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Medicine

EPIGENETIC FACTORS THAT INFLUENCE GROWTH AND DEVELOPMENT

Ramona NEDELCUŢĂ[1]
Gigi CĂLIN[2]
Oana IANA[3]
Cristian NEDELCUTA[4]
Dragoş DAVIŢOIU[5]
Dumitru BÃLEANU[6]

ABSTRACT:
EPIGENETICS IS A NATURAL AND PLAUSIBLE EXPLANATION FOR PHENOTYPIC CHANGES OCCURRING UNDER THE INFLUENCE OF ENVIRONMENTAL FACTORS.
WE WANT TO DOCUMENT HOW NUTRITION, ONE OF THE PRIMARY ENVIRONMENTAL FACTORS THAT INTERACT WITH INDIVIDUALS, CAN INFLUENCE EPIGENETIC CHANGES WITH CONSEQUENCES RESULTING IN HEALTH DEVELOPMENT.
THE STUDY CONDUCTED IN THE PEDIATRIC CLINIC OVER A YEAR DEMONSTRATED A DIRECT INFLUENCE ON THE NUTRITIONAL STATUS OF THE NEWBORN ACCORDING TO CERTAIN QUANTIFIABLE PARAMETERS (MOTHER'S NUTRITIONAL STATE, MOTHER'S STRESS, PHYSICAL ACTIVITY, MULTIPARITY, MATERNAL ANEMIA, ETC.).
A START IN LIFE WITH A WEIGHT BELOW THE PERCENTILE AGE LIMIT OR INSUFFICIENT MINERAL DEPOSITS PREDISPOSES CHILDREN TO EARLY ILLNESS (DYSTROPHY, ANEMIA).
THE IMPORTANCE OF PREVENTION IS CRUCIAL, WITH LONG-LASTING REPERCUSSIONS, AS THE PREREQUISITES FOR PROPER NUTRITION OF THE GENITORS MAKE THEIR MARK ON CHILDREN'S HEALTH. PROPHYLAXIS OF IRON DEFICIENCY ANEMIA OF PREGNANT WOMEN AND ENSURING PROPER NUTRITION DURING PREGNANCY ELIMINATES A LARGE PART OF THE NUTRITIONAL RISKS OF THE NEWBORN AND INFANT.

KEYWORDS: EPIGENETICS, NUTRITION

[1] Department of Pediatrics, University of Medicine and Pharmacy of Craiova, Romania
[2] Department of Pediatrics, University of Medicine and Pharmacy of Craiova, Romania
[3] C.I. Parhon National Institute of Endocrinology, Bucharest, Romania
[4] County Emergency Clinical Hospital from Craiova, Romania
[5] University of Medicine and Pharmacy Carol Davila, 8 Eroii Sanitari Str, 050474, Bucharest, Romania
[6] University of Medicine and Pharmacy of Craiova, 2 Petru Rares Str., 200349, Craiova, Romania

The genetic constellation of each person is established at the time of the union of the gametes and the formation of the zygote.

Genetics is a discipline that shows a spectacular evolution in recent years.

Only the genetic code, the simple succession of purine and pyrimidine bases that encode gene structure cannot explain why we are so different phenotypic, although at genome level the differences between us are 0.1% or more[7]. The explanation was given with the discovery of epigenetics, the basis of which was established in 1942 by Conrad Waddinton, which defines it as a conceptual branch of biology studying phenotypic changes in the context of interactions of environmental factors with genetic background. Practically, epigenetics studies biochemical reactions that cause different expressions of DNA due to the activation or suppression of certain genes, without altering the structure or sequence of the gene sequence[8].

The notion of "gene switch" that blocks/unlocks gene expression has been introduced following methylation/demethylation processes. There are many studies that support the role of epigenetics in modifying gene expression[9].

A proof of this is the study conducted on agouti mice. Normally the fur color of these mice varies from yellow to brown very light due to the agouti gene.

Pregnant mothers taking a diet rich in methyl groups (vitamins and amino acids) will cause the birth of offspring with a much darker brown color. The explanation is the sensitivity of the agouti gene to methylation, this chemical reaction causing the inactivation of some transposomes, structures existing in human genetic edifice[10].

Taking into account a number of quantifiable factors, a pediatric clinic studied the evolution of weight, height and the frequency of illness and the occurrence of iron anemia during 12 months of study[11].

Inborn epigenetic factors have been studied: type of birth (natural or caesarian), type of diet (natural, artificial, mixed), mother weight, maternal age, iron anemia during pregnancy[12].

EPIGENETICS AND GROWTH/NUTRITION

Intrauterine growth is influenced by a variety of factors (genetic, maternal pathology, placental pathology, etc.) plus epigenetic factors (maternal nutrition, family socioeconomic

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[7] Gluckman, P. D., and Hanson, M. A. (2004). The developmental origins of the metabolic syndrome. Trends Endocrinol. Metab. 15, 183–187. doi: 10.1016/j.tem.2004.03.002; Greally, J. M. (2017). Population epigenetics. Curr. Opin. Syst. Biol. 1, 84–89. doi: 10.1016/j.coisb.2017.01.004

[8] Greally, J. M. (2018). A user's guide to the ambiguous word ‘epigenetics'. Nat. Rev. Mol. Cell. Biol. 19:207–208. doi: 10.1038/nrm.2017.135

[9] Iurlaro, M., von Meyenn, F., and Reik, W. (2017). DNA methylation homeostasis in human and mouse development. Curr. Opin. Genet. Dev. 43, 101–109. doi: 10.1016/j.gde.2017.02.003; Janssen, A. B., Kertes, D. A., McNamara, G. I., Braithwaite, E. C., Creeth, H. D., Glover, V. I., et al. (2016). A role for the placenta in programming maternal mood and childhood behavioural disorders. J. Neuroendocrinol. 28. doi: 10.1111/jne.12373

[10] John, R. M., and Surani, M. A. (1996). Imprinted genes and regulation of gene expression by epigenetic inheritance. Curr. Opin. Cell Biol. 8, 348–353. doi: 10.1016/S0955-0674(96)80008-1; Lämke, J., and Bäurle, I. (2017). Epigenetic and chromatin-based mechanisms in environmental stress adaptation and stress memory in plants. Genome Biol. 18:124. doi: 10.1186/s13059-017-1263-6

[11] Liu, X. S., Wu, H., Ji, X., Stelzer, Y., Wu, X., Czauderna, S., et al. (2016). Editing DNA methylation in the mammalian genome. Cell 167, 233-247. e17. doi: 10.1016/j.cell.2016.08.056; Lyko, F. (2018). The DNA methyltransferase family: a versatile toolkit for epigenetic regulation. Nat. Rev. Genet. 19, 81–92. doi: 10.1038/nrg.2017.80

[12] Weaver IC et al (2004) Epigenetic programming by maternal behavior. Nature Neuroscience 7: 847-854; Lumey LH et al (2007) Cohort profile: The dutch Hunger Winter Families Study. Int J Epidemiol. 36: 1196-1204; Stein AD et al (2004) Intrauterine famine exposure and body proportions at birth: the Dutch Hunger Winter. Int J Epidemiol 33: 831-836

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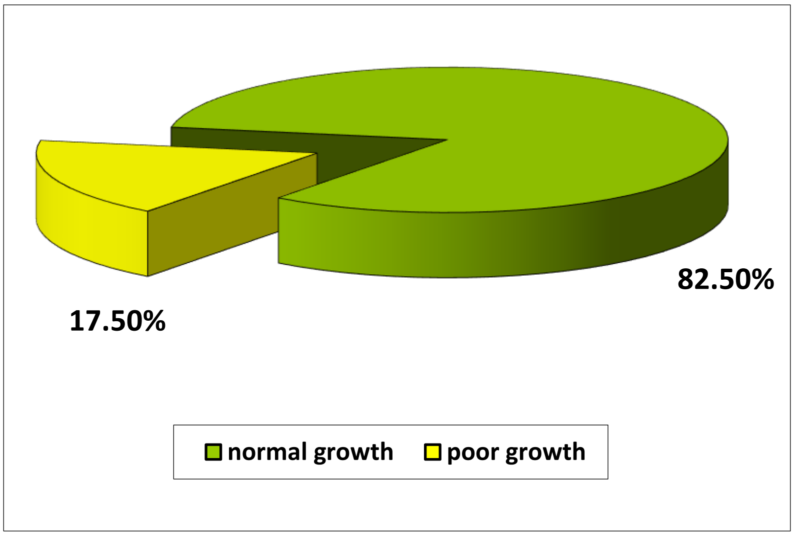
environment, stress, physical effort, pre-existing anemia in mothers, maternal multiparity or the interval between pregnancies)[13].

MATERIAL AND METHOD

485 cases of infants who were followed up for 365 days after birth were studied. The age and sex growth and development percentiles were used as working tools and at the end of the newborn period (1 month) at the age of complementary feeding (4-6 months) and at the age of 1 year.

A total of 59 children had low birth weight compared to normal birth weight.

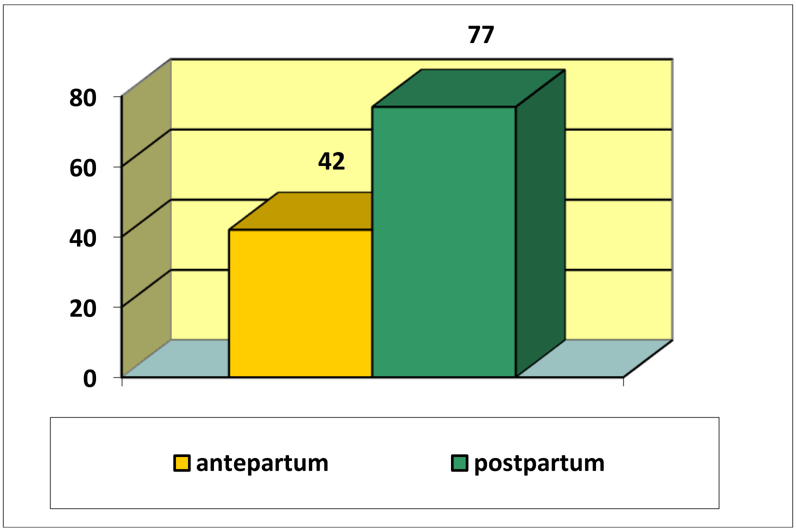
During the first year of life, growth and development deficits were detected in approximately 88 cases.



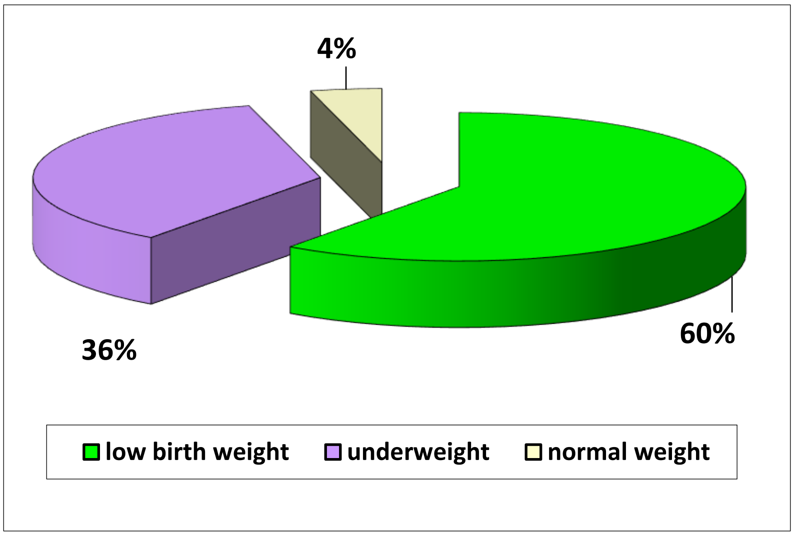
The socio-economic level of the family correlated inversely with the nutritional status of children in 84% of cases.

The iron anemia of the mother was detected antepartum in 42 future mothers and postpartum in another 77 mothers.

[13] Heijmans BT et al (2008) Persistent epigenetic differences associated with prenatal exposure to famine in humans. PNAS 17046-17049; Baedke J (2013) The epigenetic landscape in the course of time: Conrad Hal Waddington's methodological impact on the life sciences. Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences 44 : 4 Part B 756-773



Of the 42 newborns whose mothers did not receive iron prophylaxis in pregnancy, 25 had low birth weight and 15 were underweight, then during the first 6 months until the onset of complementary feeding.



Of the 77 mothers with postpartum iron anemia (87% did not perform periodic gynecological checks or haematological paraclinical determinations), 21 gave birth to younger children, and another 34 of their infants had low weight at the start of the first year.

After the onset of iron prophylaxis, nutritional recovery was achieved in about 6 months in 29 of the children.

44 of the mothers with low birth weight were multiparous and another 51 of the group with children under the age of 1 year. There was a direct correlation between the short interval between multiple births and low birth weight in 35 of the 44 mothers.

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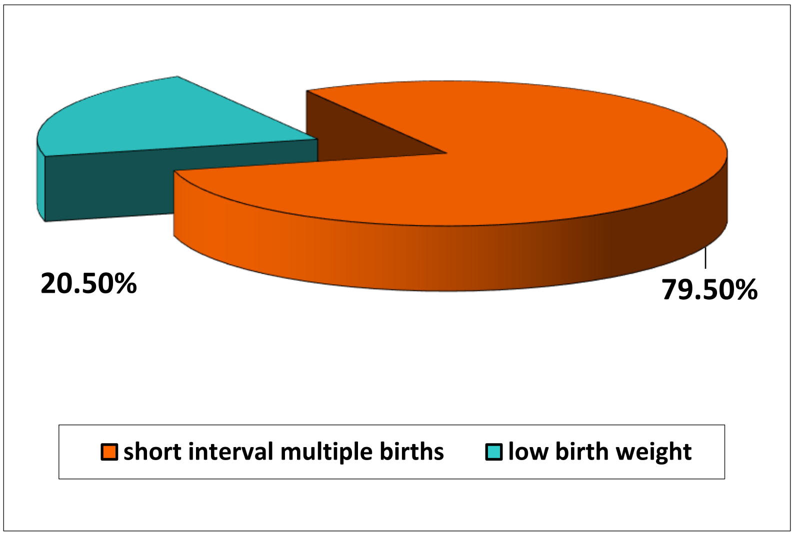
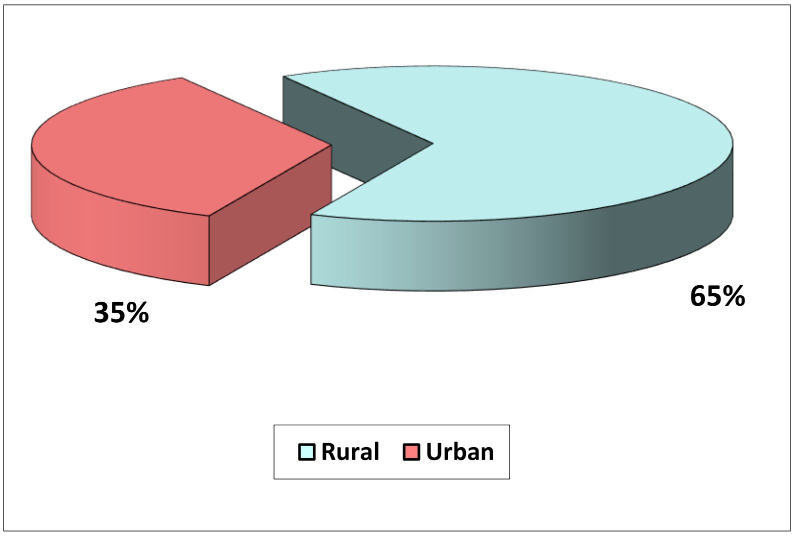


The sustained physical effort was associated with premature birth and, implicitly, small weight in 16 mothers and stress can be a multideterminist factor for a variety of conditions, including weight loss at birth, and could be objectively supported by about 20 mothers from urban areas).

The distribution on the birthplace of those with low birth weight was almost equal - 27 from urban and 32 from rural areas.



IN CONCLUSION:

- Epigenetic factors are definitely overlapped over the predefined genetic pattern influencing future evolution.
- Stress acts multifactually: engages the hypothalamic-pituitary axis - the medullary adrenal system - the production of cytokine proinflammatory and Th2 cells causing increased oxidative stress, accelerates catabolism in the detriment of anabolism, or inhibits hunger center with localization in the lateral hypothalamus.
- All these complicated actions are associated with disturbing the nutritional state of the organisms.

- Iron deficiency is associated with hypoxia or hypoxemia in the tissues, iron being a constituent of the heme, a fundamental compound of the Hb molecule. Hb is the major cellular transporter for 0_2, lack of oxygenation or nutrient deficiency is reflected in growth and development disorders.
- The socio-economic environment influences directly both the pregnant and the child's menu, the diversity of essential energy nutrients, as well as the degree of parental information regarding the prevention of nutritional deficiency and the recognition of early signs of dystrophy and addressing medical services.
- Multiparity affects the mother's nutritional "resource", knowing that the transmission and consolidation of fetal iron deposits is done during the last 3 months of pregnancy. Cesarean, on the other hand, accentuates the losses caused by intraoperative haemorrhage. The "logical" interval between pregnancies should be at least 2 ½-3 years.
- The poor feeding of the mother is directly related to the child's nutritional status.
- The preconception period is as important as the conception, in terms of the diversity of epigenetic factors that influence the nutrition of mother and child
- Establishment of preventive measures (combating stress, maternal anemia, ensuring correct pregnancy nutrition, "safe" interval between pregnancies, helps to fight poor nutrition within and after postpartum.

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REFERENCES

1. **Gluckman, P. D., and Hanson, M. A**. (2004). The developmental origins of the metabolic syndrome. Trends Endocrinol. Metab. 15, 183–187. doi: 10.1016/j.tem.2004.03.002
2. **Greally, J. M**. (2017). Population epigenetics. Curr. Opin. Syst. Biol. 1, 84–89. doi: 10.1016/j.coisb.2017.01.004
3. **Greally, J. M.** (2018). A user's guide to the ambiguous word ‘epigenetics'. Nat. Rev. Mol. Cell. Biol. 19:207–208. doi: 10.1038/nrm.2017.135
4. **Iurlaro, M., von Meyenn, F., and Reik, W**. (2017). DNA methylation homeostasis in human and mouse development. Curr. Opin. Genet. Dev. 43, 101–109. doi: 10.1016/j.gde.2017.02.003
5. **Janssen, A. B., Kertes, D. A., McNamara, G. I., Braithwaite, E. C., Creeth, H. D., Glover, V. I., et al**. (2016). A role for the placenta in programming maternal mood and childhood behavioural disorders. J. Neuroendocrinol. 28. doi: 10.1111/jne.12373
6. **John, R. M., and Surani, M. A.** (1996). Imprinted genes and regulation of gene expression by epigenetic inheritance. Curr. Opin. Cell Biol. 8, 348–353. doi: 10.1016/S0955-0674(96)80008-1
7. **Lämke, J., and Bäurle, I.** (2017). Epigenetic and chromatin-based mechanisms in environmental stress adaptation and stress memory in plants. Genome Biol. 18:124. doi: 10.1186/s13059-017-1263-6
8. **Liu, X. S., Wu, H., Ji, X., Stelzer, Y., Wu, X., Czauderna, S., et al**. (2016). Editing DNA methylation in the mammalian genome. Cell 167, 233-247. e17. doi: 10.1016/j.cell.2016.08.056
9. **Lyko, F.** (2018). The DNA methyltransferase family: a versatile toolkit for epigenetic regulation. Nat. Rev. Genet. 19, 81–92. doi: 10.1038/nrg.2017.80
10. **Weaver IC et al** (2004) Epigenetic programming by maternal behavior. Nature Neuroscience 7: 847-854
11. **Lumey LH et al** (2007) Cohort profile: The dutch Hunger Winter Families Study. Int J Epidemiol. 36: 1196-1204
12. **Stein AD et al** (2004) Intrauterine famine exposure and body proportions at birth: the Dutch Hunger Winter. Int J Epidemiol 33: 831-836
13. **Heijmans BT et al** (2008) Persistent epigenetic differences associated with prenatal exposure to famine in humans. PNAS 17046-17049
14. **Baedke J** (2013) The epigenetic landscape in the course of time: Conrad Hal Waddington’s methodological impact on the life sciences. Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences 44 : 4 Part B 756-773