

# Ten ontogenetic theses for promotion of health and primary prevention of important diseases by a prenatal and early postnatal neuro-endocrine-immune prophylaxis\*

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**Thesis 1:** Fundamental processes of life—such as sexuality and reproduction, metabolism, growth, information processing, and immune responsiveness—are controlled by the neuro-endocrine-immune system (NEIS). This comprehensive system consists of the three subsystems—the neuronal system, the endocrine system and the immune system—which are connected with each other by chemical messengers, i.e. by neurotransmitters, hormones and cytokines. The brain is the central controller of this complete system.

**Thesis 2:** In extensive experimental, epidemiological and clinical investigations we have demonstrated during the last 25 years that neurotransmitters, hormones, and cytokines represent during critical pre- and early postnatal developmental periods of the NEIS—especially of the brain—irreversibly acting organizers of the NEIS [1-2]. Thus, their environment-dependent quantity codetermines during these critical developmental periods the quality, i.e. set point of their own controllers and hence the functional and tolerance ranges of their feedback control systems (“ontogenetic basic rule”).

**Thesis 3:** Life is based on interactions between genes and the environment. Neurotransmitters, hormones, and cytokines are mediators for these interactions. Furthermore, in critical developmental periods of the

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NEIS, they act as epigenetic “ontogens.” Thus, they can affect the life-long expressivity of specific genes [1]. Hence, they can decisively codetermine the environment-dependent self-organization process of the NEIS and hence salutogenesis and pathogenesis. This thesis recently found a molecular biological confirmation by other authors [8, 10].

**Thesis 4:** Unphysiological concentrations of neurotransmitters, hormones and cytokines during critical organization periods of the NEIS can act as “endogenous teratogens,” leading to pre- and early postnatally acquired, life-long malfunctions and important diseases of reproduction, metabolism, and the cardiovascular system, of benign and malignant growth, of information processing and of the immune system. Hence, it was postulated since 25 years to supplement “structural teratology”—the science of macroscopic malformations—by “functional teratology,” i.e. the science of pre- and early postnatally acquired malfunctions, which are often associated with microscopic malformations, especially of the brain [1–7].

**Thesis 5:** This “functional teratology”—i. e. teratophysiology, teratopsychology, and teratoimmunology—opens new possibilities of a “neuroendocrine prophylaxis” and “neuroendocrine-immune prophylaxis” (NEIP), respectively, for preventive medicine, which can and will increasingly supplement and even partially substitute the curative and palliative medicine. Thus, for more than two decades 10 recommendations for a “neuroendocrine prophylaxis” were presented at several international conferences and also published, and could be even partly realized in the meantime. The aim is the prohibition and timely correction of the following burden by the environment during the prenatal and early postnatal organization periods of the NEIS, in which the mother represents the immediate environment of the unborn and newborn:

1. Iodine deficiency
2. Gestational diabetes
3. Oxygen deficiency
4. Stress
5. Gestoses, infections and vitamin deficiencies
6. Quantitative and/or qualitative malnutrition
7. Ionizing radiation, and most of all environmental chemicals which act as “neuroendocrine disruptors” and “neuro-endocrine-immune teratogens,” respectively.
8. Alcohol, nicotine and drugs
9. Psychosocial deprivation
10. Abnormal concentrations of hormones and neurotransmitters, which are caused primarily by genetic defects, but they can be prevented by a neuroendocrine substitution in good time.

Consequently, the following concrete postulates and recommendations can be concluded for a pre- and early postnatal preventive medicine:

1. Optimizing of iodine prophylaxis
2. Improvement of diagnosis and treatment of women with gestational diabetes
3. Prevention of oxygen deficiency in fetuses and newborns
4. Avoidance of stressful situations in pregnant women, newborns and infants
5. Optimizing the treatment of gestoses; prevention of infections—especially by vaccination—and prevention of vitamin deficiencies
6. Avoidance of over- and under-nutrition as well as of qualitative malnutrition; increased breast-feeding
7. Avoidance of radiation for pregnant women, embryos and fetuses; most of all, worldwide prohibition of environmental chemicals with functional-teratogenic actions; systematic testing of such substances for functional-teratogenic actions in experiments.
8. Strict avoidance of alcohol, nicotine, drugs and potentially functional-teratogenic active medications during pregnancy and breast-feeding.
9. Prevention of psychosocial deprivation in newborns, babies and infants
10. Improvement of neuroendocrine and genetic diagnoses of inborn errors of metabolism and timely corrections of genetically conditioned abnormal concentrations of hormones, neurotransmitters and cytokines.

**Thesis 6:** With the aid of such measures, e.g. optimizing the pre- and early postnatal nutrition, prohibition of environmental chemicals acting as “neuro-endocrine teratogens” and prevention of early postnatal psychosocial deprivations, can be—and could be already—prevented life-long malfunctions and important diseases in millions of human beings. Their physical, psychical and mental capacities can be clearly improved.

**Thesis 7:** For inauguration of “functional teratology” and “neuroendocrine prophylaxis” our group in Berlin organized three International Symposia during the past three decades with experts from four continents. Their proceedings as well as two monographs, about 50 articles in text- and handbooks, and about 200 original papers were published by our group on this topic in well-known Publishing Companies (Barth, Elsevier, Karger). More remarkable is that only most recently after the publication of the monograph of P. Nathanielsz [11] on “The Life in the Womb - Origin of Health and Disease” are the aforementioned cognitions and recommendations extolled worldwide by the media as newest achieve-

ments with extreme importance for health policy.

**Thesis 8:** As we had supplemented “structural teratology” by “functional teratology” 25 years ago, “structural genomics” was recently supplemented by “functional genomics” [12], in order to achieve higher performance for “Public Health.” In my opinion, “functional teratology” represents a decisive part for preventive medicine within “functional genomics,” i.e. an environment-dependent codetermination of life-long control of gene expressions.

**Thesis 9:** Therefore, the following proposals are made for the European Action Program for Environment and Health: 1. Introduction of an official interdisciplinary task force of geneticists and environmental physicians for promotion of Public Health, as it was recently done in the USA [9], and 2. Increased support of the research work for environmental and preventive medicine as well as for genetics and promotion of the cooperation between both. In my opinion, by such measures neuroendocrine prophylaxis could reach a similar importance in this century as immune prophylaxis in the last one. The past millennium was the era of curative, palliative and rehabilitative medicine plus immune prophylaxis. The new millennium should become an era of general and gene-dependent selective neuro-endocrine-immune prophylaxis (NEIP)—including worldwide birth control—plus curative, palliative and rehabilitative medicine.

**Thesis 10:** The hologenesis, existing of phylogenesis and ontogenesis, is based on changing interactions between the genome and the environment by modifications, mutations, polymorphisms, recombinations and selections. In this context, the following heuristic developmental steps and theories of the past two centuries should be mentioned:

#### *Ia First half of the 19th century*

1. Lamarck: Theory of the inheritance of acquired characteristics, which is recognized today as nongenetic, mainly materno-fetal, intergenerative transmission of persistent modifications.
2. St. Hilaire: Founder of “Structural Teratology” as science of macroscopic malformations (teras = enigma).

#### *Ib Second half of the 19th century*

1. Darwin: Theory of evolution by natural selection.
2. Haeckel: Founder of ecology.
3. Mendel: Discovery of rules for inheritance; founder of genetics.

#### *IIa First half of the 20th century*

1. Johannsen: Introduction of the terms gene, genotype and phenotype.

2. DeVries et al.: Confirmation of Mendel and introduction of the term mutation.
3. Spemann: Description of an “organizer effect” for embryogenesis.

#### *IIb Second half of the 20th century*

1. Watson and Crick: Elucidation of the spatial structure of genes, founder of “structural genomics.” Since 1980 worldwide project for the structural elucidation of the human genome.
2. Theories of “functional teratology” and “neuro-endocrine-immune prophylaxis” (Dörner et al. since 1975).
3. Beginning transition from “structural genomics” to “functional genomics,” especially by a comprehensive quantitative recording of gene expressions with the aid of “DNA/RNA-arrays” [12].

#### REFERENCES

- 1 Dörner G. Hormones and Brain Differentiation. Amsterdam-Oxford-New York: Elsevier; 1976.
- 2 Dörner G. Die Ontogenese des neuroendokrinen Systems als kinetischer Prozess. Vortrag auf der Jahrestagung der Leopoldina 1977, Nova acta Leopoldina 1980; **237**:279–291.
- 3 Dörner G, McCann SM, Martini L, editors. Systemic Hormones, Neurotransmitters and Brain Development. Basel, München, Paris, London, New York, New Delhi, Singapore, Tokyo, Sydney: Karger; 1986.
- 4 Dörner G. Significance of hormone-dependent brain development and pre and early postnatal psychophysiology for preventive medicine. In: Fedor-Freybergh PG, Vogel MLV, editors. Carforth: The Parthenon Publishing Group; 1988.
- 5 Dörner G, Plagemann A. Perinatal hyperinsulinism as possible predisposing factor for diabetes mellitus, obesity, and enhanced cardiovascular risk in later life. *Horm Metab Res* 1994; **26**:213–221.
- 6 Dörner G. Environment and gene dependent effects of hormones and neurotransmitters in mammals. *Umweltbundesamt Texte* 1998; **50**:71–81.
- 7 Dörner G, Hüllemann KD, Tembrock G, Vogel F, Wessel KF, Zänker KS, editors. *Genom und Umwelt*. Bielefeld: Kleine Verlag; 2000.
- 8 Francis D, Diorio J, Liu D, Meaney MJ. Nongenomic transmission across generations of maternal behavior and stress responses in the rat. *Science* 1999; **286**:1155–1158.
- 9 Khoury MJ. Relationship between Medical Genetics and Public Health: Changing the paradigm of disease prevention and the definition of a genetic disease. *Am J Med Genetics* 1994; **71**:289–291.
- 10 Levitt P, Harvey JA, Friedmann E, Simansky K, Murphy H. New evidence for neurotransmitter influences in brain development. *Trends Neurosci* 1997; **20**:269–274.
- 11 Nathanielsz P. *The Life in the Womb: Origin of Health and Disease*. Ithaca, New York: Promethean Press; 1999.
- 12 Phimister B, Collins FS, Lander ES, et al. Going global; microarrays and macroconsequences; array of hope. *Nature Genetics* 1999, **21 Suppl 1**:1–60.