International Journal of Nutrology
(Official Journal of the ABRAN - Brazilian Association of Nutrology)

REVIEW ARTICLE

DOI: 10.54448/ijn22303

First 2,200 days of life as a window of opportunity for multidisciplinary action regarding the developmental origin of health and disease: positioning of the Brazilian Association of Nutrology

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E-mail: dr.nogueira@me.com
DOI: https://doi.org/10.54448/ijn22303
Received: 05-10-2022; Revised: 07-20-2022; Accepted: 08-02-2022; Published: 08-25-2022; IJN-id: e22303

Abstract

Introduction: From the beginning of the 21st century, a new concept began to emerge in scientific and social circles: the first 1,000 days of life. Along the same lines, an international movement started in the same period began to discuss the "developmental origin of health and disease". Numerous problems that affect human beings throughout their life cycle begin in the early years and often can be avoided or minimized when early recognized and addressed. This document discusses, based on the scientific literature, the idea of expanding the window of opportunity for 2,200 days, encompassing the preconception phase to the end of the fifth year of life. **Methods:** Scientific articles published up to 2022 in Pubmed/Medline, SciELO, Google Scholar, and Lilacs databases, in Portuguese, English, and Spanish, were reviewed in an integrative manner. The search for articles was directed to topics related to intervention targets that could impact the present and future health of the child. **Results:** Biological, social and psychological aspects were studied in five phases: preconception, gestational, first year, second year, and third to the fifth year of life. The data obtained show the importance of expanding the period of greater professional attention at the beginning of life. **Conclusion:** The Brazilian Association of Nutrology recommends a window of 2,200 days (100 days in preconception + 270 days of gestation + 1,830 days from the first to the fifth year of life) as the ideal period of professional activity to guarantee present and children's future.

Keywords: Child health. Preconception health. Gestational health. Post-gestational health.

Introduction

From the beginning of the 21st century, a new concept began to emerge in scientific and social circles: the first 1,000 days. Considering the sum of the gestational period and the first two years of life, this "round" number helped to shape the extremely important idea, which refers to a window of opportunities for special professional care, with a focus on ensuring present health and the future of the child. Numerous studies before and after that date showed that various interventions, especially nutritional ones, in this period, led to relevant health gains, in the short, medium, and long term. On the other hand, negative stimuli also had undesirable consequences, such as obesity, cognitive losses, low immunity, and dysbiosis,

among others [1-7].

Along the same lines, an international movement that also started in the 21st century began to discuss the "developmental origin of health and disease". Numerous problems that affect human beings throughout their life cycle begin in the early years and often can be avoided or minimized when early recognized and addressed. The idea is precisely to increase the performance of health professionals at the beginning of life, aiming at better health over the years.

There is no doubt about the importance of the role of different health professionals during the first 1,000 days of life. However, one might question whether this window could not be enlarged. Many researchers have focused on the impacts on the future health of the child resulting from different conditions associated with the father and mother, even before conception [8]. Additionally, it is known that many relevant aspects, such as the development of the central nervous system and the consolidation of the microbiota, are still under construction after the second year of life [9,10].

The present document discussed, based on the scientific literature, the idea of expanding the window of opportunity for a period of 2,200 days, encompassing from the preconception phase to the end of the fifth year of life (100 days in preconception + 270 days of gestation + 1,830 days from the first to the fifth year of life).

Methods

Scientific articles published until 2022 in PubMed/Medline, SciELO, Google Scholar, and Lilacs databases, in Portuguese, English, and Spanish, were reviewed. The search for articles was directed to topics related to intervention targets, from the preconception period to the end of the fifth year of life, which could impact the present and future health of the child. Biological, social and psychological aspects were studied, which are presented, just for organization, in five phases: preconception, gestational, first year, second year, and third to the fifth year of life. In the end, based on the survey carried out, the recommendations of the Brazilian Association of Nutrology are made.

Preconception and Prenatal Periods

The first 370 of the 2,200 days of the window of opportunity refer to the 100 days before conception and the 270 days of gestation. The justification for these days to be highlighted is based on the influence, suggested by scientific evidence, that the health status of the parents has on embryogenesis, intrauterine fetal growth, and the child's future health [11,12]. Thus, the structure involved in assisting these future parents must increasingly strive to identify, prevent and treat situations that may disturb or jeopardize the health of their offspring, both in the intrauterine phase and in the early years of childhood [13].

The first 100 days of the window are unique in that they also devote attention to the paternal component. The pre-implantation period of embryo development begins with the fusion of haploid gametes provided by each parent, generating a diploid zygote [14]. This means that the first condition for the development of a healthy embryo is the good quality of the gametes. And this quality is directly related to the general health condition of the parents [15].

Behavioral factors, such as smoking and excessive alcohol consumption, and environmental factors, such as nutritional status, age, and exposure to endocrine disruptors, can impact semen epigenetics (microRNAs, long non-coding RNA, histone occupancy, and DNA methylation). composition of seminal plasma, negatively influencing embryo development, fetal growth, and potentially the long-term health of offspring [16-18].

Primary preconception care for the father is therefore rational and should be encouraged. Despite this, there are limitations, both due to the disorganization of the health system, which has not invested equally in maternal health, and the usual small involvement of the male gender [17]. There is a need to change this paradigm. The health professional can act by demonstrating paternal importance in the health of the descendant, involving him in changing habits and, eventually, with specific treatments [19]. Guidelines such as smoking cessation and high consumption of alcoholic beverages, physical exercise, less exposure to pollutants, and treatment of metabolic diseases such as obesity and diabetes are essential [17].

Regarding maternal health, the scientific literature is increasingly full of evidence demonstrating the influence of maternal health on offspring, both in the period before conception and during pregnancy. In the first moment, as well as the paternal component, in the provision of a healthy gamete [16] and, in the second, through the provision of a suitable intrauterine environment for fetal development [13].

Little is known about the biological mechanisms involved, but some health situations and/or behaviors

of women in the preconception period are shown to be associated with a worse prognosis for the health of the offspring. For example, newborns of mothers with a psychological problem before pregnancy appear to have twice the risk of increased emotional reactivity compared to those of mothers without this diagnosis **[20]**. As well as stressful situations in this period can increase the risk of mortality **[21]** or impact the weight of the newborn **[22]**. In addition, scientific evidence is increasingly strong regarding the negative impacts on offspring related to smoking, alcohol consumption, and especially low food quality and exaggerated energy intake, in addition to obesity and malnutrition **[8,22-24]**.

The medical performance at this moment is fundamental, however, complex. To be effective, both in preconception and prenatal care, it is necessary to understand the different realities and environments experienced by women, which makes it difficult to establish a universal care approach **[8,13]**. In general, in the preconception period, priorities would be folic acid supplementation for all women, guidance, and support for changes in risky habits, review of medications in use and previous obstetric history, action in pre-existing chronic diseases, and consideration of the possibility of some genetic risk **[8]**.

Prenatal care is a very opportune moment for communication, education, and intervention in women's health **[25]**. There are issues related to access and quality of this care, but, in general, pregnant women are predisposed to seek medical help and are willing to take measures to improve their quality of health. Thus, the identification of vulnerabilities and risk stratification, in addition to the implementation of established preventive and therapeutic interventions, is essential **[26-28]**.

The World Health Organization (WHO) listed 39 recommendations for prenatal care divided into 5 types of interventions: nutritional interventions, maternal and fetal assessment, preventive measures, interventions for common physiological symptoms, and interventions in health systems to improve the use and quality of antenatal care **[29]**.

Such recommendations are based on scientific evidence and most are already established in clinical practice. However, some are still discussed among researchers and lack better evidence. Thus, the supplementation of some micronutrients (vitamins and minerals) and omega-3 must be carried out according to specific needs. It is worth mentioning the difficulty of conducting clinical trials in this area due to the heterogeneity of the populations evaluated and the different possible maternal and fetal clinical outcomes **[30,31]**.

Among the unanimous recommendations in this period are healthy eating, physical exercise, adequate weight gain, and reduced exposure to cigarettes, alcohol, and substances known to be harmful to health **[32]**. Certainly, due to the global overweight and obesity pandemic and the recognized impact of energy-metabolic disorders on fetal and infant health, nutritional intervention is gaining importance and should be encouraged **[33,34]**.

Considering the complexity of the obesity disease, every pregnant woman with this diagnosis should have a multidisciplinary team including obstetricians, nutritionists, nutritionists, physical educators, and psychologists, among others, to provide information, follow-up, and effective treatment. There is a need to identify specific nutritional deficiencies, as well as control the energy balance to reduce or reverse the metabolic impacts on maternal and fetal health **[33,34]**. As a general guideline, a healthy diet during pregnancy contains adequate energy, protein, polyunsaturated fatty acids, fiber, vitamins, and minerals, obtained through the consumption of a variety of foods, including green and orange vegetables, meat, fish, beans, nuts, and cereals whole grains and fruit **[29]**.

Thus, the first 370 days, a period focused on paternal and maternal health, are the initial steps for the healthy development and healthy growth of future generations. It is very important to emphasize the role of the father, giving special attention to his nutritional status and the possible need for supplements, in addition to caring for his emotional health, factors that can influence sperm quality. In general, the omission of this care means the passage of precarious genetic information, undesirable intrauterine epigenetic manifestations, and compromised future generations' health.

The First Year Of Life

The first year of life, from birth to 12 months, is a very important period for a child's growth and development. A dynamic and continuous process of cell differentiation is observed, which begins at conception and has greater activity in the first year of life. It is dependent on the interaction of intrinsic or organic (genetic and neuroendocrine) and extrinsic or environmental factors (nutritional, geophysical, physical activity, mother-child bond). It encompasses physical growth, neurological maturation, behavioral,

sensory, cognitive, and language development, as well as socio-affective relationships **[35,36]**.

Nutrition and lifestyle, before and during pregnancy, lactation, and early childhood, have been shown to induce long-term effects on child health, including the risk of common non-communicable diseases such as obesity, diabetes, and cardiovascular problems. This phenomenon is known as "early metabolic programming of long-term health and disease" **[37]**.

In 2008, The Lancet **[38]** published a series on maternal and child malnutrition that identified the need to focus on the period from conception to the end of the child's second year of life (the first thousand days), with emphasis on good nutrition and healthy growth, which would have lifelong benefits. Since the publication of this series, the concept of the first thousand days has been adopted by academia and international non-governmental agencies and organizations **[39]**.

Currently, the WHO focuses on the first 1,000 days, but already with concern for the prevention of obesity, highlighting the importance of nutritional guidance and healthy lifestyle habits, for this age group and children over one year old **[40,41]**. Adequate nutrition during pregnancy, associated with exclusive breastfeeding for the first six months, the addition of adequate complementary foods, and continuation of breastfeeding for two years or more, in addition to maintaining good eating habits and physical activity, are basic requirements for growth and development. full child development **[37,42,43]**.

Black et al. **[43]**, Swinburn et al. **[44]**, Bergmeier et al. **[42]** and Skouteris et al. **[45]** showed that the origins of adult health and well-being derive from genetic-environmental interactions that extend from conception to age 24 months (first 1000 days) and continue through age 5 years (second 1000 days) and highlight those young children with adequate nutrition and opportunities for early learning have the best chance of thriving, even when facing biological or environmental threats **[42,43]**.

All scientific societies recognize the importance of exclusive breastfeeding for up to 6 months and complemented up to 2 years or more, for its various factors, highlighting: bonding, warmth, protection, and stimulation (affective, motor, environmental); specific proteins for gestational age and age of life; immune factors; microbiota development (digestive, cutaneous, respiratory); long-chain polyunsaturated fatty acids (LCPUFAs), minerals (macro and micro) and vitamins for brain and physical development **[46-49]**.

Complementary foods (solid and liquids, except breast milk or infant formula) should not be introduced before 4 months, but should not be delayed beyond 6 months **[46,47]**. Predominant and partial breastfeeding should also be encouraged if exclusive breastfeeding is not achieved. If this is not possible, the option is infant formula **[37,46,47,50]**. Victora, et al. **[51]** show in a meta-analysis that exclusive breastfeeding acts as the protection against childhood infections, in the prevention of dental malocclusion, guarantees the genetic potential of intelligence, and leads to probable reductions in the risk of overweight and diabetes. Indeed, Zheng, et al. **[52]** also highlight the importance of encouraging and supporting prolonged breastfeeding for the prevention of childhood obesity.

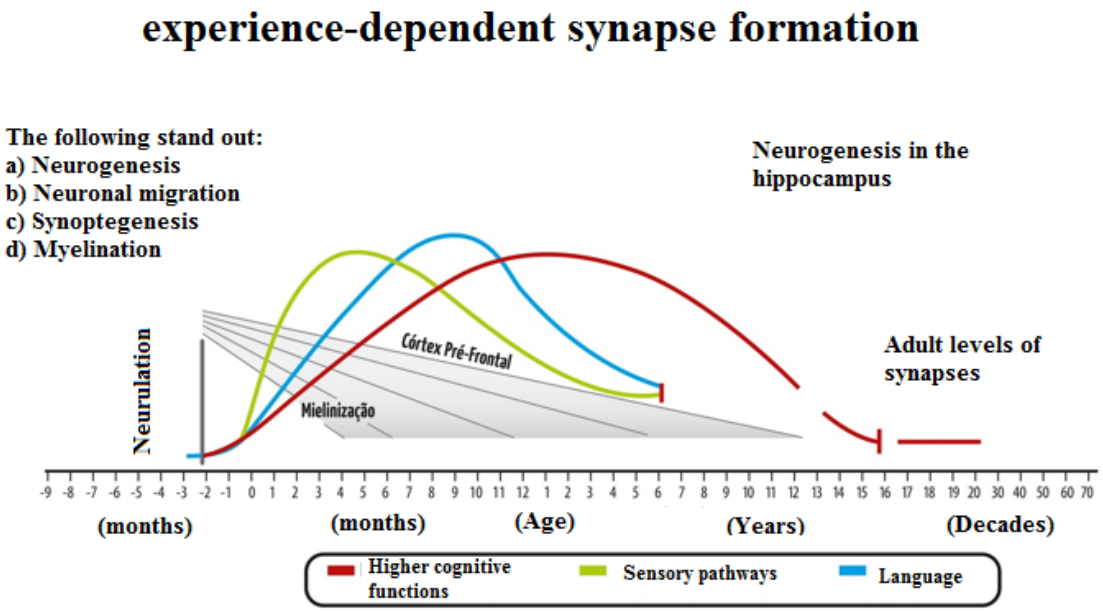
A new report by the First Steps Nutrition Trust identifies key actions needed to protect children from overweight and obesity in the first 1,000 days of life, including the requirement that services become Baby-Friendly accredited **[53]**. Victora points out that, in addition to obesity prevention, much emphasis has been placed on cognitive development and, in this sense, the intake of LCPUFAs is essential for brain development **[51]**. About 70 to 80% of the brain forms within the first 2 years of life **[51]**. During the first 1000 days, brain development is rapid, with nutrition playing an important role in the expression of the genetic code **[54]**.

The basic architecture of the brain is built through a continuous process that begins before birth and continues into adulthood. Simpler neural connections and skills form first, followed by more complex circuits and skills. In the first few years of life, more than 1 million new neural connections form every second. Sensory pathways such as vision and basic hearing are the first to develop, followed by early language skills and higher cognitive functions. Connections proliferate and are pruned, in a defined order, with later, more complex brain circuits built on top of earlier, simpler circuits. Cognitive, emotional, and social capacities are inextricably intertwined throughout life. The brain is a highly interrelated organ and its multiple functions operate in a very coordinated way, as shown in **Figure 1**. Emotional and physical health, social skills, and cognitive-linguistic abilities that emerge in the early years are important prerequisites. for success in school and later in the workplace and community **[54,55]**.

Considering that all nutrients are necessary for brain development and function, some of them have a high impact on its early development, in addition to fats (LCPUFAs - DHA), such as protein, iron, zinc,

iodine, selenium, magnesium, and vitamins A, D, E and B12. The effect is greatest in the fetal and early postnatal periods due to the high metabolic demands of the brain at this age. Breast milk contains the ideal nutrients for neurodevelopment **[56]** and the development of healthy microbiota **[56]**. Clear and consistent evidence indicates that children should be exposed to healthy food environments from conception, which also contributes to the formation of gut microbiota **[43,57]**.

Figure 1. Neurogenesis in the hippocampus.



Source: Adapted from Thompson, R. A., & Nelson, C. A **[55]**.

From the first moments of life, the human body is colonized by a wide variety of microorganisms that become present on the skin and in various mucous cavities (oral, nasal, vaginal, and pulmonary); but the vast majority of them are located in the gastrointestinal (GI) tract and are called the gut microbiota. The newborn's intestine is mainly colonized by several species of Bifidobacterium, which are also abundant in breast milk. Soon after birth, the microbiota in the infant's gut is nourished and shaped by the dietary and bioactive components of milk. The composition of the gut microbiota is thought to largely develop after birth, being influenced by early life events such as mode of delivery, nutrition, and exposure to antibiotics **[57]**. Data from 2021, obtained through gene sequencing, showed that, contrary to what was previously believed, the microbiota does not stabilize at around 3, but at 5 years of age **[58]**.

During critical time windows of development, the intestinal microbiota and its metabolites help not only locally, concerning the intestinal microenvironment, but also beyond the gastrointestinal tract, as in the physiological and structural aspects of the central nervous system (CNS) and in the programming of important body systems, such as the immune system, which, if lost, lead to irreversible changes in the normal growth and functions of these systems. The communication pathways that allow the interaction of the intestinal microbiota with the host's CNS are described as the microbiota-gut-brain axis **[59]**.

Changes in the gut microbiome are associated with pathological conditions, including inflammatory bowel disease, asthma, obesity, metabolic syndrome, cardiovascular disease, immune-mediated conditions, cow's milk protein allergy, and neurodevelopmental disorders **[59,60]**. Early modulation and preparation of the microbiota influence brain health and disease status later in life, so careful nutrition in the early years is critical **[61]**. Allergenic foods can be introduced when complementary feeding (CF) is started at any time from 4 to 6 months. Infants at high risk of peanut allergy (those families with severe eczema, egg allergy, or both) should have peanuts introduced between 4 and 11 months after evaluation by a trained specialist. Gluten can be introduced between 4 and 12 months, but consumption of large amounts should be avoided during the first few weeks and later during childhood. All babies should receive iron-rich CF, including meat products and/or fortified

foods. No sugar or salt should be added to CF and fruit juices or sweetened drinks should be avoided. Vegan diets should only be used under appropriate medical or dietary supervision and parents should understand the serious consequences of not following advice on dietary supplementation **[47,62]**.

Whole cow's milk should not be used in the first year of life due to excess protein and sodium, and lack of linoleic and linolenic acid, iron, zinc, selenium, copper, and vitamins A, C, D, E, and B3, thus predisposing obesity, iron deficiency anemia and deficiencies of the aforementioned nutrients **[47,50,62]**. Michaelsen & Greer **[63]** indicate that it is prudent to avoid high protein intake during the first 2 years of life, which leads to increased glomerular filtration rate due to increased renal solute load and increased risk of overweight and obesity later in childhood. They observed that elevated IGF-I values in early life are stimulated by protein intake and are associated with changes in body composition. This could be achieved by limiting the intake of whole cow's milk or high-protein infant formula beyond the first year of life. Singhal **[64]** 2017 highlights that the increased risk of obesity associated with a high protein intake in early life has led to recommendations to restrict or reduce cow's milk intake in infants and young children and the development of formulas with a low protein content that produces a growth pattern more similar to that of the breastfed infant, which was also highlighted in research by Koletzko et al in 2009 **[65]**, 2014 **[66]** and 2019 **[50]**.

A systematic review carried out by Carvalho et al **[67]**, of 16 studies published between 2003 and 2013 on the food consumption of Brazilian children aged between 6 months and 5 years, showed high frequencies of inadequacy in the consumption of micronutrients, especially iron, vitamin A and zinc, in addition to excess energy consumption. These nutrients play a key role in growth, cognitive development, and immunity, and excess energy predisposes to obesity. Mello et al, 2016 **[63]** presented a review on infant and preschooler feeding and observed that it is characterized by low consumption of meats, fruits, vegetables, and vegetables, high consumption of cow's milk, and inadequacy in the preparation of baby bottles, in addition to early and high consumption of fried foods, sweets, soft drinks, and salt. Nogueira-de-Almeida, et al. **[69]** in a systematic review that included 134 eligible studies, totaling 46,978 children from zero to 83.9 months, observed that in Brazil anemia is prevalent among children of 33%.

Given the evidence of nutrient intake deficiency in children's diets in the first year of life and the importance of this phase, it is essential that the professional involved in pediatric care ensure adequate growth and development of the child, offering the best alternative for nutrition. Thus, it is essential to recommend exclusive breastfeeding for up to 6 months and supplemented for two years or more, to encourage the consumption of foods of high nutritional value, to carry out standardized preventive supplements, and, whenever necessary, to supplement whatever is deficient, so that the child has its full development and future health conditions are ensured.

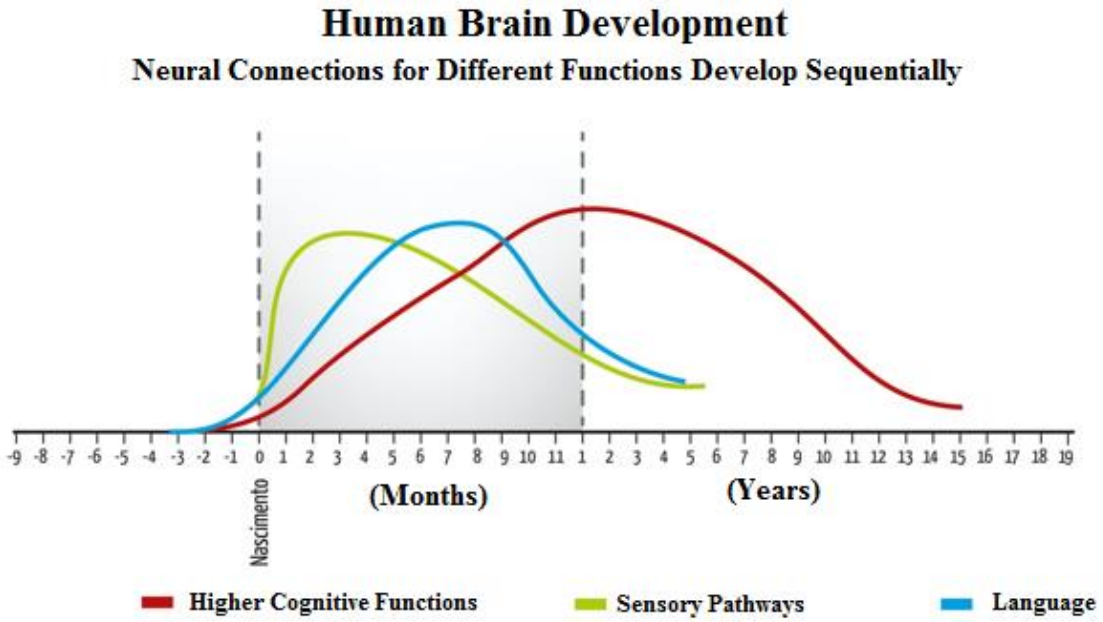
The Second Year Of Life

As in the first year, the period between the 12th and 24th month after birth is characterized by continuous and intense brain development, which is strongly shaped by interactions between genes and the environment where the child lives **[43]**. The experiences with the environment in the first days of life affect the quality of the brain architecture, establishing a solid or fragile foundation for all learning, health, and behavior that follow **[54]**. In the 24th month after birth, the first 1000 days of life end.

The second year of life is marked by the peak of the development of higher cognitive functions and by the improvement of language, motor skills and cognitive and socio-emotional development (**Figure 2**) **[54]**. At this stage, children acquire complex abilities for their development, such as autonomy and understanding of rules and limits.

The US Centers for Disease Control and Prevention (DCP) and the American Academy of Pediatrics (AAP) **[71]** have issued revised guidelines that assist in identifying developmental milestones. According to that document, most 15-month-olds can show an object they like, clap when excited, show affection, try to say a word or two, take a few steps on their own, and use their fingers to feed. At 18 months, the child is increasingly independent, tries to eat alone with a spoon, says "no" by shaking his head, scribbles, points to show something interesting, only plays with toys, tries to say three or more words, and walks alone. At 24 months the child walks more confidently, runs, kicks a ball, eats with a spoon, says at least two words together, notices when others are hurt, holds something in one hand while using the other, plays with various toys, and accepts the company of other children.

Figure 2. Human brain development and different functions that develop sequentially.

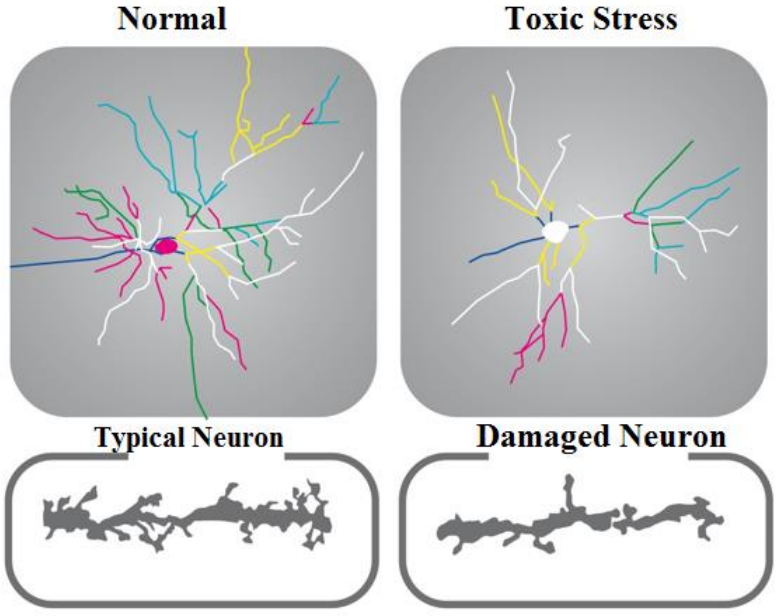


Source: Adapted from C.A. Nelson (2000) **[70]** and Center on the Developing Child (2007) **[54]**.

These advances are achieved as the CNS develops. The brain is more flexible, or "plastic", early in life, aiming to accommodate a wide range of interactions with the environment, but as it matures and becomes more specialized to take on more complex functions, it becomes less capable of reorganizing and adapt to new or unexpected challenges **[54]**. Socio-emotional well-being and adequate nutritional status provide a solid foundation for emerging cognitive skills and form the basis of human development **[54]**.

Environmental stress impairs the development of brain architecture, which can lead to lifelong problems in learning, behavior, and physical and mental health. Stress factors in early childhood include extreme poverty, poor diet, physical and psychological violence, lack of educational stimulation, and severe maternal depression, among others **[43,54,72]**. In the absence of care during this developmental window, environmental stress is built into the organism by processes that shape the architecture of the brain, which, under stress, has underdeveloped neural connections in areas important for successful learning at school and on-site. of work **[54,72]** (**Figure 3**).

Figure 3. Persistent stress and changes in brain architecture.



Source: Adapted from Radley et al (2004) **[73]**, Bock et al (2005) **[74]**, and Center on the Developing Child (2007) **[54]**.

For health professionals, it is necessary to recognize the importance of food as an environmental factor that stimulates neurodevelopment. Key nutrients that support neurodevelopment during this period include protein; zinc; iron; hill; folate; iodine; carotenoids (lutein + zeaxanthin); vitamins A, D, B6 and B12; and LCPUFAs **[30,75]**. Failure to provide essential nutrients during this critical period of development can result in lifelong deficits in brain function, even with subsequent nutrient replacement **[30,75]**.

The second year of life is also recognized as a window of opportunity for the prevention of chronic non-communicable diseases (NCDs). During this period, the child makes the transition from a diet based on milk to one with solid and varied foods. Food learning takes place during this window and it is well documented that exposures to new tastes predict food preferences and behaviors, as well as dietary patterns in adulthood **[76]**. Guidance on healthy eating is needed for the whole family, as children's eating habits are influenced by parents' practices and examples **[77]**.

Breastfeeding should be continued until two years of age or beyond. Epidemiological data show that children who were breastfed have healthier eating patterns in subsequent years **[78-80]**. In addition to the benefits mentioned above, breast milk can transmit to the child the variety of flavors of the mother's diet and shape the family's preferences and acceptance of solid foods during weaning, decreasing the risk of NCDs in adulthood **[76]**.

In general, in the period between 12 and 24 months of life, it is recommended to maintain breastfeeding (and in the absence of breast milk, early childhood formulas should be preferred to cow's milk, to limit protein intake and meet the essential fatty acid and iron requirements) **[81]**; encourage adequate food practices with a variety of flavors and textures (through the consumption of fruits, vegetables, legumes, pulses, oilseeds, grains, cereals, tubers, dairy products, and meats); avoid foods of poor nutritional quality; avoid TV and other screens turned on during meals; supplement iron and vitamin A when indicated; encourage personal hygiene and hand washing; treat intestinal parasites; encourage the practice of exercises, and ensuring sufficient time devoted to sleep **[30,82,83]**. Thus, it is possible to improve the quality of infant nutrition and help prevent severe acute malnutrition, as well as reduce the risk of obesity and cardiovascular, metabolic, and endocrine diseases **[77,83]**.

Actions at individual and collective levels must be implemented. Pediatricians, nutritionists, nutritionists, and other health professionals should familiarize themselves with food sources that provide essential nutrients needed for child development. Although most professionals are aware that exclusive breastfeeding is the best source of nutrition for the first six months, dietary advice thereafter is less robust. Awareness of which foods are "healthy", not just as alternatives to "unhealthy" food, but as positive factors for optimal development, allows professionals to make more appropriate dietary recommendations. As the infant's nutritional intake shifts from the relative protection of breastfeeding to dependence on the choices made by parents, professional guidance for appropriate food choices become increasingly important. In addition, knowing which nutrients are at risk in the infant after the first year of life (eg, zinc, iron, vitamin D) will guide dietary recommendations in the clinic **[75]**.

In the field of public health, opportunities to improve early childhood nutrition, and therefore neurodevelopment, should be focused on two areas **[75]**. First, in designing programs aimed at supporting breastfeeding and providing nutritious foods or supplements to young children. Examples in Brazil include the Baby-Friendly Hospital Initiative, the Strategy for Fortifying Infant Food with Micronutrients Powder (NutriSUS), the National Iron Supplementation Program (PNSF), and the National Vitamin A Supplementation Program (PNSVA). It is necessary to evaluate the creation of new vitamin D and omega-3 supplementation programs. And second, in the dissemination of guidelines that inform providers about the best feeding practices in early childhood.

Third To The Fifth Year

After infancy and childhood, the preschool period refers to a time of transition and transition from total and absolute dependence to preparing for school life and being away from home for longer periods. Studies to separate age groups for clinical research, characterize this age, between 2 and 5 years, as early childhood **[84]**. In Brazil, there are controversies about the nomenclature, and it can vary between 1 and 6 years, but it is usually determined that it is between 2 and 6 years.

The age group from 3 to 5 years is the period in which children are no longer fully fed by their parents and start to choose individual foods, toys, and postures, have a greater motor and developmental autonomy and begin the process of seeking alternatives to the model of total acceptance of what is

imposed on them. Negativism, exploration, and tantrum, in a scheme of intense learning and capturing new experiences, are the primary aspects of preschool.

In many places, preschoolers start their lives outside the home, attending foster or care institutions, daycare centers, preschools, recreation places, or the homes of close family members. In the first fixed separation from the family, they stay full-time or part-time in places with caregivers of different levels of expertise. From a clinical point of view, they are exposed to an environment of greater antigenic contact, which also coincides with the maturation of the immune system, predisposing the child to repeated respiratory, digestive, or dermatological processes **[85]**.

From a developmental point of view, at this age they start socializing with other children and adults different from the family environment, being subjected to behavior patterns different from those found in the first years of life. With this, they can maintain the standard of control and limits or be exposed to models that are different from the previous one. If in the first years the child plays in a centered way and with little interaction with others, from the third year onwards he can respond to patterns of interaction and socialization of contact with peers. He reacts when confronted or when an object is taken from him, but he already learns to share, share, and understand the rules of coexistence.

At the end of this phase, you are ready to start the most complex process of time developed in a single place, in a single activity, and start learning and literacy. Models of literacy readiness would show the ability to be able to develop written and reading language **[86]**. Numerous processes are concomitant in this stage of life. Autonomy begins more clearly with ambulation and the ease of being able to face new environments, now looking from above. Gait and movement stability determine exploration and greater risk of accidents. Speech and understanding skills broaden the horizon of understanding and establishing communication with family members and institutional colleagues **[87]**.

The greater fine motor capacity allows greater control of the hands, the pincer movement, the search for objects, the beginning of the drawing, the execution of copies, and greater attention. The preschool period is of paramount importance for the prevention of chronic nutritional problems since, in this period eating habits, lifestyles concerning physical activity, and behavior patterns are formed more consistently.

A study by Fisberg's group **[88]**, carried out with students from public and private daycare centers in the country, showed a prevalence of overweight of 28% in children under 6 years of age, with a higher number in private schools. Obesity data reached 9% with greater involvement in children between 4 and 6 years old. Recent anthropometry data carried out in the country by the ENANI 2019 National Child Food and Nutrition Study showed that of 14,558 Brazilian children under 5 years of age, 2.9% were underweight for their age and 7% were short stature. The prevalence of overweight and obesity reached 10%, with a significant decrease with increasing age **[89]**.

These data are noteworthy because they disagree with most of the studies recently published in the country, with an increasing sequence of overweight as age increases, with a prevalence of overweight of 40 to 50% in adolescents (ERICA study) and more than 50% in adults (POF and Vigitel) **[90]**. Anyway, it reinforces the condition of the existence of a sum of nutritional problems, such as short nutritional stature, overweight, and still many children with malnutrition. Nutritional insecurity persists in the country **[91]** and these processes are added to a high prevalence of low birth weight, the high number of premature births, and cesarean sections. All these factors determine increased risks for overweight and obesity **[92,93]**.

Another important aspect for the preschool age group is the risk of nutritional inadequacies due to food insecurity, selectivity, and inadequate eating habits. A national approach study showed important risks for the consumption of vitamins and minerals, aggravated in the age group between 4 and 6 years, with the decrease in the consumption of breast milk, infant formulas, and supplementation. There was a low prevalence of inadequate intake of vitamin B6 (<0.001%), riboflavin (<0.001%), niacin (<0.001%), thiamine (<0.001%), folate (<0.001%), phosphorus (<0.1%), magnesium (<0.1%), iron (<0.5%), copper (<0.001%), zinc (<0.5%) and selenium (<0.001%). An important number (more than 95% of the population between 4 and 6 years old) consumed less fiber than the recommendation. Approximately 30% of the sample consumed more saturated fat than recommended. The prevalence of inadequate vitamin E intake ranged from 15% to 29%. More than 90% of children had an inadequate intake of vitamin D. In children over 4 years of age, the prevalence of inadequate calcium intake was approximately 45%. Sodium intake was greater than the recommended upper intake level in 90% of children under 4 years of age and 73% of children over 4 years of age. In

general, the intake of fiber, calcium, and vitamins D and E was lower than recommended. In addition, children consumed large amounts of sodium and saturated fat **[88]**.

Another important point at this age is the continued prevalence of risk factors for low iron intake, with a lower intake of red meat. However, data from ENANI show that the prevalence of iron deficiency anemia does not reach 1.5% of children over 2 years of age **[94]**. These values are much lower than those of previous studies, recently consolidated through meta-analysis **[69]**, and may reflect the possible action of prevention and treatment programs, with the use of iron salts, or methodological problems in obtaining and analyzing the Dice.

The prevalence of low plasma zinc levels reaches 17.4% among children over 2 and under 5 years of age. Precisely in the age group of greater selectivity, a lower supply of zinc is observed, aggravating the intake in children with greater sensory risk **[95]**. The prevalence of vitamin A deficiency at this age reaches 6%, vitamin B12 deficiency at 8.5%, and vitamin D deficiency at 5.3% of the population **[96]**.

Some situations are important to analyze some risk factors and prevention of nutritional diseases at this age. The school system determines reinforcement for adequate cognitive development, especially in populations at higher nutritional risk **[25]**. Entry into the school system also determines admission to a systematized snack, access to school lunches, and food inside and outside the school, beyond the family environment. They still do not have access to canteens, but they are exposed to school lunches (brought from home, from school, or purchased).

Meals away from home need to be planned and can be very important for children with a full-time or part-time school activity. Brazilian school lunches, now regionalized and with greater possibilities for using local foods and decentralized purchases, allow for meals that are more focused on needs and less on excess food or products that are incompatible with the reality of children. However, when the school lunch is not linked to lunch, the data are different. In a national study carried out to evaluate school lunches in this age group, it was found that the morning period determines a more complete snack, with a greater presence of dairy proteins, sources of carbohydrates, and fruits (juice or fresh). The afternoon snack almost always made at home, has a greater hedonic component and a greater share of sweets, candies, and soft drinks **[97]**.

In addition to food, the preschool period can be important in determining protection for aspects linked to lower levels of access to resources. A South African study with daycare children showed that parents living together, in a stable union and higher education even in low income, protected their children from developmental delays **[98]**. In the preschool period, risks and opportunities are determined by the formation of eating habits and the first autonomous experiences of development. As it is a phase of slower growth, it can also be a risk for weight gain. Nutritional deficiencies can be addressed by school lunch and snack care programs, and the initial school environment can be favorable for obesity prevention. Pediatricians have an exponential role, as they need to make families aware of childcare care in the post-infant phase, a period in which family members fail to establish routine follow-up, starting to attend more emergency rooms and emergency services. Adequate pediatric care at this stage involves vaccination guidance for boosters, nutritional guidance inside and outside the home, initiation of physical activity, and emphasis on developmental processes.

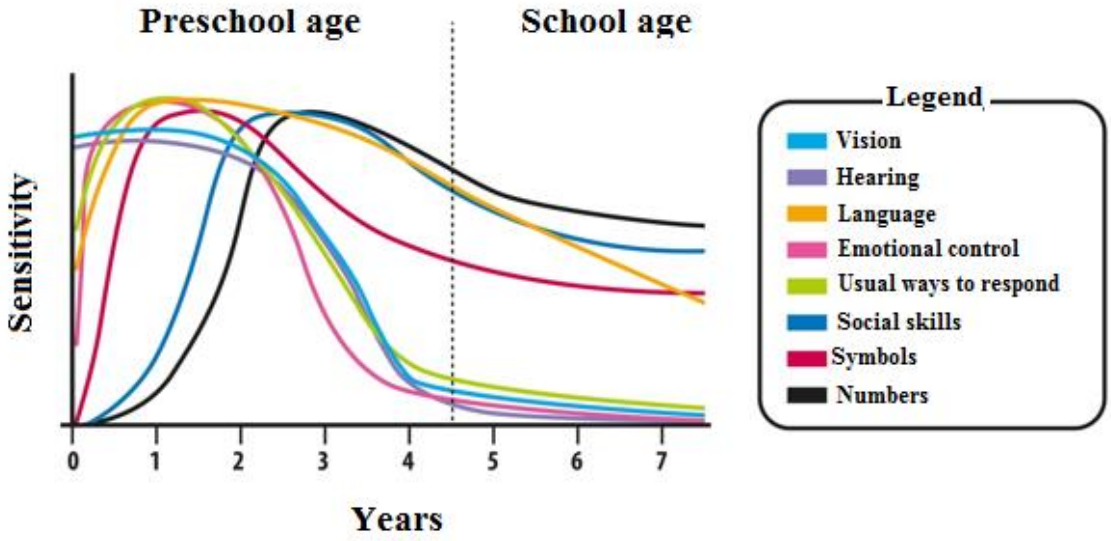
Neurodevelopmental Aspects

The human brain records and response to life experiences, archives consciousness, and bears ultimate responsibility for emotions and behavior (conditioned or "spontaneous"). Whatever genetic potential children receive from their parents, their actual experiences radically and extensively change and modify that potential; the brain is malleable. CNS formation, personality orientation, the establishment of the main lines of interest throughout life, tendencies, emotional patterns, passions, and competences occur during the first stages of an individual's life, with the beginning of life being fundamental for this process, influencing and establishing pathways in brain development that affect learning, health, and behavior throughout the life cycle **[99]**.

Figure 4 helps to visualize how basic dispositions are established before cognitive patterns. After the third year, it will be more difficult to change the personality style. But parents can look to successfully build basic language and number skills more easily through fifth grade **[100]**. Other insights are also important. By checking the "window" of the central auditory system, one can see why exposing a baby to the sounds of a second language works to lay the groundwork for their easy acquisition when appropriate. The need to involve parents in the first years of life is because the window of opportunity for maximum comfort in acquiring "peer social skills" does

not open until the third year, a skill that children need to have social contact with in children's kindergartens or other institutions.

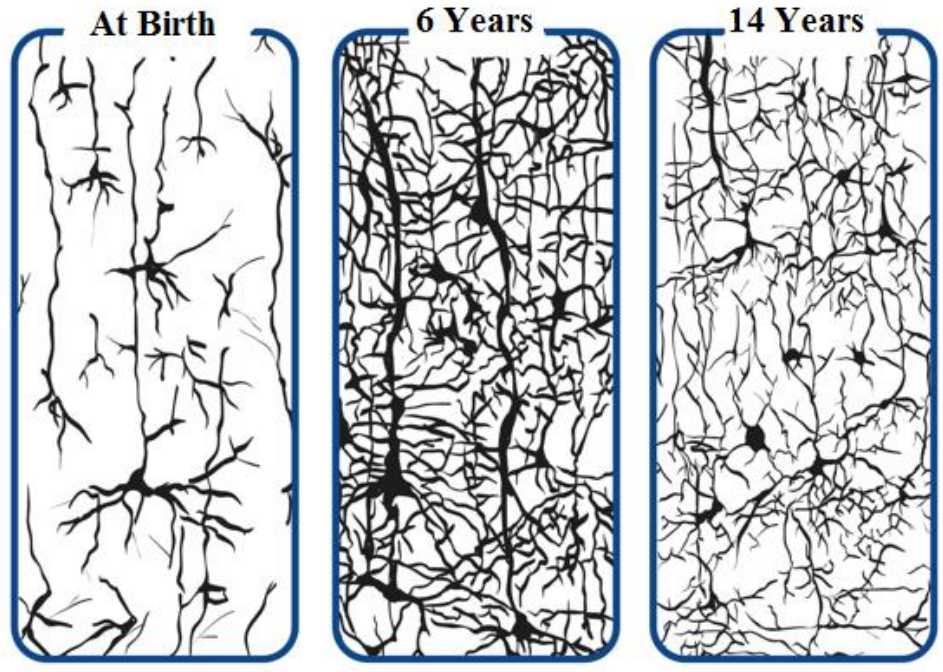
Figure 4. Basic dispositions are established before cognitive patterns.



Source: Adapted from Council for Early Child Development (Nash, 1977; Early Years Study, 1999; Shonkoff, 2000).

When synaptic densities are mapped (**Figure 5**), it is observed that, at birth, disconnected neurons are seen. The rapidity of brain growth in the early years leads to a mass of dense connections **[101,102]**. Between fifth and sixth grade, the process of "choice" begins, whereby the strongest neural pathways (ingrained observations, memories, rules for living well, skills practiced, and so on) are retained, and disconnected neurons are reabsorbed and replaced effectively disappear. This happens to allow the brain greater clarity for adult operational use, also explaining the difficulty in acquiring new knowledge. Thus, the greater the density of neural connections (pathways) in the brain before this process, the more is retained and the greater the capacity for additional learning **[101,103]**.

Figure 5. Synaptic density.



Source: "Synaptic Density". Adapted from Rethinking the Brain. Families and Work Institute. Rima Shore. 1997.

The first days of life, up to five years of age, are characterized by intense growth and motor, cognitive, and neurological development, in which children demand specific nutrients. During pregnancy, the demand for micro and macronutrients increases due to physiological changes (pregnant woman and fetus). In the first three months of pregnancy, adequate nutrition is essential for organ development and differentiation, in the second and third trimesters, feeding is more involved in optimizing fetal brain growth and development **[8,104]**.

From a neurological point of view, the importance of this phase is the susceptibility to diseases, which allows vulnerability to the growth and development of the CNS. Not only genetic factors but also environmental ones can exert influence, being the nutritional factor essential in this process. Other variables, such as stress, emotional deprivation, and socioeconomic and pathological conditions, influence the proper development of sensory systems (hearing and vision), myelination (rapidity of processing and nerve impulse), hippocampus (memory and learning), and prefrontal cortex (attention), inhibition, planning, self-regulation, multiple tasks), neurotransmitter system (monoamines), and brain circuits (associations) **[75]**.

Macronutrients (glucose, proteins, and LCPUFAs) are critical for brain development and influence cognitive ability, learning, and behavior **[105]**. LCPUFAs, a specific group of lipids, have gained prominence in recent years with numerous studies confirming their prominent role in brain development, mainly delimiting the functions of docosahexaenoic acid (DHA) and arachidonic acid (ARA), which are LCPULFAs, formed in the liver from of essential fatty acids **[106,107]**.

In the retina, DHA is the main polyunsaturated fatty acid present in the lipid membranes of the outer segments of rods and cones. In the brain, 10% of its weight and 50% of its dry weight consists of lipids, almost half of which are phospholipids, the main constituents of the double-layer membrane of neurons **[107,108]**. The fetus has limitations for LCPUFA synthesis until at least 48 weeks of gestational age, requiring maternal stock and dietary supply of DHA and ARA to be available through the placenta. Deposition occurs in the brain and retina mainly during the last trimester of pregnancy and in the postnatal phase. In the first years of life, DHA and ARA accumulate in brain tissue around 30 times compared to the third trimester of pregnancy, highlighting the importance of LCPUFA in neurodevelopment **[109]**.

The interval up to the fifth year of life is the most complex period for brain development, when the growth and differentiation of cortical neurons occurs, as well as the establishment of synaptic connections and the development of the visual and auditory cortex, together. with association areas for language reception and cognitive function. The increase in the speed of interneuronal and brain communication due to the myelination process also takes place during this period. The relationship between DHA and cognition, vision, and behavior refers to its association with increased fluidity of cell membranes and modulation of the physiology of monoamine neurotransmitters, affecting dopamine and serotonin signaling pathways **[106,110]**.

Some micronutrients are considered critical for the growth process, including iron, zinc, copper, iodine, and B vitamins **[75,109,111]**. The B vitamins have different roles in the development of the CNS **[112]**: vitamin B6 is a limiting cofactor in the synthesis of numerous neurotransmitters, such as dopamine, gamma-aminobutyric acid (GABA), serotonin, and noradrenaline; directly influences transcription and gene expression and participates in the control of glucose uptake in the brain **[113]**; folic acid (B9) acts on the synthesis of amines, nucleic acids, and cell division, being a priority for growth and also responsible for the genesis of the fetal spine, brain, and skeleton, and its deficiency is associated with neural tube defects; Vitamin B12 acts in the maintenance of the myelin sheath that surrounds neurons and also in the synthesis of neurotransmitters **[113]**.

Iron also has a great influence on the development of the CNS, contributing to several structural and functional stages. It participates in the enzymatic system that regulates brain growth, myelination, synthesis of neurotransmitters (dopamine), and energy production. It is an essential nutrient not only for normal growth, but also for proper mental, motor, and cognitive development **[114,115]**.

The period from preparing for pregnancy to five years of age is critical for the physical, cognitive, social, and emotional well-being of the child, having a direct impact on future health or the development of chronic diseases that can begin even earlier. during childhood.

Psychosocial Aspects

The expression "a mother is born, when a baby is born" is widely used in psychology to emphasize the

importance of the mother/baby dyad, a unit that is constituted from the birth of a child. From the maternal point of view, this will be a time of great challenges and learning, with the mobilization of various internal and external resources, capable not only of shaping the child's behaviors and habits but of perpetuating them into adulthood. From the baby's perspective, it can be said, in a simplistic analogy, that parents will receive a blank canvas, even with limited resources. The child, in addition to depending on a caregiver for their survival, has a primitive mind, lacking symbolization, both for physiological needs and psychic demands. During the first months and years of life, this canvas will gradually acquire colors and shapes capable of constituting the child's personality, composing their legacy of experiences and emotional experiences that will accompany them throughout their existence, making this period constitutes an extraordinary window of opportunity for psychosocial development **[116-120]**.

Although childbirth works as a temporal divider between two distinct realities, pre, and post-birth, it is known that the conception of pregnancy, in terms of mental and emotional aspects, occurs even before pregnancy, with the idealization and preparation of the parents for a new family configuration, which involves practical aspects, but also particular psychic demands. In this aspect, contemporaneity brings new challenges concerning the diversity of family formatting and constitution, which currently extrapolates the pre-existing patriarchal model, changing paradigms. This differentiation promotes the constitution of heterogeneous models of families, where the blood bond can be replaced, or coexist, with the affective bond. In addition, the new family organizations, with mothers active in the labor market, make it possible for third parties to play an important role in the care and education of children. In this way, all knowledge about motherhood can, and should, be extended to those who will exercise what is called the maternal role, which involves becoming a mother/caregiver, with all the responsibilities, dedication, and peculiarities necessary for the children's care.

Regardless of the family constitution, the decision to have a child, nowadays, becomes increasingly programmed and studied. Knowing the new challenges and trying to prepare for them allows, in the future, to better adapt to this new reality, capable of cutting edges related to practical issues, such as the previous health of the pregnant woman, or the health of the child in cases of adoption, absence from work for the caregiver, need for a support network, budget forecast of expenses, contracting health plans and insurance, among other aspects. The objective of the attempt to immerse oneself in this unknown universe is to allow a better adaptation of the environment for pregnancy and postpartum, with fewer stressors acting in a very delicate moment, which, in itself, already carries its challenges.

Unlike environmental issues, which can be pragmatically managed in advance, pregnancy and the puerperium trigger a series of neurological changes, with significant changes in functional and structural plasticity in the human maternal brain, to provide successful adaptation to parenting. The result of this adaptation, whether successful or not, is capable of promoting observable differences in the quality of the mother-infant relationship and, subsequently, in the child's developmental outcomes **[121]**.

The literature shows that these psychological changes, of an adaptive nature, which aim to elevate the woman to the status of the mother, begin to appear during the end of pregnancy and extend until the first months of the baby's life. Among others, two main ones have been listed: future mothers develop greater vigilance to threats, acquiring the ability to discriminate, for example, faces with expressions of anger and fear, a condition capable of allowing the development of the ability to protect their babies from potential threats in the environment; furthermore, they begin to exhibit greater sensitivity to infant signals, associated with increased feelings of emotional attachment towards the fetus, a condition essentially necessary for the psychological adaptation of mothers to care for their babies immediately after birth and in the following months **[121,122]**.

And, if pregnancy provides a favorable environment for the development of increased sensitivity to infant signals, birth solidifies it. Now, the maternal gaze and attention will be attached to puerile signs, such as crying, smells, and smiles, translating into the ability to perceive small baby gestures that are welcomed with exaggerations in maternal/paternal vocalizations and facial expressions during interactions with the newborn **[121,122]**. In addition to heightened sensitivity, new mothers exhibit increased neural activation in the so-called social information circuit, which is associated with empathy, self-monitoring, and reflection. In practice, this activation allows mothers to better understand their own baby's emotional and social cues during interactions and respond appropriately to these demands. The converse, represented by aberrant structures and functions, has currently been associated with serious

future impairments in social competence, such as autism **[121,122]**.

New mothers still exhibit enhanced neural activation in the emotion control circuitry, increasing their ability for effective emotion regulation. Thus, the baby's cry itself functions as a facilitator of an association capable of allowing mothers to understand the child's mental state, intuiting their intentions or needs **[121,122]**. This sensitivity of the mother/caregiver, called the maternal function, is expressed in the condition of the mother, or of the person who plays such a role, in the sense of welcoming the baby's rudimentary emotions and metabolizing them, transforming them into emotionally appropriate responses, less indigestible to the still primitive psychic apparatus of the newborn. An adequate interpretation of the baby's demands, carried out by the mother/caregiver, facilitates the regulation of appropriate responses to these demands, reducing psychological distress, and helping to shape the child's initial socio-emotional development, serving as a basis for later relationships and functioning. psychosocial life span **[116-120]**.

In this sense, the literature is solid in corroborating that children of mothers with higher levels of sensitivity and postnatal bonding present better socio-emotional and behavioral outcomes during childhood. At the other extreme, poor maternal emotional control, which arises in situations of postpartum depression or excessive stress, can negatively impact parenting, allowing for non-contingent and insensitive responsiveness and poor postnatal maternal bonding **[116,117,119,120,123]**.

It is not by chance that maternal depression, as well as severe anxiety, can cause irreparable damage to the mother/baby relationship, increasing the likelihood that these children will develop cognitive, social, emotional, and behavioral problems, often manifested in the form of Deficit Disorder Hyperactivity Disorder (DDHD), irritability, low weight, and eating and sleeping problems, among others **[124]**.

Evidently, given the extreme relevance of this period, not only for the mother/caregiver, but more specifically for the child himself, with all the repercussions that will extend into adulthood, it is important to emphasize the need for care, attention and, sometimes, intervention at that time. Taking care of the mother/caregiver and promoting a good bond with the baby is equivalent to taking care of the child's psychic development because she needs the maternal psychic apparatus to develop her own. The next moment, which comprises preschool age, is marked by contact and observation of other children and social environments, albeit in a reduced way, with less expressiveness, when compared to family social coexistence. So much so that, for example, talking about the formation of eating habits and behaviors in this age group largely involves analyzing the family environment, which demands greater care and consideration. In this regard, and emphasizing the importance of this moment, it is observed that the eating routine acquired between the second and third years of life tends to be maintained in the following years, shaping the child's relationship with food throughout their life **[120]**.

This influence and direction of the family environment reaches the formation of eating habits, but also extrapolates it, modulating emotional experiences, social and affective behavior, and cognitive development of the child, up to 5 years of age. And, despite the attempts of psychology to delimit the role of parents in child development, aiming to identify direct actions of parents that could trigger consequences in their children, in an attempt to achieve some predictability, this is a very complex task. Some researchers have managed to find compelling links between what is conventionally called parenting styles and the effects they have on children **[120]**. These profiles are defined by modulations of different degrees of responsiveness and demand applied by parents in the upbringing and education of their children. From this combination, parenting styles result, capable of positively or negatively impacting education and modulation of emotional responses, as well as children's social and affective behavior. In general, four profiles can be observed, applicable separately to the responsive, authoritarian, permissive, or absent father and mother. The search for understanding the resulting vector between the child's aspects and the different parenting proposals is, perhaps, one of the great challenges faced by professionals who work in the first years of life. Only from the understanding of this triangle of forces, in which the father, mother, and child are at the vertices, will it be possible to guarantee an effective customized service to the family nucleus.

The interval that comprises the preconception period until the postpartum period, from the point of view of psychosocial development, deserves attention and dedication from the family and health professionals who work directly in the care of the pregnant woman and baby. Additionally, early childhood, marked by the way of raising children adopted by the parents, is also capable of determining

and significantly influencing the constitution of the personality and the establishment of future relational patterns of the child that extend into adulthood **[120]**.

Conclusions and recommendations

WHEREAS:

- It can be said that a child's life begins when men and women produce their gametes;
- Several aspects, some of them modifiable, interfere with the quality of gametes and can have an impact on future health;
- The gestational period presents numerous situations, linked to health and illness, which can be modified for the benefit of the developing child;
- Pregnancy is a time of high DNA plasticity, which becomes more subject to epigenetic changes;
- Birth conditions can reflect on numerous aspects related to future health;
- The first year of life is a critical phase, in which nutrition plays a fundamental role, but the beginning of the child's life as an autonomous being requires special care in all ways, including psychosocial ones;
- During the second year of life, several characteristics are established, including nutritional, psychological, and social life habits, which can become permanent;
- Breastfeeding is the cornerstone that links to the best pediatric development, during the first two years of life, or even when continued for longer;
- Between the third and fifth year, aspects related to nutrition, neurodevelopment, and the microbiota are still being established and subject to changes that can be correlated with disease or health;
- Taking into account the days linked to the preconception and gestational period and the initial five years of life, an extended window of 2,200 days is obtained.

ABRAN RECOMMENDS THAT:

- The classic period of the "first 1,000 days" continues to be understood as important for pediatric health care;
- Additionally, the "first 2,200 days" should be considered as an expanded window of childcare and intervention, for the benefit of the present and future health of children.

Acknowledgement

Not applicable.

Funding

Not applicable.

Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

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