We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,800
Open access books available

122,000
International authors and editors

135M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS BOOK CITATION INDEX INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Chapter

Fetal-Neonatal Lifestyle Basis of the Adult Metabolic Syndrome Patients

Hashem Kilani, Abdulsalam Al-Za'abi, Areej Kilani and Laila Kilani

Abstract

Information on the health status in modern society and developed countries depicts an increase in noncommunicable diseases (NCDs) such as diabetes, overweight, obesity, and metabolic syndrome. An examination of factors related to this increase shows that there is a shift in the daily practices of the people, and especially children in all ages, as they grow older toward a more sedentary lifestyle. This chapter concentrated on the term used to describe lifelong changes in function that follow a particular event in an earlier period of the life span, which is called programming. These include the lifestyle in the fetus, pregnant woman, and parents; all of which affect pronounce metabolic syndrome in later life of adult. Therefore, regular physical activity and living systematic healthy lifestyle in the prenatal stages are of importance to genetic modification of inheritance for future generations.

Keywords: lifestyle, adult, metabolic syndrome

1. Introduction

For more than a decade, high blood pressure, arteriosclerosis, smoking, high blood sugar, and lack of movement have been dangerous factors leading to morbidity and mortality. Today, recent studies indicate that the first risk factor to rush to death is the lack of physical activity and time of daily sitting in addition to the poor selection of healthy food [1–5]. It may be the responsibility of everyone in us not to follow a healthy lifestyle that is inherited by generations, the most important factor that has led to a negative acceleration of human health. This would not have been possible without the negative use of technology for human life.

The sedentary life experienced by most people has led to an increase in such risks and a marked increase in noncommunicable diseases. So, the most important issues that urge them to take the initiative in the marketing of sports and physical activity that the movement blessing and health crown on the heads of healthy cannot be achieved without beginning to modify the behavior and the adoption of a healthy lifestyle. This includes regular physical activity and stay away from pressure exercise relaxation and selection of appropriate food and early sleep with sufficient hours (quality of sleep) [5]. Therefore, in order to do so, school sports are a productive educational activity that is of great physical interest to the student [6]. Educational institutions and organizations have converged in

recognition of the importance of school sports in maximizing the use of the time available to activate the lesson of physical education. This interest emphasizes the inclusion in many studies of its recommendations on the importance of school sports and its role in the development of students from the mental, psychological, and physical aspects [6–9].

Physical activity has much health, psychological, and social benefits. It helps to raise the level of fitness for better health and more active life. It also helps prevent many diseases or metabolic symptoms. It also reduces the risk of heart disease, diabetes, low back pain, and obesity, as well as the development of health and nutrition knowledge and the development of positive attitudes toward physical activity [2, 9–11].

Metabolic syndrome is a combination of medical disorders that increase the risk of cardiovascular disease and diabetes, which refers to all the biochemical processes that occur in the body; it is a group of metabolic abnormality-related risk factors that greatly increase the risk of developing type 2 diabetes and health problems in the heart and blood vessels. Also, their biochemical processes in the body that leads to abdominal obesity and insulin resistance causing type 2 diabetes and Cardiovascular (hyperlipidemia) [12].

2. Obesity facts

While the prevalence of obesity appears to have plateau in the United States, emphasis is not only placed in treatment but also prevention as only 8% of normal weight children will become obese adults, while those who are obese during childhood tend to be obese adults. Also, a longitudinal change in percentages of obese children in Jordan, KSA, UAE, Kuwait, and Oman has similar trends. The increased rate of obesity in childhood and in the overall population is also present in the Arab world [13]. Data from this study done by students in Seeb, Muscat, demonstrate how the proportion of children who grew into adolescents that became overweight or obese increased from a single digit (about 7 percent) to more than 20% (so we are talking that in the same cohort of children when they were 6–7 years old only one in ten was classified as obese, but by the time they are late teens, one in five is classified as overweight). Participants were assessed at the beginning of the school year during the screening that took place before entering the different levels of education [14].

Kilani et al. have also presented a similar prevalence of college students who are overweight at SQU, with a much higher proportion of students who present an unhealthy level of body fat [14]. In another survey, males and females had similar values for BMI and WC, and they maintained a normal BMI of <25 Kg/m^2. The genetic predisposition might synergize with environmentally driven factors like physical activity and diet in the etiology of obesity and overweight among Omani and Jordanian adolescents [4, 15]. So, what are some differences between normal weight and obese people? Hormone research agenda is divided into two aspects: exercise endocrinology (hormonal responses to exercise) and the role of physical activity in promoting a healthy lifestyle.

The main characteristics of the syndrome store excess fat in the abdomen as visceral fat (abdominal obesity) and "insulin resistance" [16, 17]. Firstly, obesity generally can be inherited or acquired, especially when an individual lives in an incubator environment to increase the number and size of fat cells. Prader-Willi syndrome (PWS) is rarely caused by a genetic defect that leads to physical, mental, and behavioral problems. One of the factors that contribute to childhood obesity great feeling of hunger and lack of control over eating which leads to chronic overeating (hyperphagia) and obesity [18].

Defined etiology of obesity is accounted for (3-5%) with issues related to hormonal diseases, lesions in the hypothalamus, and altered genes (Early-onset hyperphagia caused the pathologic obesity) [18].

The second is Multi-factorial obesity which results from an interaction between inherited predisposition and environment (epigenetic). PWS results from all alteration in the expression of the paternal chromosome 15, in the regions 11–13, and there are three main genetic alterations that result in the syndrome: paternal deletion, maternal uniparental disomy, and imprinting defect [19]. These causes that people with syndrome although share some common characteristics also present a wide range of abilities and disabilities. As babies, individuals with the syndrome are what we call floppy babies because of their decreased muscle tone, most of them have to be intubated as they fail to thrive, and somewhere between ages 4 and 8, an exacerbated seeking for food behavior begins which turns into hyperphagia that if it is uncontrolled it can turn into obesity [19]. Physically, they could be shorter than normal if not on growth hormone replacement therapy and have small hands and feet; some present intellectual disability, deficit in their sensorial systems and in their motor behavior [19]. Many researchers recommend to reduce weight by 10% of body weight in the first 6 months to a year and continued losing weight after reaching less than 25 in BMI. In general, recommendations include reducing calories including reducing 500–1000 calories per day [20–22].

In some studies, 9007 men and 1491 women aged 44 +/−9 years free of metabolic syndrome took measurements of waist circumference and blood pressure and fat and sugar glucose as documented in the baseline and follow-up checks. Cardiorespiratory fitness was measured by maximal treadmill test duration. During the average follow-up of 5.7 years, 1346 men and 56 women developed metabolic syndrome. Inverse associations between fitness and metabolic syndrome incidence were found, suggesting that greater cardiorespiratory fitness levels may be beneficial in the primary prevention of metabolic syndrome [23]. The purpose of this paper was to review through scientific research published to respond on to the following question: Can the conditions during fetal development program the system to result in a survival advantage, yet increase vulnerability for adult diseases?

3. Developmental plasticity

The developmental plasticity is the ability of an organism to develop in various ways, depending on the particular environment or setting [24]. This can be based on the interaction of cellular cells, which refers to direct interactions between cell surfaces that play a crucial role in the development and functions of multicellular organisms, such as complex, structural humans. These interactions allow the cells to communicate with one another in response to changes in the microbial environment [25]. This ability to send and receive signals is essential for cell survival. For instance, normal embryonic and postnatal development requires a fine regulation of cell proliferation, differentiation, migration, and apoptosis. During organogenesis, cell–cell interactions trigger events such as epithelial-mesenchymal transition (thin protective layer) and tubulogenesis (kidney development) that describes tissue that forms a thin protective layer on exposed bodily surfaces and forms the lining of internal cavities, ducts, and organs. Another example is related to cystogenesis, tubulogenesis, and kidney development [26]. Cystogenesis and tubulogenesis are important for many complex biological processes such as organ development. Again, if we compare an epidermal keratinocyte and a pancreatic acinar cell, the same genome, yet their profound morphological, physiological, and biochemical differences are entirely

the product of epigenetic modification. Keratinocyte cells are the building blocks of the skin. They are the most common type of skin cell and make keratin, a protein found in the skin, hair, and nails.

One condition that causes the pancreas to stop producing adequate enzymes is pancreatic acinar atrophy. This occurs because the disease hurts slowly and without obvious symptoms. The ability of many animals is adaptability to environmental evolution. This can make small size and slow metabolism to live and survive, while the enlarged size and accelerated metabolism are advantages of reproductive success when resources are available. Often this occurs early in life or even through inheritance from parents and even grandparents. However, fetuses who are adjusting to one environment, such as the uterus, may be at risk when exposed to other environment when they become adults [27]. Effects of prenatal exposure to the Dutch famine on adult disease in later life. Bees determine the number of larvae within the appropriate age group and begin to place these larvae to become queens. The only difference between the honeybees and the queen is the food received during the process of maturity: the workers feed potential queens royal jelly throughout their lives, while the bees are working on royal jelly during the first 2 days of the larvae [28].

4. Biological evidences

Biological evidence may be relevant to understanding human development and susceptibility to disease. With the improved nutritional status of many mothers around the world, the characteristics of their offspring—such as body size and metabolism—also changed. Their mother's prenatal response may generally respond to individuals so that they are more appropriate to the environment's expectations through the signals available in early life. If the mother is a smoker during pregnancy, it is possible that the third generation of her offspring will be smokers. Ironically, however, rapid improvements in nutrition and other environmental conditions may have adverse effects on the health of those whose parents and grandparents lived in poor conditions, as happened in World War II in Europe [29] and the famine in India early in the last century [30]. The full understanding of the patterns of human plasticity in response to early nutrition and other environmental factors will have implications for public health management.

5. Thrifty hypothesis

The thrifty gene hypothesis indicates that certain populations may have genes that determine increased fat storage, which in times of famine represent a survival advantage, but in a modern environment result in obesity and type 2 diabetes. An example of the thrifty hypothesis showed by Dutch famine study which has shown that the offspring of mothers who were pregnant during the famine have more diabetes and those who were exposed in early gestation have more atherogenic lipid profile, altered clotting, more obesity, and a threefold increase in cardiovascular disease. Explanations for the heritability of these syndromes and the environmental contribution to disease susceptibility are addressed by the "thrifty genotype" and the "thrifty phenotype" hypotheses [27]. The underlying scientific hypothesis has been developed by epidemiology studies and emphasized by Dr. David Barker in the United Kingdom. During development fetuses respond to severe malnutrition by favoring the metabolic demands of the growing brain/CNS and heart at the expense of other tissues [31, 32]. In addition, the growing brain/CNS and heart tissue may

not, however, escape entirely unscathed. The fetus is protected from death and is live-born but is more prone to diseases later in life [33]. Various studies have supported barker hypothesis.

6. Epidemiology studies

Epidemiology studies have shown that markers of malnutrition such as frank intrauterine growth retardation (IUGR), low birth weight, or small for gestation age (SGA) strongly predict the subsequent occurrence of hypertension, hyperlipidemia, insulin resistance, type 2 diabetes, and ischemic heart disease, in adult life.

It has been shown that fetuses that are growth retarded during the first trimester of development are three times more likely to be obese as adults. In the case of premature infants, at the age of 4–10 years, these children who had been born prematurely had an increase in their acute insulin response, which compensated for insulin resistance. This decrease in insulin sensitivity may predispose premature infants to type 2 diabetes mellitus in adulthood, as already demonstrated among infants born at term who are SGA [33, 34], that compared with young people from the same region of Finland who are born after a pregnancy, and young people who ranged from 18 to 27 years of age who were preterm infants have become higher in chronic insulin resistance and more prone to glucose and high blood pressure [35]. Preterm births happen on their own early means that some of what would be the third trimester is lost. This is typically a sensitive period for programming and certainly a time during which the final aspects of organogenesis occur. This is explained by spending in the more difficult environment of a hospital setting in which there are many toxic substances as well as nutritional challenges. Now that many more extremely premature babies are surviving to adulthood, ensuring their health is crucial [36]. On the other hand excessive energy supply to the fetus or infant also has adverse consequences so a U shape works similarly at the tow ends of the malnutrition (**Figure 1**).

Maternal hyperglycemia may lead to fetal hyperinsulinemia and fat deposition that influence the fetus. Offspring of obese women or women with diabetes are at greater risk for developing metabolic disorders themselves, even during childhood [37–39].

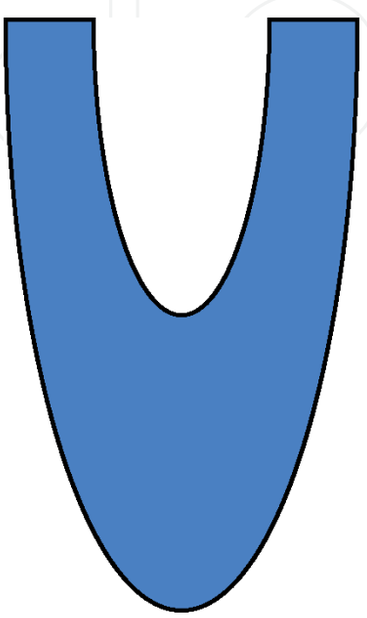

Figure 1.
Excessive energy supply to the fetus or infant also has adverse consequences.

As a consequences, an infant usually has about 5–6 billion fat cells during the third trimester when a mother is pregnant. This number increases during early childhood and puberty, resulting in a healthy adult body possessing 25–30 billion fat cells [40]. Meanwhile, excessive energy supply to the fetus or infant will increase the potential of becoming obese. Babies who depend on milk factory have the highest amount of energy, leading to an increase in body weight than children who were breastfed; it can affect the increase in obesity and its risks later in life [41]. This complicate the long-term effects due to Prenatal and postnatal nutrition during early infancy. In one study, carotid intima-media thickness at 9 years of age in 216 children of European ancestry whose mothers had energy intake in the lowest quartile during early or late pregnancy was higher than that of children whose mothers had intake in the highest quartile, implying that maternal nutrition during pregnancy can affect the subsequent risk of atherogenesis in the offspring [42].

Thus, obesity comes from an increase in the numbers of fat cells, or adipocytes, and is hence due to a shift in the activity of certain genes during development. Because to maternal malnutrition during pregnancy, the offspring later suffering from obesity in the middle of the abdomen and lack of muscle mass, change the sensitivity of insulin, change in hepatic metabolism, decreased number of nephrons, high blood pressure, with a change in appetite regulation, activity level, and control of nerve endocrine glands [42]. There are critical periods in the differentiation and maturation of the tissues and cells involved in organogenesis throughout gestation and early postnatal life. The examples of the kidney, heart, and pancreas were obvious since their functional units are formed prenatally in the human fetus [43].

7. Animal studies

Embryos of pregnant rats fed with a low-protein diet during the preimplantation period (0–4.25 days) show altered development in multiple organ systems; the offspring had reduced birth weights, relatively increased postnatal growth, and adult-onset hypertension [44].

Obviously, the preconception period is particularly sensitive, so that even the required nutrient deficiencies (B12 or folate or methionine) can have an effect on metabolism and blood pressure later in sheep [45]. It has recently been reported that the imbalance in B12 folic acid status and pain during pregnancy contributes to insulin resistance in childhood in humans [46].

Glucocorticoid management to pregnant rats at specific times during pregnancy to cause high blood pressure [47], insulin resistance in offspring later in life [48], changes in gene expression in the developing brain of offspring, and increased sensitivity to stress after the birth have been reported. The administration of glucocorticoids to the pregnant rat at specific points during gestation has been reported to cause hypertension [47], insulin resistance in the offspring in later life [49], alterations in gene expression in the developing brain of the offspring, and increased sensitivity to postnatal stress [50].

In mice, it may lack nutrition during pregnancy to breed showing later the following: visceral obesity, reduced lean body mass, changes in insulin sensitivity, different hepatic metabolism, decreased numbers of nephrons, high blood pressure, and altered endothelial function, together with altered appetite regulation, level of activity, and neuroendocrine control [51–54].

There are critical periods in the differentiation and maturation of the tissues and cells involved in organogenesis throughout gestation and early postnatal life. The examples are seen in the kidney, heart, and pancreas, since their functional units are formed prenatally in the human fetus.

In the kidney, maternal dietary imbalance may lead to developmentally induced deviations from the optimal ratio of body mass to nephron number. This increased risk of inadequate renal function and hypertension in later life [54]. A predisposition to renal failure and a potentially reduced life span are predicted [55]. In the pancreas insulin secretion is also affected. Nutritional stress in pregnant rats reduces the growth of the endocrine pancreas during organogenesis and increases beta-cell apoptosis [55], leading to hyperglycemia and impaired insulin secretion when the offspring become adults. In the adult male rat offspring of mothers on a protein-restricted diet, low birth weight is associated with reduced expression of components of the insulin signal transduction pathway in the skeletal muscle [56]. Similar abnormalities have been reported in infants of low birth weight, and together with the developmentally induced reduction in skeletal muscle mass, these abnormalities might contribute to later insulin resistance.

8. Programming

Developmentally induced epigenetic modifications of DNA are generally stable during the mitotic cell divisions that continue throughout a lifetime. So, developmental plasticity of fetus through cell-cell interaction can be understood as a set of programs. "Programming" is the term used to describe lifelong changes in function that follow a particular event in an earlier period of the life span. Evolutionary plasticity requires a constant modification of genetic expression that appears to be mediated, at least in part, by genetic processes such as epigenetic mechanisms as cells use to control gene expression by virtue of DNA methylation. The role of DNA methylation in gene expression can be found in Phillips [57], and by a histone modification which is a histone protein includes methylation that can impact gene expression [58].

Several studies show that skeletal muscle can be programmed, where early exposure to environmental stimuli leads to a constant change in the skeletal muscle phenotype in later life. This has been demonstrated in mammalian models where reduced nutrient availability during pregnancy weakens muscle fibers, muscle and skeletal formation (white/red fiber ratios), and birth size [59]. Epidemiological studies in human aging groups also suggest that low birth weight and gestational malnutrition are closely related to reduced muscle size, skeletal strength, and aging [59, 60].

This refers to changes in gene expression due to nongenetic structural alterations of DNA and/or histones [58]. So, remember that cell-cell interaction can be transferable in the fetus so memory of active person eventually will be available later in life for the offspring babies [58]. Thus, developmental plasticity requires both the genome and the genetic variability of the environment interactively by the mature phenotype and determines the sensitivity and subsequent environmental factors and the subsequent risk of the disease affects [61]. The effects of maternal nutrition and behavior clearly target the promoter regions of specific genes rather than being associated with global changes in DNA methylation. DNA modulates the rate of transcription to messenger RNA. The phenotypic effects of epigenetic modifications during development may not manifest until later in life [62].

9. Hormones

It plays an important role in childhood growth and continues to have anabolic effects in adults. As the stress hormone, norepinephrine affects the brain's amygdala, where attention and responses are controlled. It is also based on norepinephrine response to fight or flight, in addition to epinephrine, which raises the heart rate

directly, leading to the release of glucose from energy stores and increasing blood flow to the skeletal muscles. It increases the supply of oxygen to the brain [63]. Glucagon is a peptide hormone, produced by alpha cells of the pancreas that raises blood glucose levels. Its main tasks are to increase blood sugar through protein conversion in the liver (gluconeogenesis). Suppress the immune system and help with fat, protein, and carbohydrate metabolism [64]. It also affects the density of the bones negatively, and it is possible to use cortisone in various forms to treat a variety of diseases.

10. Conclusion

The term used to describe lifelong changes in function that follow a particular event in an earlier period of the life span is called programming. Nevertheless, the previous information may have a significance of pediatric obesity endocrine abnormality. GH-IGF-1 axis is partially responsive for the signal to enhance muscle and bone development. Growth hormone (GH) response to exercise may be weak in obesity and may not appear until later in life, especially if they affect genes that are responding to subsequent environmental responses, such as high-fat diet. I do not know how the genetic change instigated development window in the main systems. Exercise is the best way to do this when you exercise regularly, and you build stronger muscles, even if you do not work out with weights. Muscles use more calories than fat throughout the day, even while you are resting. Fat cells of unhealthy obese were larger than those of any other group. It was swollen and full of inflammation. The collapse and filling of their fat stores were disabled and showed a closer look that their mitochondria were not functioning well causing loss of muscle power. This is due to fat cell accumulation which reduces its ability to burn fuel and produce adenosine triphosphate, or ATP, the body's energy currency. It is natural that the behavior of the human being and his attitude of life inert to be aware of the importance of physical activity and live in the healthy lifestyle system in the prenatal stages. Thus, healthy genetic modification will be inherited for future generations.

Author details

Hashem Kilani[1]*, Abdulsalam Al-Za'abi[2], Areej Kilani[3] and Laila Kilani[4]

1 School of PE, Health and Recreation Department, University of Jordan, Amman, Jordan

2 College of Education, Health and PE Department, UAEU, Al-Ain, Abu-Dhabi, UAE

3 Internal Medicine Department, Jordan University Hospital, Amman, Jordan

4 Clinical Pharmacist, University of Jordan, Amman, Jordan

*Address all correspondence to: hashemkilani@gmail.com

IntechOpen

References

[1] Kilani H, Al-Yarobi S, Zayed K, Alzakwani I, Bererhi H, Shukri A, et al. Physical fitness attributes, vitamin D, depression, and BMD in Omani's children. European Scientific Journal. 2013;**9**(30):156-173

[2] Habsi A, Kilian H. Lifestyle of adult Omani women: A cross sectional study. Sultan Qaboos University Medical Journal. 2015;**15**(2):241-249

[3] Kilani H. Cardiovascular diseases risk, energy expenditure, and health fitness. Canadian Journal of Clinical Nutrition. 2015;**3**(2):1-4

[4] Kilani H, Alhazzaa H, Waly M, Musaiger A. Lifestyle habits: Diet, physical activity and sleep duration among Omani adolescents. Sultan Qaboos University Medical Journal. 2013;**13**(4):510-519

[5] Kilani H, Alfahdi B. What is the effect of the number of sleeping hours for military sports trainers in the Royal Air Force? European Journal of Sport Technology. 2018;**20**:2-19

[6] Al-Za'abi A, Kilani H, Bataineh M, Alnuaimi J. Perceived health benefits and barriers to physical activity among secondary school students. International Scientific Journal of Kinesiology-Sport Science Journal. 2018;**2018**:91-102

[7] Kilani H, Lala O. Fat mass percentage with hypertension and some variables of physical working capacity among students. In: Second International Scientific Conference about the latest Scientific Evidences of Physical Education. Irbid: Yarmouk University; 2007

[8] Mehana M, Kilani H. Enhancing physical education in Omani basic education curriculum: Rationale and implications. International Journal for Cross-Disciplinary Subjects in Education (IJCDSE). 2010;**1**(2):1-11

[9] Benn T, Al-Sinani Y. Physical education in Oman: Women in Oman and specialist initial teacher training. Physical Education Matters. Summer. 2007;**2**(2):57-55

[10] Laaksonen AA. Physical activity in the prevention of type 2 diabetes: The Finnish diabetes prevention study. Diabetes. 2005;**54**(1):158-165

[11] Corbin C, Lindsey R, Welk G, Corbin W. Concepts of Fitness and Wellness: A Comprehensive Lifestyle Approach. 4th ed. St. Louis: McGraw-Hill; 2002

[12] Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among U.S. adults: Findings from the third National Health and Nutrition Examination Survey. JAMA. 2002;**287**:356-359

[13] Musaiger AO, Al-Mannai M, Tayyem R, Al-Lalla O, Ali EY, Kalam F, et al. Prevalence of overweight and obesity among adolescents in seven Arab countries: A cross-cultural study. Journal of Obesity. 2012:381-390

[14] Osman YF, Muscati SK, Ganguly SS, Khan M, Al-Sharji B. Progression of obesity among Seeb school children in Oman. A preliminary study. Saudi Medical Journal. 2004;**25**(12):2038-2040

[15] Kilani H, Waly M, Yousef R. Trends of obesity and overweight among college students in Oman: A cross sectional study. Sultan Qaboos University Medical Journal. 2012;**12**(1):69-76

[16] Kilani H. Exercise and metabolic syndrome. In: Dietary Management of Metabolic Syndrome Conference organized by the Department of Nutrition and Food Sciences, AUB and The Department of Clinical Nutrition in collaboration with Lebanese Academy

for Nutrition and Dietetics; 17th May 2012; Beirut, Lebanon; 2012

[17] World Health Organization. Children Obesity Causes Global Strategy on Diet Physical Activity and Health. 2014

[18] Chen C, Visootsak J, Dills S, Graham JM Jr. Prader-Willi syndrome: An update and review for the primary pediatrician. Clinical Pediatrics (Phila). 2007;**46**(7):580-591

[19] Cassidy SB, Schwartz S, Miller JL, Driscoll DJ. Prader-Willi syndrome. Genetics in Medicine. 2012;**14**(1):10-26

[20] Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation. 2004;**109**(3):433-438

[21] Eckel RH. Obesity: Mechanisms and Clinical Management. Philadelphia (PA): Lippincott Williams & Wilkins; 2003

[22] Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet. 2005;**365**(9468):16-22, 1415-1428

[23] LaMonte MJ, Blair SN, Church TS. Physical activity and diabetes prevention. Journal of Applied Physiology (Bethesda, MD: 1985). 2005;**99**(3):1205-1213

[24] Obesity (Silver Spring). 2008; 16(7):1651-1666

[25] Bergmann F, Aulmann S, Sipos B, et al. Acinar cell carcinomas of the pancreas: A molecular analysis in a series of 57 cases. Virchows Archiv. 2014;**465**(6):661-672

[26] Mousavi SJ, Hamdy Doweidar M. Role of mechanical cues in cell differentiation and proliferation: A 3D numerical model. PLoS One. 2015;**10**(5):11

[27] Roseboom TJ. Effects of prenatal exposure to the Dutch famine on adult disease in later life: An overview. Twin Research. 2001;**4**(5):293-298

[28] Sagili RR, Metz BN, Lucas HM, Chakrabarti P, Breece CR. Honey bees consider larval nutritional status rather than genetic relatedness when selecting larvae for emergency queen rearing. Scientific Reports. 2018;**8**:7679. DOI: 10.1038/s41598-018-25976-7

[29] Scrimshaw NS. The phenomenon of famine. Annual Review of Nutrition. 1987;**7**:1-21

[30] Arnold D. The 'discovery' of malnutrition and diet in colonial India. Indian Economic and Social History Review. 1994;**31**(1):1-26. DOI: 10.1177/001946469403100101

[31] de Rooij SR, Painter RC, Holleman F, Bossuyt PM, Roseboom TJ. The metabolic syndrome in adults prenatally exposed to the Dutch famine. The American Journal of Clinical Nutrition. 2007;**86**:1219-1224

[32] Barker DJP. Mothers, Babies and Health in Later Life. Edinburgh: Churchill Livingstone; 1998

[33] Barker DJP, Osmond C, Forsén TJ, Kajantie E, Eriksson JG. Trajectories of growth among children who have coronary events as adults. The New England Journal of Medicine. 2005;**353**:1802-1809

[34] Rooij WH Sr, Yonker JE, Painter RC, Roseboom TJ. Prenatal undernutrition and cognitive function in late adulthood. Proceedings of the National Academy of Sciences of the United States of America. 2010;**107**:16881-16886

[35] Hofman PL, Regan F, Jackson WE, et al. Premature birth and later insulin resistance. The New England Journal of Medicine. 2004;**351**:2179-2186

[36] Hovi P, Andersson S, Eriksson JG, et al. Glucose regulation in young adults with very low birth weight. The New England Journal of Medicine. 2007;**356**:2053-2063

[37] Boney CM, Verma A, Tucker R, Vohr BR. Metabolic syndrome in childhood: Association with birth weight, maternal obesity, and gestational diabetes mellitus. Pediatrics. 2005;**115**(3):e290-e296

[38] Julie R. Ingelfinger, prematurity and the legacy of intrauterine stress. The New England Journal of Medicine. 2007;**356**:20

[39] Hillier TA, Pedula KL, Schmidt MM, Mullen JA, Charles MA, Pettitt DJ. Childhood obesity and metabolic imprinting: The ongoing effects of maternal hyperglycemia. Diabetes Care. 2007;**30**:2287-2292

[40] Kronemer C. Uncovering the Biology Behind Fat Cells. NFPT CEC. 2012. Available from: https://www.nfpt.com/blog/uncovering-the-biology-behind-fat-cells

[41] Reusens B, Remacle C. Programming of the endocrine pancreas by the early nutritional environment. The International Journal of Biochemistry and Cell Biology. 2006;**38**:913-922

[42] Harder T, Bergmann R, Kallischnigg G, Plagemann A. Duration of breastfeeding and risk of overweight: A meta-analysis. American Journal of Epidemiology. 2005;**162**:397-403

[43] Ozanne SE, Jensen CB, Tingey KJ, Storgaard H, Madsbad S, Vaag AA. Low birthweight is associated with specific changes in muscle insulin-signalling protein expression. Diabetologia. 2005;**48**:547-552

[44] Kwong WY, Wild A, Roberts P, Willis AC, Fleming TP. Maternal undernutrition during the preimplantation period of rat development causes blastocyst abnormalities and programming of postnatal hypertension. Development. 2000;**127**:4195-4202

[45] Sinclair KD, Allegrucci C, Singh R, Gardner DS, Sebastian S, Bispham J, et al. DNA methylation, insulin resistance, and blood pressure in offspring determined by maternal periconceptional B vitamin and methionine status. Proceedings of the National Academy of Sciences of the United States of America. 2007;**104**:19351-19356

[46] Yajnik CS, Deshpande SS, Jackson AA, Refsum H, Rao S, Fisher DJ, et al. Vitamin B12 and folate concentrations during pregnancy and insulin resistance in the offspring: The Pune maternal nutrition study. Diabetologia. 2008;**51**:29-38

[47] Levitt NS, Lindsay RS, Holmes MC, Seckl JR. Dexamethasone in the last week of pregnancy attenuates hippocampal glucocorticoid receptor gene expression and elevates blood pressure in the adult offspring in the rat. Neuroendocrinology. 1996;**64**:412-418

[48] Nyirenda MJ, Lindsay RS, Kenyon CJ, Burchell A, Seckl JR. Glucocorticoid exposure in late gestation permanently programs rat hepatic phosphoenolpyruvate carboxykinase and glucocorticoid receptor expression and causes glucose intolerance in adult offspring. The Journal of Clinical Investigation. 1998;**101**:2174-2181

[49] Welberg LA, Seckl JR, Holmes MC. Prenatal glucocorticoid programming of brain corticosteroid receptors and corticotrophin-releasing hormone: Possible implications for behaviour. Neuroscience. 2001;**104**:71-79

[50] Vickers MH, Breier BH, Cutfield WS, Hofman PL, Gluckman PD.

Fetal origins of hyperphagia, obesity, and hypertension and postnatal amplification by hypercaloric nutrition. American Journal of Physiology. Endocrinology and Metabolism. 2000;**279**:E83-E87

[51] Langley-Evans SC, Welham SJ, Jackson AA. Fetal exposure to a maternal low protein diet impairs nephrogenesis and promotes hypertension in the rat. Life Sciences. 1999;**64**:965-974

[52] Brawley L, Itoh S, Torrens C, Barker A, Bertram C, Poston L, et al. Dietary protein restriction in pregnancy induces hypertension and vascular defects in rat male offspring. Pediatric Research. 2003;**54**:83-90

[53] Vickers MH, Breier BH, McCarthy D, Gluckman PD. Sedentary behavior during postnatal life is determined by the prenatal environment and exacerbated by postnatal hypercaloric nutrition. American Journal of Physiology. Regulatory, Integrative and Comparative Physiology. 2003;**285**:R271-R273

[54] Aihie Sayer A, Dunn R, Langley-Evans S, Cooper C. Prenatal exposure to a maternal low protein diet shortens life span in rats. Gerontology. 2001;**47**:9-14

[55] Gale CR, Javaid MK, Robinson SM, Law CM, Godfrey KM, Cooper C. Maternal diet during pregnancy and carotid intimamedia thickness in children. Arteriosclerosis, Thrombosis, and Vascular Biology. 2006;**26**:1877-1882

[56] Ijuin T, Hatano N, Hosooka T, Takenawa T. Regulation of insulin signaling in skeletal muscle by PIP3 phosphatase, SKIP, and endoplasmic reticulum molecular chaperone glucose-regulated protein 78. Biochimica et Biophysica Acta. 2015;**1853**:3192-3201

[57] Phillips T. The role of methylation in gene expression. Nature Education. 2008;**1**(1):1-16

[58] Chen Z, Zang J, Whetstine J, Hong X, Davrazou F, Kutateladze TG, et al. Structural insights into histone demethylation by JMJD2 family members. Cell. 2006;**125**:691-702

[59] Sharples AP, Stewart CE, Seaborne RA. Does skeletal muscle have an 'epi'-memory? The role of epigenetics in nutritional programming, metabolic disease, aging and exercise. Aging Cell. 2016;**15**:603-616

[60] Patel H, Jameson K, Syddall H. Developmental influences, muscle morphology, and sarcopenia in community-dwelling older men. The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences. 2012;**67**:82-87

[61] Patel HP, AlShanti N, Davies LC, Barton SJ, Grounds MD, Tellam RL, et al. Lean mass, muscle strength and gene expression in community dwelling older men: Findings from the Hertfordshire Sarcopenia Study (HSS). Calcified Tissue International. 2014;**95**:308-316

[62] Jaenisch R, Bird A. Epigenetic regulation of gene expression: How the genome integrates intrinsic and environmental signals. Nature Genetics. 2003;**33**(Suppl):245-254

[63] Bateson P, Barker D, Clutton-Brock T, et al. Developmental plasticity and human health. Nature. 2004;**430**:419-421

[64] Tanaka M, Yoshida M, Emoto H, Ishii H. Noradrenaline systems in the hypothalamus, amygdala and locus coeruleus are involved in the provocation of anxiety: Basic studies. European Journal of Pharmacology. 2000;**405**(1-3):397-406. DOI: 10.1016/S0014-2999(00)00569-0. PMID: 11033344