

Allergic enteritis in children

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Gastroenterology Rev 2017; 12 (1): 1–5
DOI: <https://doi.org/10.5114/pg.2017.65677>

Key words: food allergy, children, enteritis, enteropathy.

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Abstract

The gastrointestinal form of food allergy is very common in children. The most frequently observed types are allergic proctitis and proctocolitis. In most cases the symptoms subside within the first 2 months of life. The babies seem healthy, and the only abnormality is a small amount of blood in stool. Symptoms can also include small intestine inflammation and colitis. Patients may present with irritability, abdominal pain, flatulence, colic, postprandial vomiting, chronic diarrhoea, and hindered physical development. The diagnosis of allergic enteritis is based on the clinical examination and the results of additional tests including an endoscopy of the lower digestive tract with histopathological assessment. Cow's milk proteins are the most common nutrition proteins responsible for the development of the symptoms of allergic enteritis. The most essential method of treating allergic enteritis is the elimination diet. The symptoms should subside within 1–2 weeks from the beginning of the diet.

One of the effector organs for food allergy is the gastrointestinal tract. The gastrointestinal form of food allergy is very common in children. It may manifest itself in different ways depending on which section of the digestive system it involves [1, 2]. This includes allergic eosinophilic oesophagitis, gastritis and enteritis, inflammation of the small intestine and colon, inflammation of the rectum, and also an enteropathy caused by an ingestion of allergenic food [2, 3]. Allergic enteritis in infants is thought to be caused by increased permeability of the immature mucosa and the immaturity of the immune system in the digestive tract [4]. The disease mainly affects infants fed exclusively with breast milk, since their digestive tract is exposed to the food allergens from their mother's milk [3, 5–12].

Another supposed cause of allergic enteritis is the disturbance of the microbial ecosystem of the digestive tract. Smehilová *et al.* [13] analysed the differences in the composition of the intestinal microflora between 28 healthy breastfed babies and 16 breastfed ones with allergic enteritis. It has been shown that in healthy babies the dominating bacterium is *Bifidobacterium*, while in allergic babies *Clostridium* is found to be more abundant.

Among all forms of allergic enteritis, the most common 1 in paediatric patients is the food protein-induced

proctocolitis (FPIP). It usually occurs in young infants within the first 2 months of life [8, 14]. However, this does not mean that the disease will not occur in older children [3, 4, 15]. It is believed that the onset usually falls on the 2nd–6th week of life, but there have been cases of onset in the first day of life [1, 3–5].

Faber *et al.* [16] described a case of a prematurely born neonate who suffered from a gastrointestinal bleeding of a later confirmed allergic aetiology. The bleeding occurred as soon as in the first day of life, after the first feeding, and repeated after the next feedings. Kumar *et al.* [17] described as many as 3 cases of allergic enteritis that occurred in the first day of life. The diagnosis was confirmed by excluding infections and anatomical causes of the bleeding (a sigmoidoscopy was performed). The symptoms subsided after an elimination diet was started (elimination of milk from the mother's diet, a mixture based on a strong casein hydrolysate or free amino acids).

Sierra Salinas *et al.* showed that approximately 80% of children present the first symptoms at the age of 0–3 months [6].

Infants with FPIP seem healthy, they usually develop normally, and the only abnormality that can sometimes be observed is a small amount of blood in their stool (e.g. in the form of streaks), a perianal intertrigo, slightly

loose stools, or mucus in stools [1, 3, 4, 18]. Sierra Salinas *et al.* [6] described 13 cases of infants with allergic enteritis, whose only symptom was passing stools with mucus and blood, while neither the clinical examination nor the laboratory tests showed any health abnormalities. The diagnosis was only confirmed by an endoscopic examination.

Baldassarre *et al.* [10] described prematurely born, breastfed twins, who passed bloody stools but apart from that were clinically healthy. The bleeding subsided once elimination diet was started.

If it is the distal section of the digestive tract that is mainly involved, general symptoms such as disturbances of growth are very rare. Constipations also belong to possible manifestations [15]. It is indicated that this disease entity is usually caused by an IgE-independent sensitivity of a cellular reaction mechanism [5, 19].

Frequently, although slightly less frequently than proctocolitis, it is food protein-induced enterocolitis syndrome (FPIES), which is also most common in infants but can be observed in older children as well [3, 20–22]. It is believed that FPIES is less common in breastfed infants compared to FPIP (breastfeeding is in this case believed to have a protective function) [23]. Patients are frequently allergic to more than one food product [23]. They may present with irritability, abdominal pain, flatulence, colic, postprandial vomiting, chronic diarrhoea, and hindered physical development [2, 3, 17, 21–23]. At times there may also be blood in their stools or microscopic blood, which can be confirmed in laboratory tests (faecal occult blood test) [3, 7]. Thus, a child can suffer from anaemia resistant to iron therapy [3, 20]. The course of FPIES can involve incidents of symptom aggravation (e.g. following ingestion of larger amounts of allergenic food) with acute diarrhoea, dehydration, and metabolic disturbances [3, 23]. Chronicity of the symptoms may ultimately lead to the malabsorption syndrome with protein loss [22, 24].

If the two intestinal syndromes described above are not treated, there is a risk of food protein-induced enteropathy [3]. Intestinal villi can be damaged or even destroyed [4]. In such cases a child suffers from chronic diarrhoea, hindered growth, decreased appetite, and frequently also complains of gastrointestinal symptoms. Impaired digestion and absorption, the symptoms of which are dominant in the clinical picture of the disease, lead to anaemia, hypoalbuminaemia, and other deficiencies [3–5].

The diagnosis of the allergic enteritis is based on the clinical examination (including the patient's history of the symptoms and family history) and the results of additional tests [15]. Allergic enteritis must be diagnosed differentially to rule out other diseases. Both

the acute conditions (including the ones requiring surgical intervention such as intestinal torsion, intussusception, necrotic enteritis) and the conservative treatment (bacterial infections of the digestive system, pseudomembranous enterocolitis) must not be disregarded. The chronic character of the symptoms frequently indicates the presence of chronic conditions such as Hirschsprung's disease or non-specific enteritis. Also, it is necessary to take into account the parenteral conditions such as coagulation disturbances. Thus, in differential diagnosis it may prove useful to conduct laboratory tests, imaging scans, and endoscopy [4].

It has been shown that children with allergic enteritis have decreased iron levels, thrombocytosis, and eosinophilia more frequently than healthy children [9, 25].

Among the examinations that are useful in the diagnosis of the disease endoscopy of the lower digestive tract with histopathological assessment of biopsies is important. Xanthakos *et al.* [26] showed that in the case of suspected enteritis, the endoscopic examination is crucial for making a decision on the possible dietary treatment. It turned out that among the infants suspected of allergic enteritis studied by this study group (suspicion based on clinical symptoms such as lower digestive tract bleeding), changes typical for allergic inflammation were found in only 14/22 (64%) children. Non-specific inflammatory changes were found in 3 (14%) children, and in as many as 5 (23%) there were no changes at all.

The microscopic picture in allergic enteritis can reveal inflammation, extravasations, erythema, bleeding, and sometimes also a swelling and aphthous erosions of the mucosa [1, 5, 8, 24]. Sierra Salinas *et al.* [6] observed that the sigmoid colon is the most frequent location of endoscopic changes (75% of patients).

Typical changes observed in the microscopic examination include the infiltration of eosinophils and the folliculosis [1, 4, 5, 24, 27, 28].

Molnar *et al.* described folliculosis and aphthous ulcerations in 83% of infants with clinically diagnosed allergic enteritis. Infiltrations of eosinophils were revealed in the histological assessment. Yu *et al.* [29] also described 5 infants with allergic enteritis, who presented with an infiltration of eosinophils. Sorea *et al.* [8] performed an endoscopic examination in 6 infants below the age of 3 months, whose only symptom was passing bloody stool. They found a swelling of the mucosa in all patients and extravasations and petechiae in 4 of them. In 5 children a histopathological examination was performed and in all cases the presence of infiltrations of eosinophils was revealed. Sierra Salinas *et al.* [6] observed infiltrations with neutrophils and eosinophils in the biopsies of their patients. Diaz *et al.* [14]

found infiltrations of eosinophils in the rectal mucosa in 18 out of 20 infants with lower digestive tract bleeding and confirmed allergy to cow's milk proteins. Fagundes-Neto and Ganc [21] described 5 cases of allergic enteritis in infants younger than 6 months with colitis and lower digestive tract bleeding, which subsided once cow's milk was eliminated from their diet. Macroscopically, the colonoscopy showed hyperaemia and spontaneous bleeding during the procedure, and microscopically – microerosions and infiltrations with eosinophils. Cordero Miranda *et al.* [30] found folliculosis and heavy infiltration with eosinophils in a 50-day-old infant passing bloody stools. However, emerging from our own experience is the conclusion that the histopathological picture is sometimes not clear and does not explain the aetiology of bleeding in infants [31]. In such cases only some further observation can allow for a final diagnosis.

Cow's milk proteins are the most common nutrition proteins responsible for the development of the symptoms of allergic enteritis. However, the allergy can also be caused by proteins from chicken eggs, fish, corn, soya beans, and rice [5, 19, 22]. In order to identify the allergy-inducing food proteins allergy diagnosis is conducted. However, it is emphasised that the test results are frequently false-positive. Thus, they should always be verified based on the case history and the elimination and provocation test results [1].

Yu *et al.* [29] analysed the significance of standard allergy tests in infants with allergic enteritis. Highly positive prick test results for milk were found in 5 infants, but it did not correlate with the sIgE level against cow's milk proteins. The significance of the atopy patch tests (APT) is more and more often emphasised [22, 23]. Lucarelli *et al.* [11] performed prick tests in 14 breastfed infants with FIPC and measured the sIgE concentration against common food allergens. The results were normal. On the other hand, the results of APT tests were abnormal (positive) in all patients and in 50% of them showed allergy to more than one food allergen. It was revealed that cow's milk was the most frequent allergen (50%), followed by soya beans (28%), eggs (21%), rice (14%), and wheat (7%).

The most essential method of treating allergic enteritis is the elimination diet. The symptoms should subside within 1–2 weeks from the beginning of the diet [4]. Symptoms usually become weaker or subside completely after a shorter time (72–96 h) but in some cases as much as 2–4 weeks is needed [5, 20, 24]. Cordero Miranda *et al.* [30] described an infant with allergic enteritis, in whom symptoms subsided as quickly as after 48 h after elimination diet was started. Pumberger *et al.* [12] presented the cases of 11 breastfed infants in whom bleeding from the digestive tract was

caused by allergy to cow's milk protein. The allergen was excluded from the mothers' diet and the bleeding subsided after 72–96 h.

After 1–4 weeks of elimination diet it is necessary to conduct a provocation test. If symptoms recur, the diet should be applied again until the child reaches the age of 9–13 months and for at least 6 months [5, 32].

The time period between the beginning of the diet and the subsidence of symptoms is longer in the case of enteropathy (up to approximately 6 weeks) [20]. If a child is breastfed, it is recommended to remove the allergenic food products from the mother's diet. In such cases, the mother's diet should be supplemented with vitamins and minerals, including calcium in the amount of at least 1000 mg/day [5].

Breastfed infants suffering from more severe symptoms, or not showing any improvement despite the mother's elimination diet, may need a mixture of a strong hydrolysate or even a mixture of free amino acids [4, 5].

Molnár *et al.* [9] described 31 breastfed infants who presented with bleeding from the digestive tract. The bleeding subsided once milk was eliminated from the children's diet. The subsidence was quicker in infants that were fed with an elimination mixture based on free amino acids than in those that were breastfed. However, after 3 months, none of the children suffered from bleeding. Baldassarre *et al.* [10] described twins with allergic enteritis manifested with bleeding from the lower digestive tract, in whom the elimination diet turned out to be an effective treatment. Similarly, Kumar *et al.* [17], Rossel *et al.* [18], and Fagundes-Neto and Ganc [21] observed a subsidence of bleeding from the lower digestive tract in infants with allergic enteritis once milk-free elimination diet was started. Petenaude *et al.* [7] also observed a remission of dramatic symptoms in a breastfed 8-week-old boy with allergic enteritis (vomiting, agitation, blood stools) after milk elimination from the mother's diet.

As pointed out by Sorea *et al.* [8], in the case breastfed infants the application of the mother's elimination diet is not always effective. In 5 of 6 studied infants clinical remission was obtained, but in 1 child the bleeding subsided only after breastfeeding was terminated. Also Sierra Salinas *et al.* [6] showed that in 10 out of 13 cases applying elimination diet in the mothers did not cause symptom remission. An improvement was observed only after a hydrolysate of cow's milk proteins was used.

In a premature neonate described by Faber *et al.* [16] the use of even a strong protein hydrolysate was not effective. Only after the introduction of a mixture based on free amino acids did the bleeding from the digestive tract subside.

In the case of enteropathic symptoms, especially if intestinal villi are damaged, a mixture of medium-chain triglycerides (MTC) can be considered [4].

Xanthakos *et al.* [26] warn against hasty diagnosis of allergic enteritis and ill-conceived application of the elimination diet. They found that in infants who do not show typical allergic changes in the endoscopic examination, the bleeding subsides without elimination diet; unless it is caused by some other serious organic disease (in 1 of the patients non-specific enteritis was diagnosed). Also, they showed that as many as 84% of doctors empirically recommend the elimination diet in infants with bleeding from the lower digestive tract, which is frequently completely unjustified. Jang *et al.* [33] described 16 neonates who presented with bleeding from the lower digestive tract. Endoscopic changes were found in all patients, but histopathological changes that could fulfil the criteria of allergic inflammation were confirmed in only 10 of the cases. In only 2 (12.5%) children the allergy was confirmed in the elimination and provocation test. The elimination diet was applied in them. In the remaining 14 (87.5%) cases the bleeding subsided spontaneously after 4 days on average (1–8 days). A diagnosis of idiopathic enteritis of infants was established. Those authors also warn against premature use of the elimination diet.

For many years, the significance of probiotic bacteria supplementation has been increasing in value in the treatment of gastrointestinal diseases and food allergies. *Lactobacillus rhamnosus* GG (LGG) is a thoroughly investigated bacterium [10, 34]. Baldassarre *et al.* [35] compared the effectiveness of treatment using an elimination diet and a strong casein hydrolysate with and without LGG in infants with allergy to cow's milk suffering from bleeding from the lower digestive tract. They found that after 4 weeks of such a diet, none of the children receiving the probiotic supplement suffered from bleedings, while 5 out of 14 children receiving the mixture without the probiotic still suffered from bleedings. It was also shown that within 4 weeks, in the group that was more supplemented than the control group, the concentration of faecal calprotectin decreased.

Glycocorticosteroids are sometimes used during remission induction. In the case of steroid dependence, antileukotriene drugs can be administered. Antihistamine and antidegranulation drugs (cromoglicic acid) are used as well [1]. There are single reports of the benefits of pancreatic enzyme use as a supplement of the mother's diet. It is believed that they break up proteins ingested by the mother, which decreases their allergenicity once they get into the milk [5]. Biological treatment (omalizumab, mepolizumab) is a novelty [1].

The prognosis for patients with allergic enteritis is good [4, 24]. It is a common belief that allergic enteritis (especially in its mild course) is a self-limiting disease [15, 19].

Molnár *et al.* [9] showed that regardless of the type of feeding and the initial therapeutic result of the diet, after 3 months from the diagnosis, none of the children suffered from bleeding.

According to most authors, children aged 1–2 years do not have any symptoms of the disease [19–21]. Some authors believe that in the case of changes located in the upper sections of the intestine, the symptoms may last longer, i.e. up to the age of 3 years [23].

Roseel *et al.* [18] described 9 neonates who suffered from allergic enteritis manifested by bleeding from the lower part of the digestive tract. The symptoms subsided once milk was eliminated from the diet. After 12 months the provocation test was conducted with the cow's milk proteins in 6 children (3 did not report). It showed acquired tolerance in 3 children and sustained allergy in 3 children.

For over 2 years Sorea *et al.* [8] observed 6 children with allergic enteritis diagnosed at the early neonatal age. They found that all children acquired tolerability to milk, which had previously been an allergen to them. However, the tolerance in particular children appeared at different ages, ranging between 6 and 23 months.

To sum up, allergic enteritis is an important manifestation of food allergy, especially in neonates, and it should be considered in all children (especially neonates) presenting gastrointestinal symptoms. It is most crucial if the clinical symptoms had their onset shortly after changes in child's diet had been introduced or if the child's mother had eaten some allergenic food.

Conflict of interest

The authors declare no conflict of interest.

References

1. Alfadda AA, Storr MA, Shaffer EA. Eosinophilic colitis: epidemiology, clinical features, and current management. *Therap Adv Gastroenterol* 2011; 4: 301-9.
2. Lake AM. Dietary protein enterocolitis. *Curr Allergy Rep* 2001; 1: 76-9.
3. Kaczmarek M, Wasilewska J, Jarocka-Cyrta E, et al. Polskie stanowisko w sprawie alergii pokarmowej u dzieci i młodzieży. *Post Dermatol Alergol* 2011; 28 (Supl. 2): 75-116.
4. Barnard J. Gastrointestinal disorders due to cow's milk consumption. *Pediatr Ann* 1997; 26: 244-50.
5. Academy of Breastfeeding Medicine. ABM Clinical Protocol #24: Allergic Proctocolitis in the Exclusively Breastfed Infant. *Breastfeed Med* 2011; 6: 435-40.

6. Sierra Salinas C, Blasco Alonso J, Olivares Sánchez L, et al. Allergic colitis in exclusively breast-fed infants. *An Pediatr (Barc)* 2006; 64: 158-61.
7. Patenaude Y, Bernard C, Schreiber R, et al. Cow's-milk-induced allergic colitis in an exclusively breast-fed infant: diagnosed with ultrasound. *Pediatr Radiol* 2000; 30: 379-82.
8. Sorea S, Dabadie A, Bridoux-Henno L, et al. Hemorrhagic colitis in exclusively breast-fed infants. *Arch Pediatr* 2003; 10: 772-5.
9. Molnár K, Pintér P, Györfy H, et al. Characteristics of allergic colitis in breast-fed infants in the absence of cow's milk allergy. *World J Gastroenterol* 2013; 19: 3824-30.
10. Baldassarre ME, Capiello A, Laforgia N, et al. Allergic colitis in monozygotic preterm twins. *Immunopharmacol Immunotoxicol* 2013; 35: 198-201.
11. Lucarelli S, Di Nardo G, Lastrucci G, et al. Allergic proctocolitis refractory to maternal hypoallergenic diet in exclusively breast-fed infants: a clinical observation. *BMC Gastroenterol* 2011; 16: 82.
12. Pumberger W, Pomberger G, Geissler W. Proctocolitis in breast fed infants: a contribution to differential diagnosis of haematochezia in early childhood. *Postgrad Med J* 2001; 77: 252-4.
13. Smehilová M, Vlková E, Nevorál J, et al. Comparison of intestinal microflora in healthy infants and infants with allergic colitis. *Folia Microbiol (Praha)* 2008; 53: 255-8.
14. Diaz NJ, Patricio FS, Fagundes-Neto U. Allergic colitis: clinical and morphological aspects in infants with rectal bleeding. *Arq Gastroenterol* 2002; 39: 260-7.
15. Troncione R, Discepolo V. Colon in food allergy. *J Pediatr Gastroenterol Nutr* 2009; 48 (Suppl. 2): 89-91.
16. Faber MR, Rieu P, Semmekrot BA, et al. Allergic colitis presenting within the first hours of premature life. *Acta Paediatr* 2005; 94: 1514-5.
17. Kumar D, Repucci A, Wyatt-Ashmead J, et al. Allergic colitis presenting in the first day of life: report of three cases. *J Pediatr Gastroenterol Nutr* 2000; 31: 195-7.
18. Rossel M, Ceresa S, Las Heras J, et al. Eosinophilic colitis caused by allergy to cow's milk protein. *Rev Med Chil* 2000; 128: 167-75.
19. Boné J, Claver A, Guallar I, et al. Allergic proctocolitis, food-induced enterocolitis: immune mechanisms, diagnosis and treatment. *Allergol Immunopathol (Madr)* 2009; 37: 36-42.
20. Maloney J, Nowak-Węgrzyn A. Educational clinical case series for pediatric allergy and immunology: allergic proctocolitis, food protein-induced enterocolitis syndrome and allergic eosinophilic gastroenteritis with protein-losing gastroenteropathy as manifestations of non-IgE-mediated cow's milk allergy. *Pediatr Allergy Immunol* 2007; 18: 360-7.
21. Fagundes-Neto U, Ganc AJ. Allergic proctocolitis: the clinical evolution of a transitory disease with a familial trend. *Case reports. Einstein (Sao Paulo)* 2013; 11: 229-33.
22. Nowak-Węgrzyn A, Muraro A. Food protein-induced enterocolitis syndrome. *Curr Opin Allergy Clin Immunol* 2009; 9: 371-7.
23. Leonard SA, Nowak-Węgrzyn A. Manifestations, diagnosis, and management of food protein-induced enterocolitis syndrome. *Pediatr Ann* 2013; 42: 135-40.
24. Lake AM. Food-induced eosinophilic proctocolitis. *J Pediatr Gastroenterol Nutr* 2000; 30 (Suppl.): 58-60.
25. Coviello C, Rodriguez DC, Cecchi S, et al. Different clinical manifestation of cow's milk allergy in two preterm twins newborns. *J Matern Fetal Neonatal Med* 2012, 25 (Suppl. 1): 132-3.
26. Xanthakos SA, Schwimmer JB, Melin-Aldana H, et al. Prevalence and outcome of allergic colitis in healthy infants with rectal bleeding: a prospective cohort study. *J Pediatr Gastroenterol Nutr* 2005; 41: 16-22.
27. Villanacci V, Manenti S, Antonelli E, et al. Non-IBD colitides: clinically useful histopathological clues. *Rev Esp Enferm Dig* 2011; 103: 366-72.
28. Müller S, Schwab D, Aigner T, et al. Allergy-associated colitis. Characterization of an entity and its differential diagnoses. *Pathologe* 2003; 24: 28-35.
29. Yu MC, Tsai CL, Yang YJ, et al. Allergic colitis in infants related to cow's milk: clinical characteristics, pathologic changes, and immunologic findings. *Pediatr Neonatol* 2013; 54: 49-55.
30. Cordero Miranda MA, Blandón Vijil V, Reyes Ruiz NI, et al. Eosinophilic proctocolitis induced by foods. Report of a case. *Rev Alerg Mex* 2002; 49: 196-9.
31. Bata G, Swincow G, Rytarowska A, et al. Nieswoiste czy alergiczne zapalenie jelita grubego u małych dzieci – trudności diagnostyczne. *Med Wieku Rozwoj* 2006; 10: 475-82.
32. Koletzko S, Niggemann B, Arato A, et al. Diagnostic approach and management of cow's-milk protein allergy in infants and children: ESPGHAN GI Committee practical guidelines. *J Pediatr Gastroenterol Nutr* 2012; 55: 221-9.
33. Jang HJ, Kim AS, Hwang JB. The etiology of small and fresh rectal bleeding in not-sick neonates: should we initially suspect food protein-induced proctocolitis? *Eur J Pediatr* 2012; 171: 1845-9.
34. Vanderhoof JA, Mitmesser SH. Probiotics in the management of children with allergy and other disorders of intestinal inflammation. *Benef Microbes* 2010; 1: 351-6.
35. Baldassarre ME, Laforgia N, Fanelli M, et al. Lactobacillus GG improves recovery in infants with blood in the stools and presumptive allergic colitis compared with extensively hydrolyzed formula alone. *J Pediatr* 2010; 156: 397-401.

Received: 27.04.2015

Accepted: 21.09.2015