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CORRECTIVE FACTORS OF INTESTINAL MICROFLORA DISORDERS IN THE PERINATAL PERIOD

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ABSTRACT

Intestinal microflora is found at approximately 10^4 bacteria per ml of intestinal fluid. Although this ecosystem is very diverse with dynamic changes taking place within it, there is a certain stability in the type and number of species, referred to as the core microbiome, found in 95% of the human population. Genetic variation of microorganisms is relatively small, and their functions are strictly defined and highly conservative. The microbiome exists symbiotically with the host, protecting it against colonization by pathogenic microorganisms, providing essential metabolites, and stimulating the immune system. Colonization begins prenatally and its development is greatly influenced by the course of pregnancy, method of delivery, food supplied to the child during the first moments of life, and post-birth environment. The appropriate intestinal microflora composition is a key determinant of health and homeostasis, and any intestinal dysbiosis can be associated later in life with the development of obesity, diabetes, allergies or cancer. Due to the increasing number of hospitalised pregnancies and deliveries, affecting the intestinal microflora of a newborn, efforts are being made to minimize this process and restore the newborn's microbiome. The use of the Vaginal seeding procedure raises up great hopes, but also some fears concerning its safety. Some very simple and most natural factors have been recently also appreciated and promoted, such as breastfeeding or direct contact of the baby's skin with the mother's skin, which are allies to probiotic bacteria. The purpose of this paper is to emphasize the importance of microbial colonization of the human body and to present the latest and most effective procedures that are designed to correct the existing dysbiosis or to reduce the risk of its occurrence. The literature for the compilation of this study has been obtained from databases such as PubMed, Google Scholar, Web of Science.

KEYWORDS: caesarean section, intenstial microflora, vaginal seeding, breastfeeding, probiotics

Does the method of termination of pregnancy influence the formation of neonatal microflora?

The manner in which pregnancy is terminated is very important in the context of the health of both the mother and the child. The development of a normal microflora depends on the number and type of bacteria species acquired during delivery. Newborns, born physiologically, breastfed, not subjected to antibiotic therapy [1] are considered to possess the most optimal composition of the intestinal microflora – they have a direct contact with the bacterial flora of the vagina and gastrointestinal tract of the mother. Immediate skin to skin contact and breastfeeding are also of great importance. The positive health effect is attributed mainly to *Lactobacillus* and *Bifidobacterium* [2] – colonization with these bacteria is much greater in children who were born naturally than in those whose delivery was terminated in a surgical procedure. The latter in the first weeks of life are much more often colonized by mother skin microorganisms and hospital strains, i.e.: *Enterococcus, Clostridium, Klebsiella, Streptococcus, Haemophilus* and *Veillonella* [2] – while colonization with *Bifidobacterium* bacteria is

delayed by about 180 days in comparison with physiologically born infants [2]. Children born by caesarean section, apart from differences in microbial formation, are more likely to develop adaptive disorders, which additionally prevents the skin contact between the mother and her child and delay the start of breastfeeding. Their presence also often prolongs the time of newborn's hospitalization and the need to implement antibiotic therapy. Planned caesarean sections often take place before the due date of delivery – it is connected with shortening the third trimester of pregnancy, during which the fetus swallows non-sterile amniotic fluid, which also leads to colonization of the gastrointestinal tract with bacteria from the mother [3,4]. The ever-growing number of scheduled Caesarean sections also coincides with the increasing incidence of non-communicable diseases such as food allergies, asthma, obesity, diabetes and autism spectrum disorders, prompting researchers to study the possible causal relationship between these factors.

This work is for illustrative purpose only; it has been compiled on the basis of an analysis of the results of scientific research published in peer-reviewed journals in the years 2000–2018. The following terms were used in electronic search: # cesarean section, # intestinal microflora, # vaginal seeding, # breastfeeding, # probiotics, in databases such as: PubMed, Google Scholar, Web of Science.

Vaginal seeding – innovation or standard?

In connection with the reports of impaired intestinal microflora coupled with the occurrence of many diseases later in life, there are more and more ideas to restore the natural microbiome. One of the most recent procedures is vaginal seeding – it is a aimed at transferring bacteria from the mother's vagina to the newborn, who was born by caesarean section and thus had no contact with the natural microflora from the mother's birth canal. This procedure starts before the surgery, by removing the secretion from the woman's reproductive tract and the colonizing bacteria into a sterile gauze, and then storing it in a sterile container until the baby is born. The next step is to wipe the face and the rest of the newborn's body with the gauze, so that the colonization with bacteria from the mother can begin. In a study conducted in 2016, swabs from the oral cavity, skin and anus were taken from 18 newborns: 7 born naturally and 11 by caesarean section, 4 of whom were subjected to vaginal seeding. Samples were collected from both newborns and their mothers 6 times within one month from the date of delivery (1, 3, 7, 14, 21, 30 days). The results of the study show that in children born by caesarean section, who underwent vaginal seeding treatment, the microbe was similar to the one of children born naturally. Moreover, on the first day after the delivery, the microflora of children born naturally and subjected to vaginal seeding was more similar to that of the mother's vagina, whereas the microflora of children born by caesarean section resembled that of the mother's skin [5]. The results of the study are very promising, however, further formation of the microbiome in children undergoing the study and its impact on their long-term health is not known. Since only four children underwent the procedure, this study is not sufficiently reliable to draw proper conclusions and confirm the safety of the procedure [6].

There are also critical opinions about this procedure – it is believed that during vaginal seeding many pathogenic microorganisms may be transmitted from a mother to a child, which at the moment do not cause active infection and the pregnant woman is not aware of the carrier. *Chlamydia trachomatis, Neisseria gonorrhoeae,* human papillomavirus, cytomegalovirus and group B streptococci are just some of the potentially life-threatening microorganisms that newborns can be infected with [7]. At the moment, with the current state of the scientific knowledge, the American College of Obstetricians and Gynaecologists does not recommend vaginal seeding until more extensive research and more detailed data is obtained in the context of the safety of the procedure.

Use of probiotics and prebiotics and their effect on infant's health

If the delivery was performed without complications, there was no need to apply antibiotic therapy to a mother or a child and the newborn is breastfed, the intestines colonize with probiotic bacteria, whose presence is optimal and allows for proper development of the child. However, the intestinal microflora in children born as a result of a hospitalised labour differs significantly from the microflora of their peers. One way of restoring normal microbial activity is through the supply of probiotics. While the best source is of course breast milk, when children cannot be breastfed, preparations containing different species of beneficial microorganisms and adapted for newborns are used. Probiotic bacteria are also present in artificial mixtures recommended for infant feeding. In the current recommendations of the Polish Society of Neonatology (PTN) from 2015, a cautious approach to routine use of probiotics in newborns has been retained [8]. However, the experts from the World Allergy Organization (WOE) suggests the administration of probiotics in several clinical situations: pregnant and breastfeeding women (where there is a high risk of allergy development in their children) and newborns with a high risk of developing allergies. Probiotics can help prevent autoimmune diseases such as type 1 diabetes. In a large TEDDY study, it was shown that administration of probiotics – mainly *Lactobacillus* and *Bifidobacterium* – during the first 27 days of life was associated with a lower risk of autoimmunization against pancreatic beta cells islets, especially in newborns at risk of developing type 1 diabetes (compared to children who

did not receive probiotics or received them after 27 days of life) [9]. As with all medical devices, probiotics have certain restrictions as to their use, such as sepsis, NEC and post-surgical conditions in the gastrointestinal tract. The situation with prebiotic substances is completely different, they are common in food, but they are also produced on an industrial scale. Prebiotics have a beneficial effect on human health, among others: the addition of prebiotic saccharides to the diet of newborns not fed with breast milk, accelerates the colonization of bifidobacteria in the gastrointestinal tract [9]. Fructan, commonly known as fructooligosaccharides (FOS), are also considered prebiotics. They stimulate the proliferation of bacteria that have a positive effect on the human body. On the other hand, they inhibit the development of pathogenic microflora**,** including carcinogens (factors that affect the development of cancer), improve digestion, facilitate the absorption of many elements and reduce the amount of toxins in the body. Prebiotics are also readily available, as they are commonly found in food products such as yoghurts, fruits and vegetables.

Breastfeeding – constantly appreciated since prehistoric times

In the pre-Neolithic period, prior to the domestication of farm animals, mother's milk was the only way to feed babies – however, with the development of civilization, attempts at artificial feeding began to emerge. Despite the great convenience and salvage for children who were deprived of their mother's milk, the appreciation of natural breastmilk has not ceased. In ancient Egypt and Mesopotamia, a new form of employment appeared – a wet-nurse. Such a woman was employed to breastfeed orphans. Nowadays, most of the beneficial properties of breast milk have been recognized. It is one of the safest and most beneficial ways to influence the development of proper intestinal microflora of a newborn. The goal to be pursued in newborn nutrition is to provide exclusive breastfeeding during the first six months of life. Female breastmilk produced in sufficient quantities by a healthy, well-nourished mother fully satisfies the newborn's need for all necessary nutrients, at the same time ensuring its proper development in the first half-year of life [10]. The benefits of breastfeeding are enormous for both sides of the process. In a woman who is breastfeeding, oxytocin is secreted, which reduces the length of postpartum period. In addition, the risk of developing breast cancer and ovarian cancer is also decreed [11]. Breast milk contains a number of natural oligosaccharides that stimulate the growth of pro-health bacteria in the baby's intestine and over 300 different species of bacteria and their genetic material, including *Staphylococcus, Streptococcus, Veillonella, Leptotrichia, Prevotella, Lactobacillus, Enterococcus, Staphylococcus, Bifidobacterium* – they are found in sulphur as well as in transitional and mature milk. It has been demonstrated that *Enterococcus faecalis* bacteria and lactic acid bacteria (*Lactobacillus sp.*) show antimicrobial activity directed against *Staphylococcus ureus* [2]. Epidemiological studies in the United States have reported that 64-82% of skin infections caused by meticillin-resistant *Staphylococcus aureus* concerned newborns delivered by caesarean section [12]. Such a large variety of bacteria present in breast milk contributes to its anti-infectious and immunomodulatory properties. Consumption of such many natural prebiotics and probiotics by a child facilitates proper digestion and positively influences the development of its immune system. An extremely important element of newborn care is administration of colostrum (infant milk), which, due to its composition and properties, has a significant impact on the proper colonization of the neonate's digestive tract [13]. Compared to mature milk, it contains more protein and vitamin A, less fat and less lactose. This accelerates the excretion of meconium and prevents jaundice in newborns. It contains *Bifidobacterium* and *Lactobacillus* bacteria and a significant number of oligosaccharides that promote their growth and has high levels of antibodies (Class A secretory immunogolobulin – IgA), cytokines as well as anti-inflammatory factors.

Delayed colostrum secretion in the mother after caesarean section and postponement of natural feeding adversely affect the development of newborn microflora [14]. Breastfeeding is a natural and safe way to restore proper colonization of newborn mucous membranes after caesarean section or antibiotic therapy as well as a chance for proper development, since even the best mixtures dedicated to newborns will not replace breastmilk. Numerous studies suggest that it is possible to restore normal composition of the bacteria that inhabit a child's body, even if the child or pregnant woman has undergone perinatal antibiotic therapy by feeding the newborn only with natural food from the mother.

Conclusions

Since conception, a man is exposed to the influence of medication and supplements as well as many other factors that can affect his intestinal microflora in either way. In connection with the development of science and microbiological research, the beneficial effects of microorganisms on the human body have been appreciated with attempts made to explain when exactly the symbiosis between a man and probiotic bacteria begins. It has been proved that there is a correlation between abnormal composition of human intestinal microflora and the occurrence of many allergic, autoimmune and other diseases. As a result, numerous ideas have emerged aimed at restoring proper microbiota, including vaginal seeding. However, due to the still relatively small number of studies in this field, there are no clear recommendations for the use of these methods. It can therefore be concluded that the most beneficial for the human body is being subjected to everything that is as close to nature as possible and from the earliest moments of life.

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