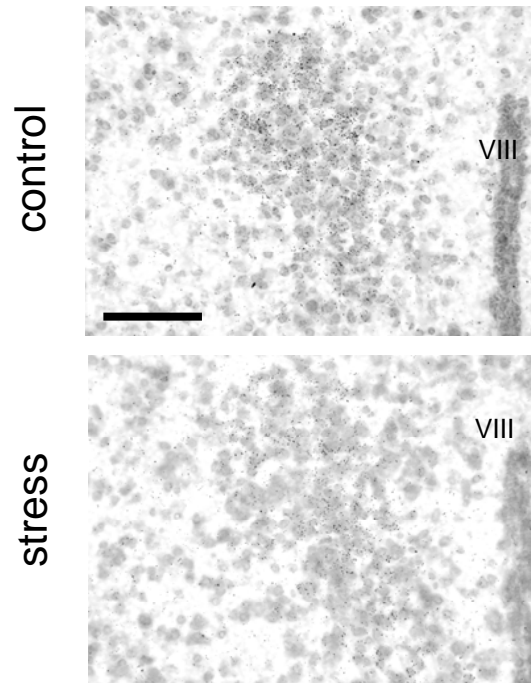
A Stress Mouse Model



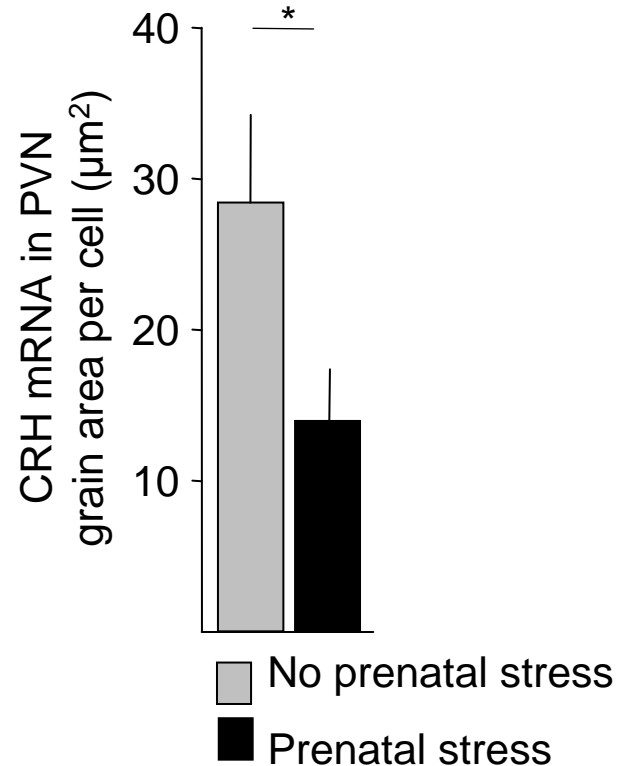
Prenatal Stress Challenge is Associated with Airway Hyperresponsiveness in Murine Adult Offspring



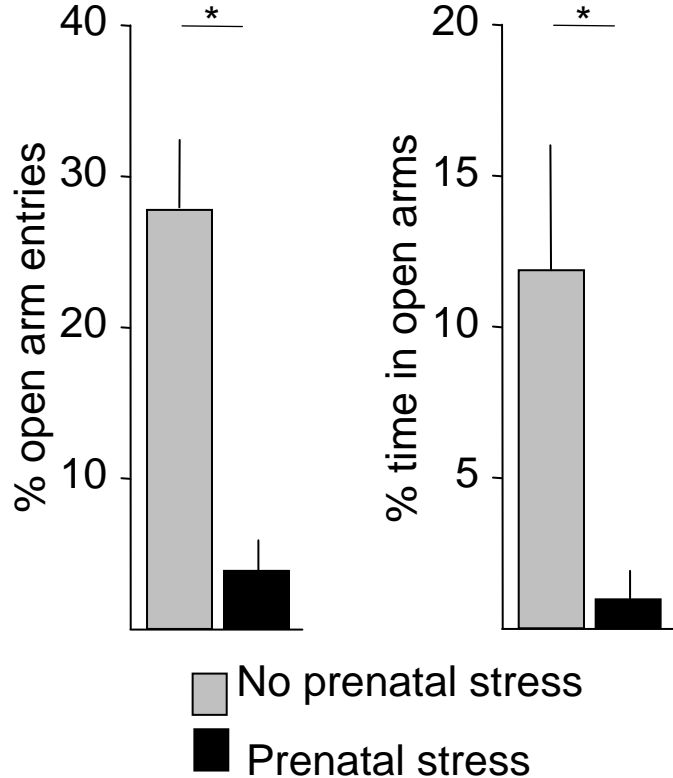
Prenatal Stress Reduces Expression of CRH mRNA in the Paraventricular Nucleus of Mice



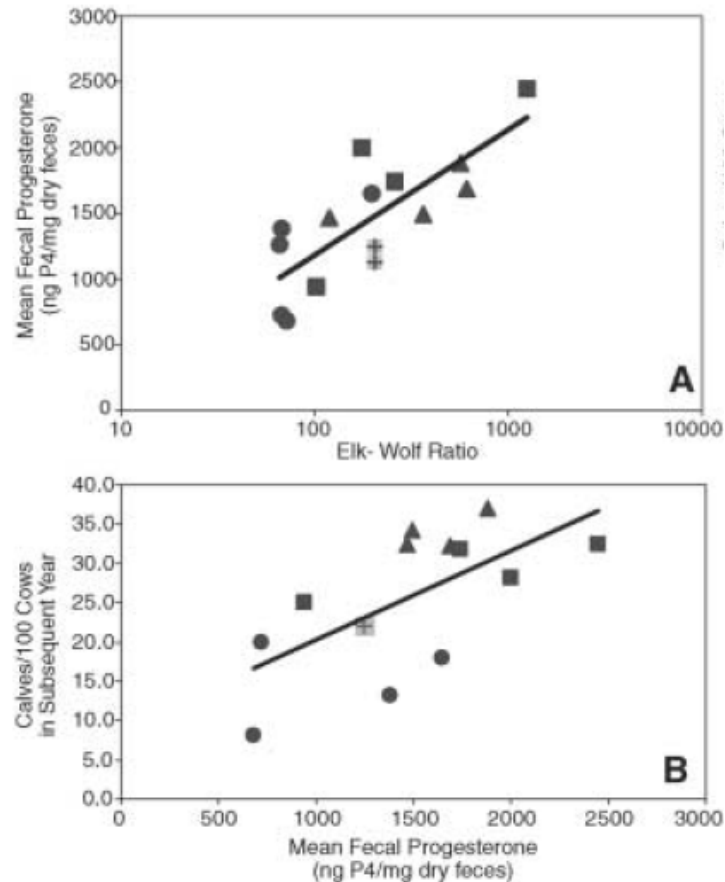
VIII= third ventricle



Prenatal Stress Increases Anxiety in Mice



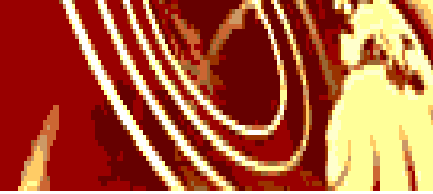
Prenatal Stress Decreases Progesterone Levels in Elks



Risk Factors for Spontaneous Miscarriage

<i>Parameter</i>	<i>Normally progressing pregnancy</i>	<i>Subsequent spontaneous abortion</i>
Age, median (years)	29.6 (297)	31.2 (38)
BMI, median (kg/m ²)	22.1 ^a (288)	20.6 ^a (37)
Progesterone, median (ng/ml)	14.7 ^b (298)	12.7 ^b (37)
QoL-SF12, median (PCS)	52.0 (286)	51.7 (38)
Previous miscarriage (%)	25.3 (150)	20.8 (24)
Living with partner (%)	97.6 (292)	97.4 (38)
University degree (%)	32.4 (296)	44.7 (38)
ADS (score)	10.0 (290)	9.2 (38)
Social support (score)	4.73 (295)	4.73 (38)
PSQ (score)	28.8 (292)	31.7 (37)
PSQ demands (score)	33.3 ^c (295)	40.0 ^c (37)
Chronic disease ^d (%)	9.4 (298)	15.8 (38)
Medication ^e (%)	10.1 (298)	5.3 (38)
Employed (%)	83.4 (296)	73.7 (38)

Values in parentheses are the number of study participants for whom data were available. Values not in parentheses are median values, unless otherwise stated. Values with the same superscript letter are significantly different: ^a*P* = 0.024, ^b*P* = 0.037, ^c*P* = 0.024.



Soaring stress hormones hit pregnancy





Continuation of Prospective Birth Cohort

1st Trimester

- Recruitment
- P Analysis

- Miscarriage

Birth

- Birth Weight

Children's Age 3 Years

- Incidence of Atopic Diseases

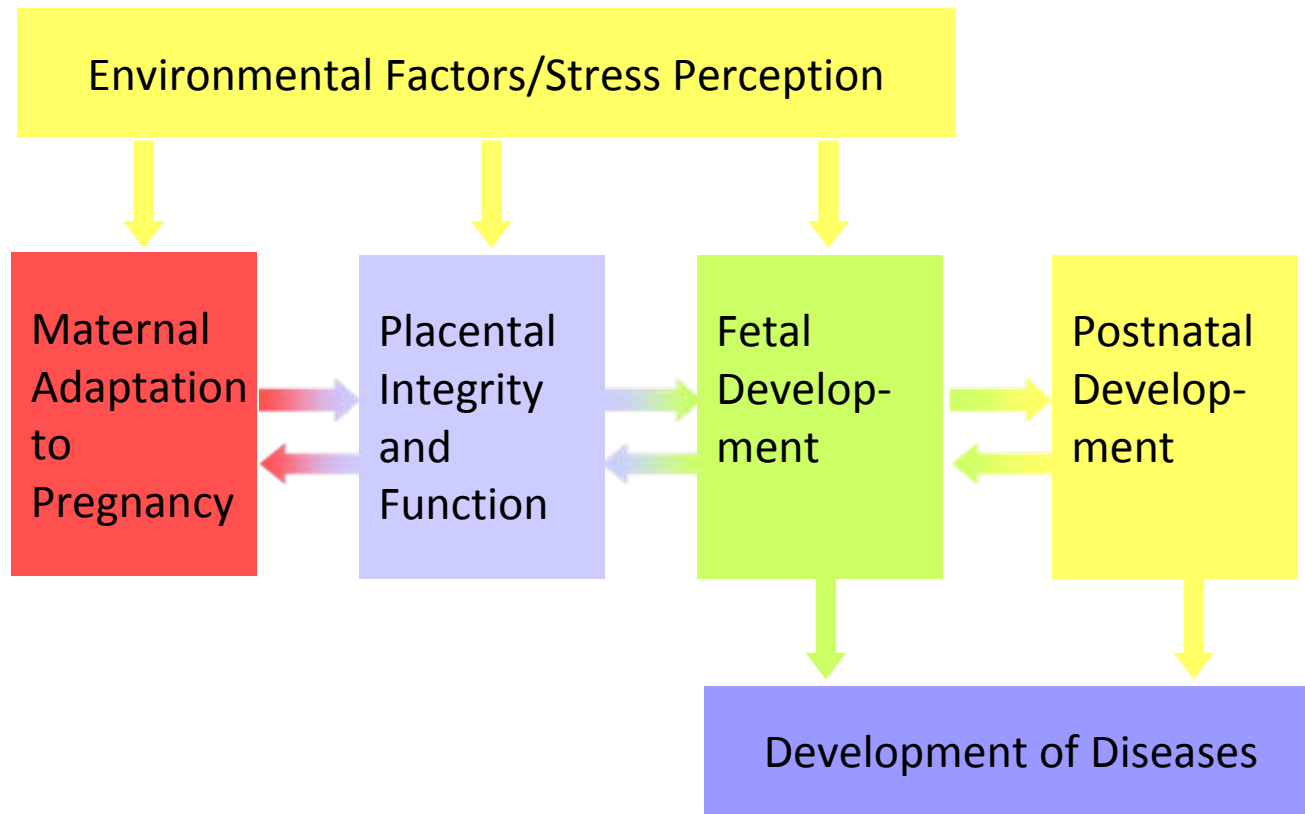


Association between Progesterone in Early Pregnancy and Atopic Dermatitis in Children

Parameters	Boys (n=149)			Girls (n=124)		
	Crude OR ^a	95% CI	p-Value	Crude OR ^a	95% CI	p-Value
<i>Endocrine</i>						
Progesterone (ng/ml) *	0.99	0.93-1.06	0.78	0.83	0.73-0.94	0.004
Estradiol (ng/ml) *	1.00	0.99-1.00	0.87	1.00	0.99-1.00	0.40
<i>Parental</i>						
2 allergic parents	5.22	1.43-19.1	0.01	4.30	0.56-32.9	0.16
1 allergic parent	3.03	0.97-9.44	0.05	0.63	0.20-2.03	0.44
No allergic parent	1	-	-	1	-	-

Log. Regressionsanalyse, * = per unit increase

Simplified Scenario on Pathogenesis of Fetal Origin of Diseases



Equalize Life Chances

