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The Impact of Mode of Delivery on the Development of Gut Microbiota and the Risk of Atopic Diseases in Children: A Literature Review

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Abstract

Introduction: In recent years, the prevalence of atopic diseases among children has increased. Increasing evidence suggests that early gut microbiota development, shaped in part by the mode of delivery, feeding practices, and perinatal antibiotic exposure, may play an important role in the pathogenesis of these conditions.

Aim: This study aimed to investigate the association between mode of delivery, early-life gut dysbiosis, and the risk of developing atopic diseases in children, including atopic dermatitis, allergic asthma, allergic rhinitis, and food allergies.

Methods: A review of observational studies, cohort studies, meta-analyses, and review articles published between 2005 and 2025 was conducted using the PubMed and Google Scholar databases.

Results: Vaginal delivery promotes favourable colonization of the neonatal gut, whereas caesarean section is associated with delayed maturation of the gut microbiota and a predominance of bacteria typically found on the skin and in the hospital environment. In numerous studies, caesarean section has been associated with an increased risk of asthma, allergic rhinitis, atopic dermatitis, and food allergy. Breastfeeding demonstrated a protective effect, while perinatal antibiotic exposure may further disrupt microbiota homeostasis. Probiotics and synbiotics are being considered as potential tools for microbiota modulation; however, their efficacy has not been conclusively confirmed.

Conclusions: Caesarean section should be considered a potential risk factor rather than a direct cause of atopy. Supporting the proper development of the gut microbiota may be an important component of the early prevention of atopic diseases in children.

Keywords: atopic diseases, gut microbiota, dysbiosis, caesarean section, vaginal delivery, breastfeeding, allergy, gut–immune axis

1.Introduction

Over the past decades, a steady global increase has been observed in the number of children affected by atopic diseases, which constitutes a significant public health concern [1]. In the pathogenesis of allergic diseases, an excessive immune response to allergens is observed, resulting in the overproduction of allergen-specific immunoglobulin E (IgE). By binding to mast cells, IgE leads to the release of inflammatory mediators such as histamine, thereby triggering allergic symptoms [2]. The most common atopic diseases include atopic dermatitis, allergic rhinitis, and allergic asthma [1]. In children, the so-called atopic march is commonly observed, in which atopic dermatitis typically develops first and may subsequently be followed by allergic rhinitis and allergic asthma [3]. Their etiology is complex and primarily involves immune dysregulation as well as genetic and environmental factors [1].

A key role in the development and maturation of the immune system is played by the gut microbiota, a community of microorganisms forming a complex ecosystem within the gastrointestinal tract. The first 1000 days of life are considered critical for the proper development of the gut microbiome, which in turn determines the normal maturation of the immune system. Therefore, the mode of delivery as well as the method of feeding are very important factors influencing the composition of the gut microbiome [4]. During vaginal delivery, the newborn is colonized by bacteria present in the mother's birth canal, gastrointestinal tract, and skin. In contrast, caesarean section deprives the infant of direct exposure to the birth canal and maternal gut flora, thereby limiting the transfer of the maternal microbiota [5]. It has been observed that the microbiota of infants born vaginally is characterized by a predominance of beneficial bacteria such as *Bacteroides*, *Bifidobacterium*, and *Parabacteroides*, whereas in infants delivered by caesarean section, bacteria typical of the hospital environment and the skin, including *Staphylococcus*, *Corynebacterium*, and *Propionibacterium* [1]. This, disturbances in early colonization by gastrointestinal bacteria may be reflected in the shaping of the immune system [4].

The aim of this study was to present the relationship between the occurrence of atopic diseases and gut dysbiosis in newborns depending on the mode of delivery, and to identify possible early preventive strategies aimed at reducing the risk of developing these immune disorders.

2. Allergic Diseases in Children: Definition and Classification

Allergic diseases are among the most common chronic disorders of childhood. According to the World Allergy Organization, they affect 30–40% of the population, with a considerable burden observed among children in industrialized countries [6]. They include atopic dermatitis, allergic rhinitis, food allergy, and allergic asthma [1]. In children, a characteristic temporal sequence in the development of atopic diseases, known as the atopic march, is often observed. It is earliest manifestations most commonly include food allergies and atopic dermatitis, followed later by the possible development of other allergic diseases, such as allergic asthma and allergic rhinitis. It should be emphasized, however, that this progression does not always occur in the same way. Nevertheless, the concept of the atopic march underscores the shared immunological basis of these conditions and their tendency to coexist [3].

Allergic diseases constitute a group of disorders in which the principal underlying mechanism is an abnormal and exaggerated immune response to specific antigens known as allergens [7]. Their pathogenesis is based on type I hypersensitivity reactions mediated by IgE antibodies. Initial exposure to an allergen leads to sensitization through activation of the Th2 immune response and the production of allergen-specific IgE antibodies. Subsequent exposure to the same allergen triggers the activation of basophils and mast cells, resulting in the release of inflammatory mediators such as histamine and leukotrienes [8]. These mediators are responsible for the main clinical manifestations of allergic diseases, including vasodilation, increased vascular permeability, bronchoconstriction and pruritus [7].

The first 1000 days of life represent a critical window for the development of the gut microbiota, which is essential for proper immune system maturation. Disruptions in microbial homeostasis during this period may be associated with long-term health consequences, including an increased risk of inflammatory and immune-mediated diseases. This suggests that the gut microbiota may play an important role in the pathogenesis of atopic diseases by influencing the development and regulation of immune responses [4].

2.1 Atopic Dermatitis

Atopic dermatitis is a chronic, relapsing inflammatory skin disorder. It is main clinical manifestations include skin lesions characteristic of eczema accompanied by intense pruritus. These lesions are typically distributed in characteristic locations, such as the flexural areas of the elbows and knees, and on the cheeks in infants. The disease course is characterized by periods of exacerbation and remission [9].

In a study by Pantazi et al. (2024), the gut microbiota of 121 infants with symptoms of atopic dermatitis was evaluated. Children with atopic dermatitis showed an increased abundance of proteolytic bacteria, mainly *Enterobacter* species, *Klebsiellas* species, and *Escherichia coli.* At the same time, their gut microbiota demonstrated a significantly lower abundance of acidifying bacteria, represented by *Enterococcus* species, *Lactobacillus*, and *Bifidobacterium*. These findings indicate clear differences in gut microbiota composition between healthy infants and those with atopic dermatitis, suggesting a potentially important role of the gut microbiota in the pathogenesis of the disease [10].

2.2 Allergic Asthma

Allergic asthma is the most common chronic respiratory disease in childhood. It is caused by bronchial hyperresponsiveness in response to inhaled allergens and is characterized by recurrent episodes of wheezing, dyspnoea, and cough [11]. It is development results from the interplay of both environmental and immunological factors. An important role in the pathogenesis of asthma is also played by the gut microbiota, as well as the microbiota of the respiratory tract [12].

In a study conducted among children and adolescents by Fiuza et al. (2024), significant differences in gut microbiota composition were demonstrated between individuals with type 2 asthma and healthy controls. It was observed that patients with asthma had a higher proportion of bacteria of the genus *Bacteroides* in their gut microbiota compared with healthy individuals. In contrast, a greater abundance of bacteria of the genus *Prevotella* was found in healthy participants. Interestingly, the abundance of *Bacteroides* correlated with IL-4 concentrations in nasal lavage samples [13]. As is well established, IL-4 and IL-13 play an important role in the pathogenesis of asthma [14]. This may indicate the involvement of the gut microbiota in the modulation of immune responses in asthma and consequently, suggest the possibility of prevention through probiotic supplementation [13, 15].

According to Hsieh et al. (2021), the key factor may lie not so much in the structure of the microbiome itself as in an impaired immune response between the host and commensal bacteria. In patients with asthma, the IgA response to certain commensal bacteria was weakened. The authors drew particular attention to reduced IgA binding to bacteria of the genera *Blautia* and *Ruminococcus*, as well as to the family *Lachnospiraceae*. This abnormal immunological profile was more common in children with more severe and poorly controlled asthma. These findings suggest that not only dysbiosis itself, but also impaired immune tolerance to the gut microbiota, may play an important role in the pathogenesis of asthma [16].

2.3 Allergic Rhinitis

Allergic rhinitis is an inflammation of the nasal mucosa triggered by exposure to inhaled allergens. It is characterized by watery nasal discharge, sneezing, nasal obstruction, and pruritus. It may be seasonal, for example during grass pollen season, or perennial, for example in cases of allergy to house dust mites [17].

In a study by Zhou et al. (2021), significant differences in gut microbiota composition were observed in individuals with allergic rhinitis. Patients showed a markedly reduced abundance of bacteria belonging to the phylum Firmicutes and of the genera *Blautia* and *Eubacterium* compared with healthy individuals [18]. It is worth noting that some species within the genera *Blautia* and *Eubacterium* have been described in the literature as important producers of short-chain fatty acids (SCFAs), which are involved in immune system maturation; therefore, maintaining their proper levels is of importance [18, 19, 20]. The analysis also demonstrated that SCFA concentrations were significantly lower in patients with allergic rhinitis than in the control group. A positive association was thus identified between SCFA levels and the abundance of *Blautia* and *Eubacterium* [18].

Similar observations were also reported in studies involving children with allergic rhinitis induced by house dust mites. In these patients, the composition of the gut microbiota differed markedly from that observed in healthy controls. Li et al. (2025) drew particular attention to the reduced abundance of *Escherichia fergusonii*. The abundance of this bacterium was negatively correlated with the levels of allergen-specific IgE antibodies against house dust mite allergens. Moreover, in an animal model, oral administration of this bacterium led to an alleviation of allergic symptoms. This may suggest a potential protective role of *E. fergusonii* in allergic rhinitis [21].

2.4 Food Allergies

Food allergy is characterized by an immunological reaction to specific food components. In infants and young children, the most common food allergens are cow's milk proteins and hen's egg proteins. Clinical manifestations may involve the respiratory, gastrointestinal, and integumentary systems. The most common cutaneous manifestations include urticaria and exacerbation of atopic dermatitis. Gastrointestinal symptoms most often include nausea, vomiting, abdominal pain, and diarrhoea. Respiratory manifestations may include laryngeal stridor, dyspnoea, and cough [22].

Growing evidence also suggests that the gut microbiota may play an important role in the pathogenesis of food allergy. Hara et al. (2024) demonstrated significant differences in gut microbiota composition between 18-month-old children with food allergy and their healthy peers. Children with food allergy exhibited a greater abundance of bacteria from the genera *Escherichia* and *Anaeromassilibacillus*, and a lower abundance of *Bacteroides*, *Oscillibacter*, *Hungateiclostridium*, *Anaerotaenia*, and *Ruminococcus*. Based on these findings, the authors suggested that, in children with food allergy, the gut microbiota profile shifts toward a more pro-inflammatory pattern, accompanied by a reduced abundance of bacteria involved in supporting immune tolerance [23].

3. Gut Microbiota and the Development of the Immune System

The human gut microbiota consists of trillions of bacteria, reaching up to 10^12 organisms per gram of faeces, as well as viruses and fungi [24]. Numerous reports indicate that the gut microbiota plays a crucial role in the proper development of the immune system. From the earliest days of life, the gut microbiota influences the immune system by modulating processes responsible for immune maturation [19].

Thus, infancy and early childhood represent a critical period for the proper development of the immune system. There is also evidence that maternal microbiota influences immune system development already during fetal life. Of particular importance are metabolites derived from the maternal microbiota, especially short-chain fatty acids (SCFAs). These metabolites are capable of crossing the placenta and thereby influence the maturation of the fetal immune system [19, 25]. SCFAs strengthen the epithelial barrier and increase the number of intestinal FOXP3+ regulatory T cells (Tregs) [26].

In mouse studies, Lin et al. (2005) demonstrated a stronger allergen-associated inflammatory response in mice with the FOXP3 gene knocked out [27]. Another mechanism of SCFA action is the inhibition of histone deacetylases in macrophages, neutrophils, monocytes, and dendritic cells. This results in reduced production of pro-inflammatory cytokines, thereby promoting the maintenance of immune homeostasis [24].

One of the most important SCFAs is butyrate. It can induce the differentiation of CD4+ lymphocytes into Tregs, support food tolerance, and exert anti-inflammatory effects [24, 26]. The gut microbiota also influences the development of myeloid cells. Therefore, gut dysbiosis may reduce the pool of immune cell precursors and weaken the early antibacterial response [24].

Another mechanism modulating immune system development involves innate lymphoid cells (ILCs), whose maturation depends on the gut microbiota. The ILC family includes, among others, classical cytotoxic natural killer (NK) cells, lymphoid tissue inducer (LTi) cells, and non-cytotoxic ILC populations. Stimulation by microbial signals increases IL-1β secretion, which in turn activates ILC3 cells to produce IL-2, thereby inducing the expansion of regulatory T cells (Tregs) and contributing to immune homeostasis in the intestine [24].

4. Influence of Mode of Delivery on Gut Microbiota Composition

Mode of delivery is one of the most important factors determining early colonization of the neonatal gastrointestinal tract, as at birth the infant is exposed for the first time to microorganisms of maternal origin[28, 29, 30]. In the case of vaginal delivery, newborns acquire bacterial communities that closely resemble the maternal vaginal microbiota, with predominance of the genera *Lactobacillus*, *Prevotella*, and *Sneathia* spp. In contrast, newborns delivered by caesarean section exhibit a microbial profile typical of the maternal skin surface, dominated by such genera as *Staphylococcus*, *Corynebacterium*, and *Propionibacterium* spp. [28]. These differences are of considerable importance for the subsequent maturation of the gut microbiota and may influence the development of immune responses, and consequently also the risk of chronic diseases later in life [28, 31].

The influence of delivery mode on the microbial profile of infants is also highlighted by the findings of Azad et al. (2013), who reported a poorer representation of the genera *Escherichia-Shigella* and *Bacteroides* in infants delivered by caesarean section compared with those born vaginally, thereby confirming the impact of delivery mode on the shaping of gut microbiota composition already in early infancy [29].

Further confirmation of the important role of delivery mode in shaping the early gut microbiota comes from additional observational studies conducted in neonatal and infant populations. In the study by Hill et al. (2017), both mode of delivery and gestational age were shown to significantly affect the composition of the neonatal gut microbiota in early life. Among term infants delivered by caesarean section, a greater abundance of bacteria from the phylum *Firmicutes* and a lower abundance of *Actinobacteria* were observed after the first week of life compared with newborns delivered vaginally. However, the authors also noted that, over time, the microbiota in this group gradually became more similar to the profile characteristic of infants born vaginally. Despite the initial differences, the microbial profile of these children gradually normalized, showing increasing similarity to the microbiota of infants born by vaginal delivery [30].

The effect of mode of delivery on gut microbiota composition may also be influenced by infant feeding practices. Coker et al. (2021) demonstrated that infants delivered by caesarean section were characterized by lower gut microbiota alpha diversity during the first year of life; however, a longer duration of breastfeeding partially modified this effect. In infants from this group, an increased abundance of *Bacteroides fragilis* and *Lactobacillus* was observed, suggesting that the impact of mode of delivery on microbiota development is not entirely permanent and may also be shaped by postnatal environmental factors [32].

The association between mode of delivery and gut microbiota composition is further supported by prospective studies conducted by Stokholm et al. (2020). In a study involving 700 children, cesarean delivery was shown to be associated with distinct alterations in gut microbiota composition as early as the first week and first month of life. However, by the age of 1 year, the differences between children delivered by cesarean section and those born vaginally had become considerably smaller. Persistence of cesarean section-associated dysbiosis over a longer period was strongly correlated with an increased risk of asthma in the study population. These findings suggest that the increased risk of childhood asthma may be related not so much to cesarean delivery itself, but rather to prolonged disturbances in gut microbiota maturation. At the same time, they indicate that proper microbiota development may exert a protective effect and partially reduce the adverse consequences of operative delivery with regard to the development of atopic diseases [31].

In fine, the available data indicate that vaginal delivery promotes a more natural transfer of maternal microorganisms and supports proper maturation of the gut microbiota, whereas caesarean section is associated with a different pattern of colonization and may lead to delayed maturation of the gut microbiota [29, 30, 31, 32].

5. Mode of Delivery as a Risk Factor for Atopic Diseases in Children

Mode of delivery, particularly caesarean section, has been postulated as a potential factor influencing the risk of developing atopic diseases in children, including allergic asthma, allergic rhinitis, conjunctivitis, atopic dermatitis, and food allergy [33, 34]. The relevance of this factor is primarily attributed to differences in early microbial colonization between newborns delivered vaginally and those born by caesarean section. These differences may subsequently affect gut microbiota maturation and immune system development, thereby influencing susceptibility to allergic diseases [28, 33].

In a meta-analysis of cohort studies, Zhong et al. (2023) evaluated the association between caesarean section and asthma in children and adolescents. The authors included 35 cohort studies, allowing for a broad assessment of the relationship between mode of delivery and asthma risk. The results showed that children born by caesarean section were more likely to develop asthma than those delivered vaginally. However, the authors emphasized the substantial heterogeneity of the included studies, indicating that this association requires further investigation [34].

In a meta-analysis by Liu et al. (2023), encompassing 22 studies and 1 464 868 participants, a significant association was found between caesarean section and an increased risk of allergic rhinitis in children. The authors reported that caesarean section was associated with higher odds of allergic rhinitis in children (OR = 1.19; 95% CI: 1.12–1.27; $P < 0.001$), with a stronger association observed among children with a positive family history of allergy (OR = 1.82; 95% CI: 1.36–2.43; $P< 0.001$). These findings suggest that perinatal factors, particularly mode of delivery, may affect immune system maturation and predispose children to the development of allergic diseases [35].

In a meta-analysis by Yang et al. (2023), including 9 650 children delivered by caesarean section and 20 418 children delivered vaginally, aged 0–3 years, food allergy was found to be more common among children born by caesarean section. In the analysed cohort, food allergy was reported more frequently in children delivered by caesarean section (7.8%) than in those born vaginally (5.9%). Caesarean section was also associated with higher odds of food allergy (OR = 1.45; 95% CI: 1.03–2.05), with the strongest association observed for cow's milk protein allergy (OR = 3.31; 95% CI: 1.98–5.53). Moreover, among children delivered by caesarean section with a positive family history of allergy, the odds of food allergy were even higher (OR = 2.60; 95% CI: 1.28–5.27) [36].

In a meta-analysis by Liu et al. (2024), which included 113 studies, caesarean section, compared with vaginal delivery, was found to be associated with increased odds of asthma in the offspring (OR = 1.20), allergic rhinitis or conjunctivitis (OR = 1.15), atopic dermatitis or eczema (OR = 1.08), food allergy (OR = 1.35), and allergic sensitization (OR = 1.19). These findings suggest that the effect of mode of delivery may not be limited to a single disease entity but may extend to various manifestations of atopy observed in children [33].

It should be emphasized, that not all studies have consistently confirmed this association. In a study conducted by Tamai et al. (2025), which included 2 114 children followed up to 9 years of age, no significant association was found between mode of delivery and the risk of atopic dermatitis, food allergy, bronchial asthma, or allergic rhinitis and conjunctivitis. These findings may indicate that the effect of caesarean section on the development of allergic diseases is complex and likely also depends on population-specific and environmental factors [37].

The evidence gathered to date suggests that caesarean section itself is not a direct cause of atopic diseases, but it may represent one of the factors contributing to their development, by affecting the establishment of the gut microbiota and immune responses in early life [28, 33, 34, 35, 36, 37].

6. Breastfeeding and Gut Microbiota

Environmental factors that shape gut microbiota development in early life include feeding practices, mode of delivery, and antibiotic exposure. In a meta-analysis by Ho et al. (2018), exclusive breastfeeding during the first 6 months of life was associated with a gut microbiota profile more characteristic of early infancy, whereas non-exclusively breastfed infants exhibited greater bacterial diversity. These differences could persist beyond 6 months of age [38].

Similar findings were reported by Ma et al. (2020) and Odiase et al. (2023), who demonstrated that breastfed infants more often show a predominance of bacteria with potentially beneficial effects, such as *Bifidobacterium*, *Lactobacillus*, and *Bacteroides*. In contrast, formula-fed infants were more frequently found to microorganisms considered less beneficial, including *Streptococcus*, *Enterococcus*, *Clostridioides* and *Lachnospiraceae* [39, 40].

Breastfeeding may play a particularly important role in children delivered by caesarean section, as studies suggest that it may partially compensate for disturbances in early gut colonization associated with operative delivery [32, 41]. In children born by caesarean section who were breastfed for at least 6 months, the microbiota profile was more similar to that observed in children delivered vaginally than in infants breastfed for a shorter period. In this group, longer breastfeeding duration was associated with an increased abundance of *Bacteroides fragilis* and *Lactobacillus*, which may indicate a partial restoration of a more favourable microbiota profile. These findings suggest that the duration of breastfeeding plays an important role in the restoration of the gut microbiota in children born by caesarean section [32].

7. Perinatal Antibiotic Therapy

Antibiotic therapy administered during the perinatal period is regarded as one of the key factors that may influence the development of the neonatal gut microbiota, particularly during the first weeks and months of life [42, 43]. This effect applies both to antibiotics administered to the mother during labour - most commonly as prophylaxis against group B streptococcal infection or in the context of caesarean section - and to neonatal antibiotic exposure in the early postnatal period [42, 44]. Azad et al. (2016) demonstrated that intrapartum antibiotic use, both during vaginal delivery and caesarean section, was associated with disturbances in infant gut microbiota homeostasis, although breastfeeding may partially attenuate some of these changes [43].

8. Probiotics

Probiotics are currently being considered as a potential approach for modulating the gut microbiota and immune responses in children with atopic diseases. However, their effectiveness appears to depend on the specific strain used, the timing of supplementation, the child’s age, and the type of allergic disease [45, 46, 47]. At present, the available evidence does not allow for firm conclusions regarding the efficacy of probiotics and synbiotics in the prevention of allergic diseases. Although no serious adverse effects related to their use have been reported, the introduction of these preparations into routine clinical practice requires further investigation [47].

9. Conclusions

The relationship between mode of delivery, gut microbiota development, and the development of atopic diseases in children is multifactorial. Based on the available evidence, it may be concluded that one of the key factors influencing immune system maturation in early life is the proper establishment of the gut microbiota. Particular importance should be attributed to the first 1000 days of life, during which immune mechanisms, immune tolerance, and the balance between pro-inflammatory and anti-inflammatory responses are formed.

The most important conclusion emerging from the reviewed studies is that caesarean section is associated with a distinct pattern of early gastrointestinal colonization compared with vaginal delivery. Children born vaginally show a greater abundance of maternally derived microorganisms, particularly bacteria considered beneficial, such as *Bacteroides*, *Bifidobacterium*, and *Lactobacillus*. In contrast, newborns delivered by caesarean section are more frequently colonized by bacteria typical of the hospital environment and the skin. Such differences may result in delayed gut microbiota maturation and, consequently, disturbances in immune response development.

Available research findings further indicate that gut dysbiosis may be associated with the development of specific atopic diseases, such as atopic dermatitis, allergic asthma, allergic rhinitis, and food allergies. Each of these conditions is characterized by distinct alterations in microbiota composition, including both a reduced abundance of bacteria with potentially protective and anti-inflammatory properties and an increased abundance of microorganisms associated with intensified inflammatory processes. This suggests that the gut microbiota is involved in modulating immune responses and may influence a child's susceptibility to the development of atopy.

It should be emphasized, that caesarean section should not be regarded as a direct cause of atopic diseases, but rather as one of the risks factors whose significance becomes apparent in combination with other elements, such as genetic predisposition, feeding practices, antibiotic exposure, and environmental conditions. This means that the mode of delivery itself does not determine whether the disease will occur, but it may contribute to development.

Breastfeeding appears to have an important protective role, as it supports the development of a beneficial gut microbiota profile and may partially compensate for the adverse effects of caesarean section. Longer breastfeeding duration promotes the growth of bacteria associated with immune maturation and may reduce the colonization disturbances observed in children delivered operatively. Perinatal antibiotic therapy, by contrast, may further disrupt the microbial balance of the neonatal gut.

It is also worth noting that although probiotics and synbiotics are currently being considered as potential methods for modulating the microbiota and supporting the prevention of atopic diseases, the available evidence does not yet allow for definitive recommendations regarding their routine use.

In summary, the most justified approach to the early prevention of atopic diseases appears to be supporting the proper development of the gut microbiota from the earliest stages of life. This primarily includes avoiding unnecessary caesarean sections, promoting breastfeeding, and ensuring the rational use of antibiotics during the perinatal period. Further research on the gut-immune axis may, in the future, enable the development of more precise and effective strategies for preventing atopic diseases in children.

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