

Healthy Children - A Healthy Nation: Modern Approaches of Pediatricians to The Prevention of Childhood Diseases

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ABSTRACT

The article investigates modern approaches in pediatrics to the prevention of childhood diseases. The author notes that today it is necessary to monitor the health of the younger generation, because in the future children should become full-fledged citizens of their country, and their health is a potential, which in the full sense of the word is the “building material” of the foundation of any state. It must be remembered that lifestyle-related variables and inadequate environment that surround children and adolescents can affect their cardiovascular health, which can cause serious health problems in the future.

The connection between obesity, hypertension, hyperglycemia in childhood and cardiovascular risk in adults is quite consistent, and it is possible to overcome the negative impact of the above factors if appropriate prevention programs for childhood diseases are developed already in childhood, within which not only medical professionals, but also parents and educational organizations should act.

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INTRODUCTION

Children act as a continuation of the family, but they are also the future for their country. For this reason, children's health is the most important factor that determines the future of the nation as a whole. Unfortunately, appropriate attention is not always paid to ensuring healthy and full-fledged development of children.¹

In 2019, approximately 38.2 million children under the age of 5 were overweight or obese in the world. Once considered a problem in high-income countries, overweight and obesity are increasing in low- and middle-income countries, especially in urban areas. In Africa, the number of overweight children under the age of five has increased by almost 24% since 2000. In Brazil, obesity in the age group from 5 to 9 years reached 17.6% and 12.4% of girls and boys, respectively. In this age group, about a third of children are overweight, which is a warning sign of childhood obesity risk. Obesity threatens to undo the gains made in increasing life expectancy over the past two centuries, and has become one of the most important global health problems in the 21st century.

All of the above was further aggravated during the COVID-19 pandemic. The researchers found an increase in overweight and obesity, especially in children aged 5 to 11 years, the percentage of which increased by 8.7% during the pandemic. Among adolescents aged 12 to 15, overweight increased by 5.2% compared to the period before the pandemic, and among people aged 16 to 17, the increase was 3.1%.

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An increase in the prevalence of overweight in children has contributed to an increase in the global burden of chronic diseases, such as obesity in adulthood, mental health problems, diabetes, cardiovascular diseases and some types of cancer. The anthropogenic environment, one of the factors responsible for the increase in obesity rates in children and adolescents, is defined as “the sum of the influences that the environment, opportunities or living conditions have on the development of obesity in individuals or groups of the population.” Modifiable environmental factors have an indirect effect on human eating behavior and physical activity.

The mechanisms explaining the relationship between multiple urban exposure and the development of childhood obesity are still poorly understood. Air pollution can affect the molecular mechanisms involved in the pathogenesis of obesity. Noise has been linked to sleep deprivation and increased production of stress-related hormones. Green spaces, built-up environment and vehicle traffic can partially determine the levels of air pollution and noise and, in turn, affect the prevalence of overweight. In addition, the urban environment can modulate various behaviors related to weight, including well-known risk factors for obesity, such as diet, physical activity, sedentary lifestyle, sleep duration and well-being.

Separate studies have shown a strong link between air pollution and obesity in the childhood age group through biological and behavioral mechanisms, while greater accessibility and exposure to green spaces were associated with increased levels of physical activity and sleep duration. A better understanding of the relationship between the impact of the urban environment and overweight behavior is necessary to develop effective strategies for promoting health in society.

The purpose of the study is to consider modern approaches in pediatrics to the prevention of childhood diseases.

MATERIALS AND METHODS

In the process of writing the work, articles and publications were considered within the framework of the research topic, the analysis of the material was carried out using the comparative method and the synthesis method.

RESULTS

In the early period of life, represented by the intrauterine period and the first years of life, cells, tissues, organs and systems are immature and have greater plasticity, therefore, in their development and maturation, they are more susceptible to the influence of the environment and nutrition factors.

Exposure can be defined as a cumulative effect to which an organism can be exposed from birth to death, affecting health or the development of diseases. This impact can be both endogenous (for example, infections and psychological stress) and exogenous (for example, environmental pollution and smoking). Some of these impacts can lead to responses, such as epigenetic changes secondary to environmental and nutritional factors.; consequently, exposome may be associated with the risk of developing chronic non-communicable diseases, such as obesity.²

Environmental and nutritional factors can modify the exposome due to constant structural changes, accelerated cell aging and modification of gene expression (epigenetic factors).

Epigenetic factors include DNA methylation, histone acetylation, and the presence of microRNAs. They interfere with DNA transcription and translation in a complex and dynamic way, increasing or decreasing gene expression. The main target of epigenetic factors is CpG sites, which are regions located close to the regions of the gene activator.

DNA methylation occurs when a methyl group is incorporated into the structure of one or more genes. The expression of methylated and hypomethylated genes is suppressed and elevated, respectively. Histones are structures in which DNA is folded and compacted; when they are in a deacetylated (grouped) form, DNA transcription is difficult, and in an acetylated (relaxed) form, the DNA chain is more open and, therefore, may be easier to transcribe. Micro-RNAs are small RNAs (from 21 to 24 nucleotides) that affect the translation of matrix RNA and, consequently, protein synthesis.

During pregnancy, the nutritional status of the mother (malnutrition and obesity), diseases (diabetes and hypertension), infections, exposure to chemical factors (tobacco, dioxins, pesticides, etc.) and stress affect the risk of obesity in offspring through epigenetic factors. Smoking and paternal obesity are also associated with epigenetic markers in germ cells that increase the risk of obesity in offspring throughout life.³

Publications related to the Dutch Winter Hunger Cohort describe the long-term effects of acute malnutrition during pregnancy on the health of offspring (children and grandchildren). Children of malnourished women in the early stages of pregnancy were at greater risk of developing cardiovascular diseases, diabetes, obesity and certain types of cancer; in turn, male grandchildren of women who starved at the end of pregnancy are at greater risk of obesity, especially perivisceral type.

Some of these results of the Dutch Winter Hunger Cohort can be attributed to epigenetic factors. In those exposed to hunger in the prenatal period, almost six decades later, DNA methylation of the insulin-like growth factor 2 (IGF-2) gene - an important mediator of cell proliferation, growth and differentiation - was reduced compared to those who were not exposed.

The practice of breastfeeding is one of the factors associated with protecting against obesity throughout life. A systematic review has shown that breastfeeding is associated with a reduction in the risk of overweight in adulthood by about 25%. Some of the proposed mechanisms to explain this relationship include the composition of breast milk, which adapts to the needs of the infant, including aspects related to the amount of nutrients; the presence of adipokines, such as leptin, which affect the hypothalamic center of hunger/satiety; they also described how the baby empties the breast (more slowly compared to feeding milk from a bottle), self-regulation of appetite and, more recently, epigenetic factors in this process.

Breastfeeding affects the expression of several genes through DNA methylation and the presence of numerous microRNAs in breast milk; these micro-RNAs are species-specific and affect energy expenditure, the immune system, the inflammatory response and the maturation of the gastrointestinal tract.

A cohort study compared the effect of breastfeeding on DNA methylation in infants exclusively, partially breastfed or exclusively artificially fed. The authors showed that exclusive breastfeeding up to 4-6 months of life was associated with a higher percentage and diversity of DNA methylation between birth and ten years of age.

World Health Organization (WHO) and Food and Agriculture Organization (FAO) of UN has been recommending governments to compile food reference books for more than 20 years. After all, people consume foods, not specific nutrients. These guidelines should ultimately provide advice and encourage people to lead healthier lifestyles and make better food choices. Thus, food reference books are an important medical technology for improving food and nutrition standards and promoting public health.⁴

In the requirements for the organization of a healthy diet, products are divided into four groups: fresh and minimally processed, culinary ingredients, processed and ultra-processed. Ultra-processed food (UPF) should be avoided; these are industrial formulations that mainly include substances extracted from food (oils, fats, sugar, starch, proteins), obtained from food components (hydrogenated fats, modified starch) or synthesized in the laboratory (dyes, flavors and flavor enhancers). Their label lists more than five ingredients; they are very tasty, easy to cook, and they have a longer shelf life. Moreover, they harm the environment due to the large amount of packaging in which this type of food is located. These products are aggressively advertised by the food industry to encourage their purchase and shape food preferences, and children are the main consumers of UPF.

Recently, the link between endocrine disruptors (ED) and the global obesity epidemic has also gained prominence. Some experimental studies show that these substances, also called obesogenic substances, can influence the development and progression of obesity.

ED is defined as chemicals exogenous to the body that can affect hormonal axes and cause adverse consequences for human health, his offspring and the environment. More than 800 chemicals are listed in the World Health Organization's book/The list continues to grow, including industrial products, pesticides, plastic products, phytoestrogens and several heavy metals.⁵⁻⁷

Obesogens can act directly on fat cells, causing hyperplasia or hypertrophy of adipocytes, but they can also act indirectly, controlling hunger/satiety, reducing the rate of basal metabolism and affecting the intestinal microbiota. Obesogens can cause changes in hormonal function by activating or inhibiting nuclear receptors (estrogen receptor, androgen receptor, thyroid hormone receptor, retinoic acid receptor X alpha/gamma receptor activated by proliferator peroxisome (PPARG), glucocorticoid receptor).

A recent systematic review included several articles from different countries with studies on the relationship between various types of ED and obesity in children and adults. The authors found a positive relationship between bisphenol A exposure and obesity (both generalized and centripetal) in adults, as well as between phthalate exposure (in particular,

some types of phthalates) and obesity in children and adolescents.

Epidemiological studies show that prolonged and persistent exposure to low concentrations of organic pollutants, such as pesticides, may be associated with the risk of obesity and complications such as high blood pressure, diabetes and dyslipidemia.

The food industry and packaging are common sources of ED; therefore, it can be assumed that food and beverage packaging may also be associated with an increased risk of obesity, since they contain plastic compounds such as bisphenol A. Some authors suggest that anti-obesity policies should take into account substances that cause obesity.

DISCUSSION

The growing concentration of families in cities with less mobility increases violence in cities, and the lack of places available for games, recreation and sports plays an important role in the development of obesity.

Sedentary lifestyle in the children's age group, manifested by low physical activity and a lot of screen time, is a serious public health problem. Only 23% and 19% of children aged 11 and 13, respectively, achieve the recommended level of physical activity, which is 60 minutes of moderate or high activity per day, according to a survey conducted in 38 countries. At the same time, data suggest that today's children and adolescents spend less time outdoors than their parents at the same age. Unfortunately, this situation has worsened significantly since the outbreak of the COVID-19 epidemic.

A change in this scenario, according to a recent study, is associated with an increase in the impact of an adequate environment for outdoor leisure. Places with less car traffic, houses with access to the backyard and the presence of green spaces in the vicinity are associated with more time for games and recreational activities in general, and these changes in habits are associated with a decrease in sedentary lifestyle and improved cardiorespiratory endurance in children and adolescents.

The school also contributes to the practice of lifestyle changes and increased physical activity in order to prevent and reduce excess weight/obesity in the child age group in developed and developing countries.⁸

The intestinal microbiota plays an important role in the formation of a healthy lifestyle of a child. The intestinal microbiota consists of trillions of microorganisms, the number of genes of which is more than 100 times the number of genes in the human genome. These microorganisms living in the gastrointestinal tract, mainly in the distal colon, are of great importance for maintaining the homeostasis of the host metabolism.

The human microbiota develops from birth to the age of two and is relatively stable after one and a half years of life. During birth, a newborn is exposed to several types of bacteria, depending on factors such as the type and duration of labor and oxygenation. The magnitude of the influence of these factors on the microbiota is still controversial in the literature.

After birth, the growth of the intestinal microbiota continues, and after about 31 months, the microbiota becomes similar to an adult and is unique for each person. The microbiota depends on factors such as the type of diet, the presence and duration of breastfeeding of the mother, the use of antibiotics, physical activity, hygiene, sleep quality and stress. The host genome is necessary to control the composition of the intestinal microbiota, but external factors can also contribute to changing populations of intestinal microorganisms.⁹⁻¹²

Obesity is more associated with a reduction in the diversity of microorganisms (less diversity of gene load) than with the number of each species. Studies have shown that people with a lower number of microbial genes also have a higher risk of insulin resistance, high concentrations of leptin, free fatty acids and triglycerides, in addition to a greater pro-inflammatory profile.

One of the mechanisms of action of the microbiota in the control of metabolism is the fermentation of indigestible dietary fibers with the formation of short-chain fatty acids (SCFAs), which are responsible for 10% of daily energy needs. Each receptor can be activated by different SCFA and has different actions. For example, activation of GPR41 and GPR43 induces the secretion of peptide YY (PYY) by intestinal cells. PYY acts directly on the hypothalamic centers, reducing food intake. Moreover, activation of GPR 41 also increases the expression of leptin by adipocytes. Activation of these receptors reduces lipolysis, reducing the concentration of free fatty acids in the serum and contributing to an anti-inflammatory state.¹³

SCFAs stimulates the secretion of glucagon-like peptide-1 (GLP-1), and the total concentration of SCFAs, propionate and acetate are inversely proportional to insulin resistance.

Another mechanism of action is mediated by a decrease in the activity of fasting-induced fat factor (FIAF). This factor inhibits lipoprotein lipase (LPL) and is produced by the intestines, liver and adipose tissue. The intestinal microbiota suppresses FIAF in the ileum and increases LPL activity and therefore increases cellular uptake of free fatty acids and triglyceride accumulation in adipocytes.

The microbiota also plays an important role in the metabolism of bile acids. A change in the population of intestinal microorganisms prevents the conversion of primary bile acids, which leads to their accumulation and a decrease in secondary bile acids. Primary bile acids act more specifically on G-protein-coupled receptors (TGR5), while secondary bile acids act mainly on the farnesoid X-receptor (FXR). Activation of these receptors leads to changes in lipid and carbohydrate metabolism, energy consumption and inflammation.

Another important role of the microbiota is to strengthen the barrier of the intestinal mucosa. Damage to this barrier is associated with an increased risk of infection, sluggish inflammation and increased oxidative stress.

Consequently, the intestinal microbiota has an important effect on the host's metabolism. However, in the case of obesity and related diseases, it is still difficult to determine what is the cause or effect due to conflicting studies, differences in responses in animal and human studies, and the complex interaction of trillions of microorganisms and the host. with

the activation of several molecular mediators. There remains a large area of research not only to determine the molecular mechanisms involved, but also to search for an intervention that can lead to a healthier microbiota and thus contribute to improving metabolic balance.

Also, studies show that poverty has a negative impact on the development of a child. The study of the impact of poverty on the development of a child has shown that poverty determines a set of undesirable characteristics:

- 1) high physical and psychological stress;
- 2) high exposure to toxic substances;
- 3) low access to medical care;
- 4) low access to healthy food choices;
- 5) limited access to safe places for physical exercise. When these socio-ecological conditions occur in an associated and chronic way, biological and behavioral adaptation predisposes to a protective phenotype - neuroendocrine changes that regulate body stress, behavior, sexual development and the immune system. This response leads to the possibility of greater protection with the development of a pro-inflammatory profile and accelerated puberty.¹⁴

This programming of the immune system is associated with a tendency to pro-inflammatory conditions, with high activation of pro-inflammatory cytokine pathways and high monocytic activity, which causes chronic inflammation. This association - exposure to an unfavorable environment in childhood and a tendency to pro-inflammatory processes in adults - persists even when other pro-inflammatory factors in adulthood, such as obesity, hypertension and dyslipidemia, are under control. The influence of this process is especially great if the injury occurred in early childhood, during the maturation of the immune system. This pro-inflammatory condition seems to have other consequences, such as increased impulsivity to immediate rewards and, consequently, increased behaviors such as tobacco use, alcohol abuse and the use of illicit drugs.

Chronic hunger in childhood also increases the risk of a sparing somatic phenotype characterized by low growth, slow metabolism and less active behavior. Moreover, in adults who suffered from hunger in childhood, there is a tendency to increase food intake without hunger, due to a violation of homeostasis in the regulation of hunger-satiety; therefore, they belong to a high-risk group for obesity in adulthood.¹⁵

Two German case-control studies analyzed the risk of stroke in adults who experienced poverty and its complications in childhood. The first one showed that this chance is 77% higher in exposed individuals (95% CI: 1.2-2.6) than in non-exposed individuals, regardless of the profession of the parents, living conditions or family income. Another study showed that adverse conditions cause a high risk of smoking, alcohol abuse and a sedentary lifestyle, factors that, when controlled, had less influence on this relationship.¹⁶

CONCLUSION

Thus, today it is necessary to monitor the health of the younger generation, because in the future children should become full-fledged citizens of their country, and their health is a

potential, which in the full sense of the word is the “building material” of the foundation of any state. It must be remembered that lifestyle-related variables and inadequate environment that surround children and adolescents can affect their cardiovascular health, which can cause serious health problems in the future. The relationship between obesity, hypertension, dyslipidemia and hyperglycemia in childhood and cardiovascular risk in adults is quite consistent, and it is possible to overcome the negative impact of the above factors if appropriate prevention programs for childhood diseases are developed already in childhood, within which not only medical professionals, but also parents and educational organizations should act.

AUTHOR CONTRIBUTIONS

All authors contributed in reviewing the final version of this paper.

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