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## Infection cases in infants and small children with atopic dermatitis – own observations

### Różnego typu infekcje u niemowląt i małych dzieci chorych na atopowe zapalenie skóry – obserwacje własne

#### Authors' Contribution:

- A** Study Design
- B** Data Collection
- C** Statistical Analysis
- D** Data Interpretation
- E** Manuscript Preparation
- F** Literature Search
- G** Funds Collection

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#### Summary

##### Introduction:

The purpose of the work is to estimate the frequency of occurrence of various infections in infants and small children, aged between 0 and 36 months with atopic dermatitis in the practice of a family doctor.

##### Material/Methods:

The study has been conducted on the basis of the retrospective analysis of medical documentation of disease among children born in 2005–2008 treated in Outpatient Clinic of the Polish Mother's Memorial Hospital in Lodz.

##### Results:

Children suffering from atopic dermatitis are more prone to develop infectious diseases.

##### Conclusions:

Infectious diseases in children with atopic dermatitis are of more chronic nature and more often require antibiotic therapy. Such children often manifest chronic diarrhea and their stool contains *Staphylococcus aureus*. They are more often hospitalized because of difficulty in setting a diagnosis and applying treatment in outpatient clinics.

##### Key words:

infants • small children • infection • atopic dermatitis

#### Streszczenie

##### Cel:

Celem pracy była ocena różnego typu infekcji u niemowląt i małych dzieci, w wieku 0–36 miesięcy, chorych na atopowe zapalenie skóry w praktyce lekarza rodzinnego.

##### Material/Metody:

Badanie było przeprowadzone na podstawie analizy retrospektywnej dokumentacji medycznej dzieci urodzonych w latach 2005–2008 leczonych w Poradni Podstawowej Opieki Zdrowotnej Instytutu Centrum Zdrowia Matki Polki w Łodzi.

##### Wyniki:

Dzieci chore na atopowe zapalenie skóry są bardziej podatne na różnego typu infekcje.

##### Wnioski:

Choroby infekcyjne u dzieci chorych na atopowe zapalenie skóry mają bardziej przewlekły charakter i częściej wymagają antybiotykoterapii. U dzieci tych często występują biegunki, a w kale stwierdza się obecność gronkowca złocistego. Są one częściej hospitalizowane ze względu na trudności w postawieniu diagnozy i prowadzeniu leczenia ambulatoryjnego.

##### Słowa kluczowe:

niemowlęta • małe dzieci • infekcje • atopowe zapalenie skóry

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## INTRODUCTION

There is a steady increase in the number of allergic diseases. In infants and small children atopic dermatitis is definitely the most common. Alongside, various acute infections are the most frequent reasons for complaint. In infants, respiratory tract diseases might appear even a few times during one year. In most cases they are non-complicated infections of the upper respiratory tract. Pneumonia is the most frequent reason for hospitalization, especially in the youngest children [10].

The most common infectious diseases of the respiratory system diagnosed in outpatient clinic include: cold, nosopharyngitis, laryngitis, bronchitis, pneumonia.

Some findings show that viruses are the most common reasons for the incidence of infections of the respiratory system in children. They might constitute as many as 75–90% of the total number of infections of the respiratory system [7,9].

Bacteria inducing respiratory system infections are the most known group of microorganisms because of the fact they are easily to isolate. Though they are not so common, they often result out of viral infections of the respiratory system and take a form of secondary superinfections.

In everyday medical practice it is difficult to isolate an etiological factor. However, a detailed examination of a child manifesting symptoms of infections of the respiratory system enables a doctor to determine what kind of infection the child suffers from.

A very common disorder in the practice of a family doctor is a viral infection of the alimentary tract. In some patients, symptoms of infections of the respiratory tract accompany the infection of the alimentary tract.

The most essential etiological factors of gastroenteritis in infants and small children are viruses, much less frequently – bacteria or their exotoxins. Medical literature describes a lot of research on atopic dermatitis. In not many works, however, the authors underline greater susceptibility to various infections in this group of children [22].

The purpose of the work is to estimate the incidence of various infections in infants and small children with atopic dermatitis in comparison to the group of children at the same age without features of allergy.

## MATERIAL AND METHODS

The analysis was conducted in a group of children born in 2005–2008 treated in Outpatient Clinic of the Polish Mother's Memorial Hospital in Lodz. 365 patients were divided into two groups.

The examined group consisted of 116 infants and small children with at least once diagnosed atopic dermatitis. The control group consisted of 136 children without allergy features.

The control group did not include children with any atopic symptoms. The study was based on the retrospective analysis of the individual medical documentation from Outpatient Clinic of the Polish Mother's Memorial Hospital.

The analysis was conducted using the data from the interview and physical examinations, the results of additional examinations and the information taken from the hospital record.

The analysis of the incidence of upper and lower respiratory tract infections in children with atopic dermatitis and in the control group was conducted using the data from the anamnesis and physical examination which included: frequency of respiratory tract infections in subsequent years examined in outpatient clinics, frequency of application of antibiotic therapy, frequency of the x-ray tests of the chest. The results of the analysis of infections of the alimentary tract emphasized the frequency of diarrhea episodes and/or vomiting as well as positive stool culture in outpatients.

Other, less common infectious diseases were analyzed on the base of the symptoms, physical examination and additional examinations.

In statistical analysis the CHI-Square test and the Fisher's exact test were used. The results were obtained using the statistical package (STATISTICA).

## RESULTS

In the group of children with atopic dermatitis the total number of hospitalizations was visibly higher than in the control group ( $p < 0.001$ ). The most frequent reasons for hospitalizations of children with atopic dermatitis were the infections of the lower respiratory tract ( $p < 0.01$ ). Other common reasons for hospitalization were also diarrheas (Fig. 1, 2).

A substantial difference in the percentage of hospitalizations of children with atopic dermatitis and the control group is especially visible in the youngest children (born in 2007,  $p < 0.05$ ) and infants (born in 2008,  $p < 0.001$ ) (Fig. 3).

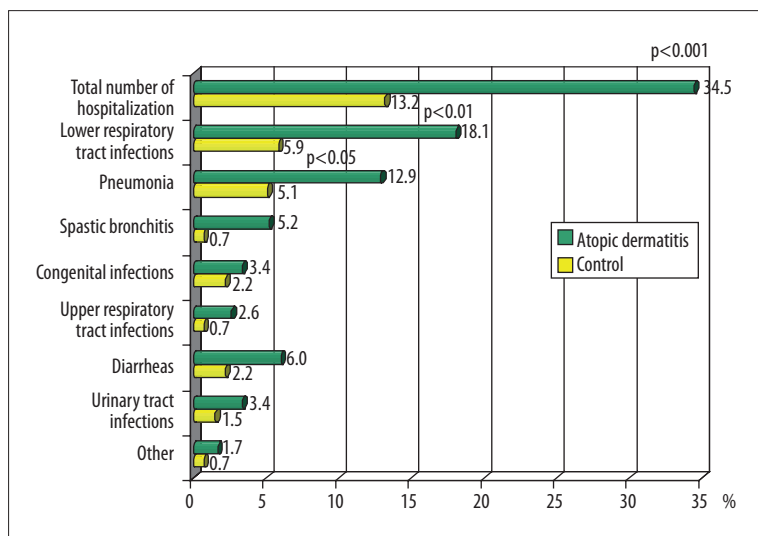


Fig. 1. The percentage of hospitalizations due to infections in children with atopic dermatitis and the control group

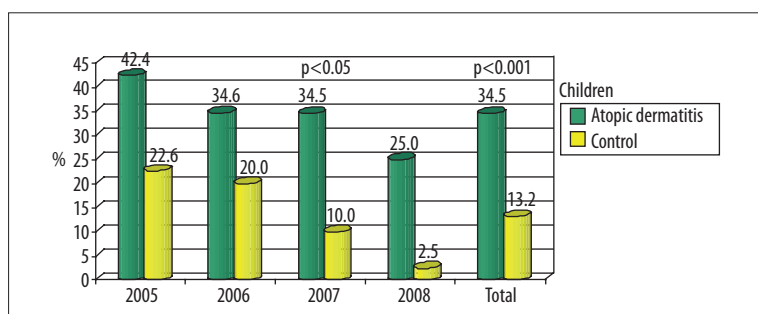


Fig. 2. The percentage of hospitalizations due to infections in children with atopic dermatitis (100%) and the control group (100%) born in a particular year

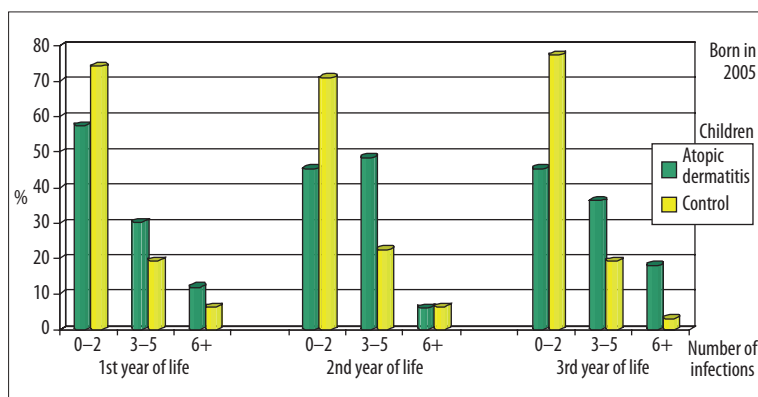


Fig. 3. The frequency of respiratory tract infections in children with atopic dermatitis born in 2005 in subsequent years of life

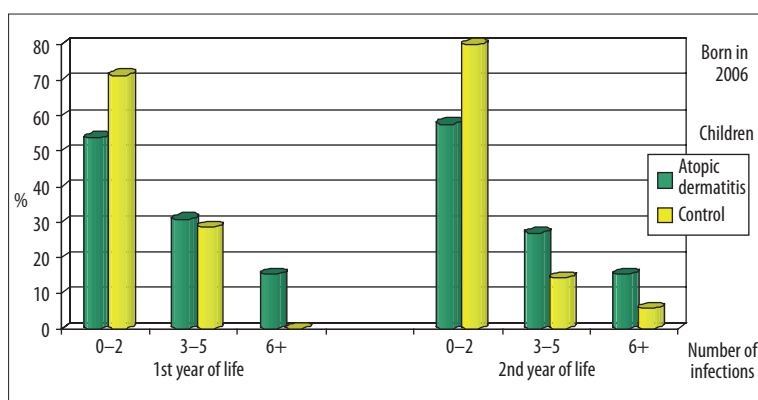


Fig. 4. The frequency of respiratory tract infections in children with atopic dermatitis born in 2006 in subsequent years of life

The percentage of children with atopic dermatitis born in 2005, who developed a high number of infections: 3–5. 6 and more in a year is significantly higher in the first and

third year of life. A high percentage, i.e. 70% of children hardly ever developing infections (up to 2 in a year) appears only in the control group (Fig. 4).

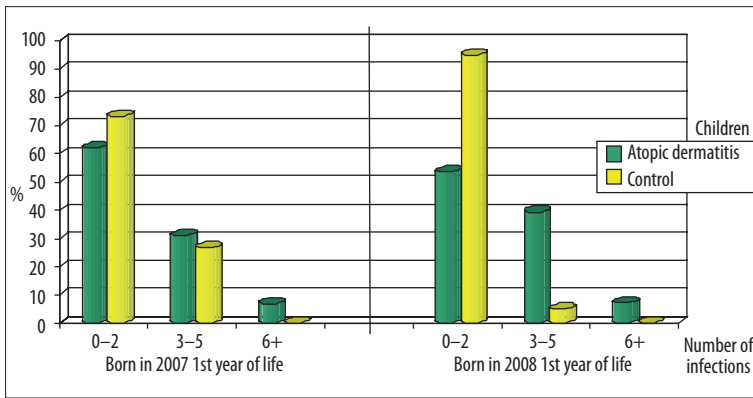


Fig. 5. The frequency of respiratory tract infections in children with atopic dermatitis born in 2007 and infants with atopic dermatitis born in 2008

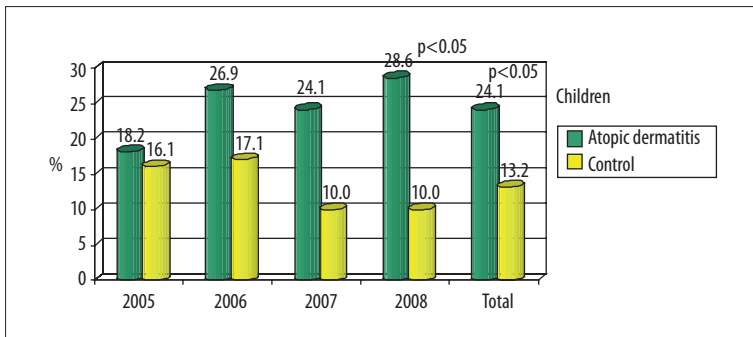


Fig. 6. The percentage of children with atopic dermatitis diagnosed with x-ray test due to pneumonia in comparison to the control

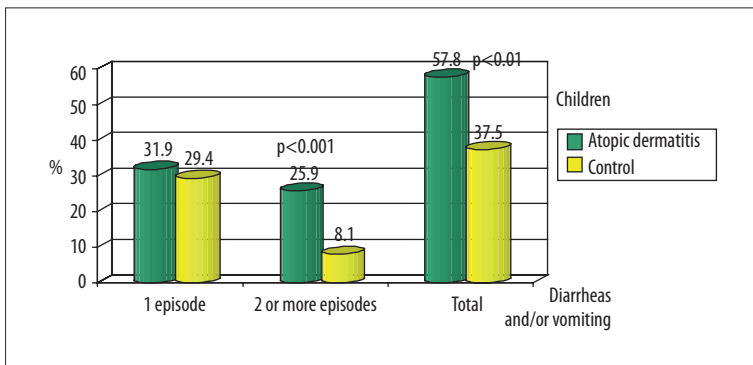


Fig. 7. The percentage of children with atopic dermatitis who manifested episodes of gastroenteritis in comparison to the control group

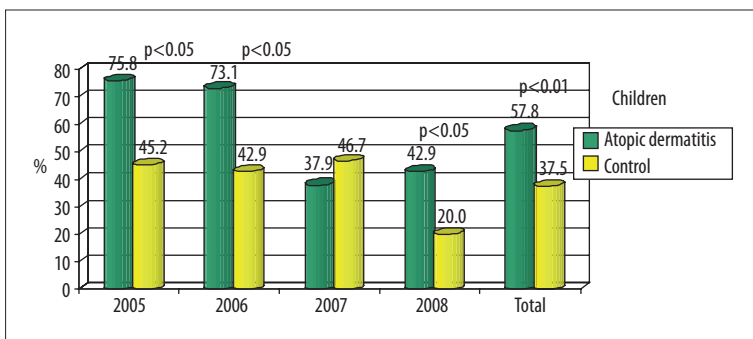


Fig. 8. The percentage of children with atopic dermatitis who manifested any episodes of gastroenteritis in comparison to the control group

Children with atopic dermatitis born in 2006 are more prone to infections than those who belong to the control group. It should be emphasized that in comparison to the children with atopic dermatitis children in the control group hardly ever develop respiratory tract infections (Fig. 5).

In the group of children with atopic dermatitis born in 2007 and 2008, and especially infants born in 2008 respiratory tract infections are more frequent (3–5, 6 or more infections

in a year). Infants (born in 2008) from the control group infrequently developed respiratory tract infections (0–2 infections in a year in up to 90%) (Fig. 6).

The percentage of children who had to have their chests x-rayed is higher and statistically significant (p<0.05) in the total number of children with atopic dermatitis. Moreover, there are more indications for x-ray tests of chest in the group of infants born in 2008 (p<0.05) (Fig. 7, 8).

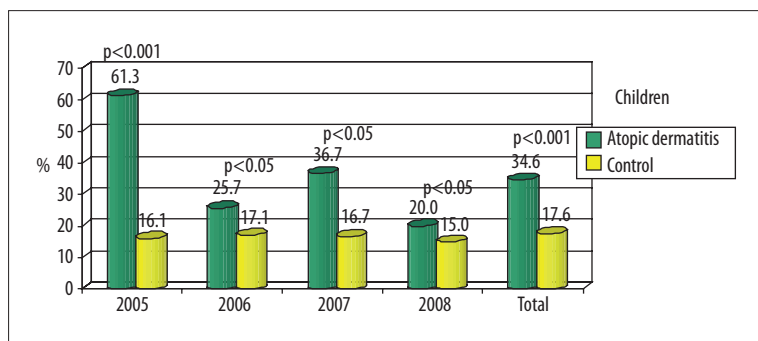


Fig. 9. The percentage of stool culture indicating an infection factor in children with atopic dermatitis in particular years in comparison to the control group

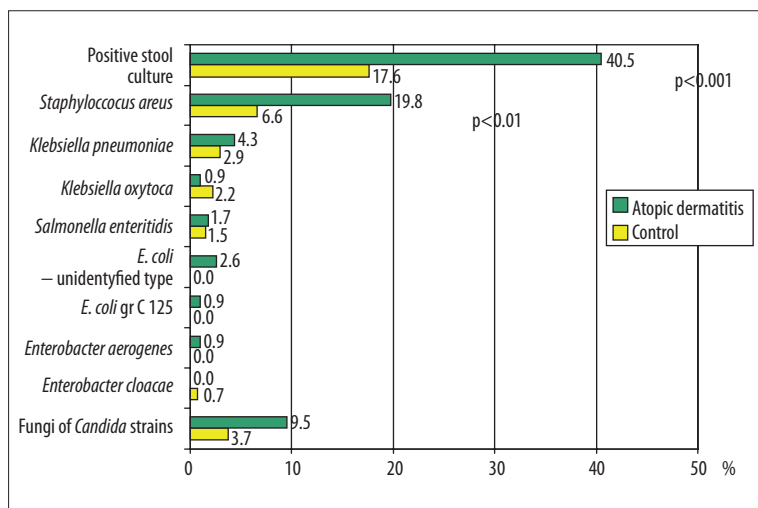


Fig. 10. The percentage of children with positive stool culture depending on the cultured pathogen in children with atopic dermatitis

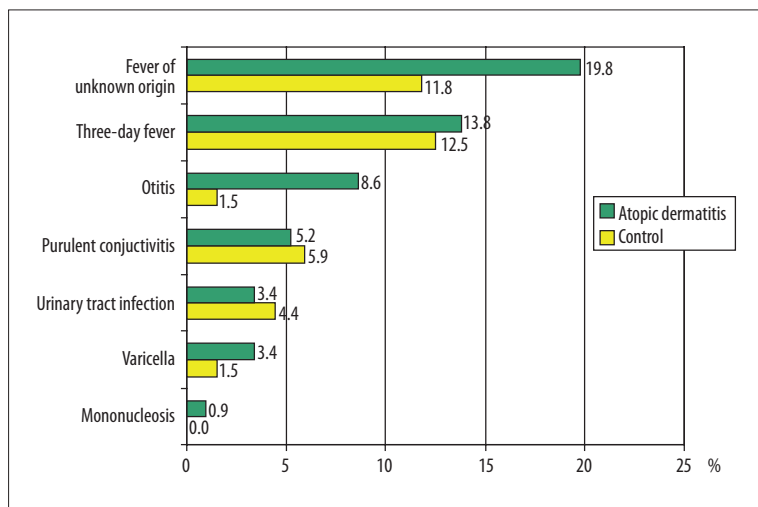


Fig. 11. The percentage of other infectious diseases observed in children with atopic dermatitis in comparison to the control group

As many as 57.8% children with atopic dermatitis manifested episodes of diarrheas and/or vomiting (p<0.01) (Fig. 9).

The total percentage of positive stool culture is significantly higher in children with atopic dermatitis (34.6%, p<0.001). Also in children born in particular years, pathogenic factors in stool are more frequent in those with atopic dermatitis than in those who belong to the control group (Fig. 10).

The most common pathogen cultured in stool is *Staphylococcus aureus*. In children with atopic dermatitis the presence of this pathogen is definitely higher and statistically significant (p<0.01). It should be stressed that

fungi of *Candida* strains, the pathogen which causes chronic diarrhea in children with atopic dermatitis, are frequent in this group of children (Fig. 11).

Among other infectious diseases the occurrence of otitis in children with atopic dermatitis is statistically significant. Such children also suffer from fever of unknown origin (Fig. 12).

The number of children who had to be administered antibiotics in the first and second year of life was statistically significant in infants born in 2008 (p<0.01) and three-year old children born in 2005 (p<0.05). It should be stressed

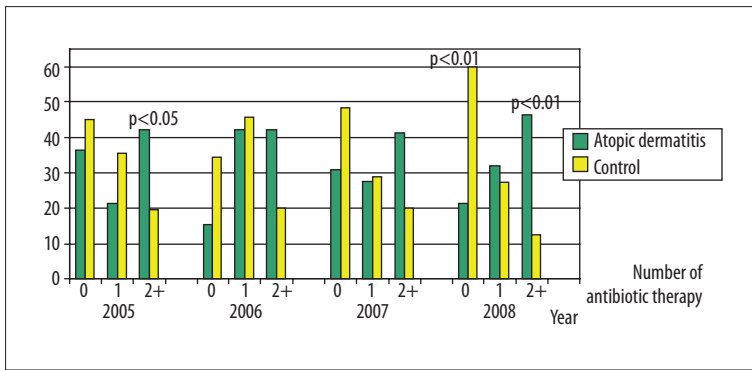


Fig. 12. The percentage of infants subjected to antibiotic therapy due to any infectious diseases in particular years

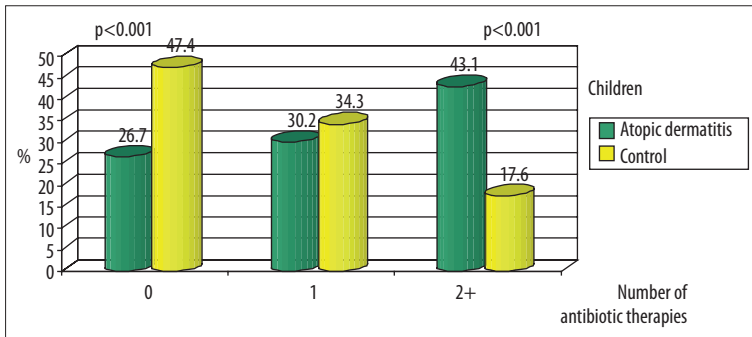


Fig. 13. The percentage of children with atopic dermatitis and the children of the control group to whom antibiotic therapy was administered in the first 12 months of life

that infants born in 2008, belonging to the control group hardly ever took antibiotics ( $p < 0.01$ ) (Fig. 13).

The application of antibiotics as early as in infancy in children with atopic dermatitis in comparison to the control group is more frequent, therefore statistically significant ( $p < 0.001$ )

## DISCUSSION

Lower respiratory tract infections (spastic bronchitis and pneumonia) in infants and young children have always been a clinical problem and the reason for hospitalization in child population [8].

The incidence of pneumonia in the youngest children is a few times higher than in adolescents and adults and is 40 cases per 1000 people per year [21]. Those who definitely require hospitalization are newborns and infants in the first quarter of the year, children remaining in the critical state, children with concomitant diseases which deteriorate their health state after the patients have developed pneumonia.

A common reason for hospitalization of the youngest children is acute gastroenteritis. Direct indications for parenteral hydration are: dehydration, consciousness disorders, persistent vomiting, insufficient oral hydration, and early age of the patient.

In our study we analyzed reasons for hospitalization due to infectious diseases on the basis of the information taken from the hospital record. It was concluded that the most common reasons for hospitalization in the two groups were lower respiratory tract infections, especially pneumonia, which made up 40% of the total number of hospitalizations. The findings correspond to the findings of other sources [10].

In the group of children with atopic dermatitis the total number of hospitalizations was much higher and the level of significance was  $p < 0.001$ . Children with atopic dermatitis are more frequently hospitalized due to pneumonia ( $p < 0.01$ ). A much higher frequency of hospitalizations of infants with atopic dermatitis indicates that in this group it is much more difficult to set a diagnosis and administer the right therapy than in a group of children of the same age who do not suffer from allergy. This phenomenon might result from the fact that the immune system in such young children is not yet fully developed anatomically and therefore does not function properly. The development of the atopic process, as well as the relationship with Th2 profile polarization, is mentioned by many authors [13].

It should be stressed that the children in the control group in the first months of life were hardly ever referred to hospital due to respiratory system infections and were perceived as more healthy. A group of scientists, who analyzed the influence of various environmental factors causing atopic dermatitis, drew similar conclusions. They stated that infants and young children with atopic dermatitis more frequently develop respiratory system infections. The authors emphasize that atopic dermatitis appears in infancy [6].

Kramer et al. in their extensive research done in a group of children with atopic dermatitis did not find significant differences in the incidence of respiratory system infections in the first year of life in comparison to the children without allergy. The scientists make a conclusion that stands in opposition to hygienic theory according to which frequent allergies result from decreased exposure to infections in early childhood [15]. The conducted analysis corresponds to the final conclusions drawn by Kramer et al. The increase in number of infections in children with atopic dermatitis presented in the author's own research is also in opposition to hygienic hypothesis.

Kummeling et al. proved that various environmental factors, including infection ones, in early infancy might lead to atopic manifestations. To prove it, further research is required [16]. Similar observations on RSV were made by Peebles. He showed that asthma and allergy symptoms in later childhood are related to respiratory tract infections caused by RSV in infancy [22].

We wanted to emphasize a high frequency of pneumonia diagnosed with an x-ray test of chest. It was concluded that in the group of all children with atopic dermatitis, pneumonia was diagnosed with an x-ray test in 28 cases, which constituted 24.1% of the examined group and was statistically significant compared to the control group (13.8%). By examining the children with atopic dermatitis born in each year separately, the significant difference ( $p < 0.05$ ) was visible only in the group of infants born in 2008. Thus it might be concluded that in infancy it is difficult to diagnose pneumonia, especially in children with atopic dermatitis.

Acute diarrheas and vomiting are also serious problems in the population of young children. Especially infants are susceptible as their mucous barrier is not well developed yet; therefore production of immunoglobulin A is insufficient. The role of IgA is the protection of the organism against pathogens which penetrate through the alimentary tract as well as the decrease in permeability of the intestinal mucous membrane for alimentary allergens [14].

While analyzing the medical documentation of the examined group symptoms of gastroenteritis were taken into consideration in individual disease records.

It was concluded that in the total number of children with atopic dermatitis diarrheas and vomiting are statistically more significant than in the control group ( $p < 0.01$ ). It, however, refers only to multiple episodes of gastroenteritis ( $p < 0.001$ ). As for a single episode of diarrhea, no statistical significance was observed.

The analysis of children with atopic dermatitis born in subsequent years, single or multiple episodes of gastroenteritis were taken into consideration. In almost all the examined age groups a statistical significance was observed ( $p < 0.05$ ).

Our analysis of the findings shows that children with atopic dermatitis develop gastroenteritis significantly more frequently. Black et al. draw similar conclusion. They state that children with atopic dermatitis manifest a smaller tolerance to intestinal pathogens, especially when it is accompanied by alimentary intolerance [4].

According to the most recent findings published in 2009 by Reimerink et al. past viral inflammation of the alimentary tract caused by rotaviruses and noraviruses in the first year of life results in the increased risk of wheezing in sick children in the subsequent year of life [23].

In our stud we show that children with atopic dermatitis more frequently develop diarrhea and wheezing in bronchia in comparison to a group of children of the same age who do not manifest features of allergy.

Possible viral etiology of these diarrheas might imply a certain relation to wheezing in bronchia because of presence of intestinal pathogens. It would require detailed virological tests, which is highly difficult to perform in a basic medical care.

To establish the cause of chronic diarrhea a detailed analysis of microbiological stool culture was carried out. The analysis of positive stool culture proved a considerable role of *Staphylococcus aureus*. It was cultured in 23 children with atopic dermatitis, which makes up 19.8% of the whole examined group. In other words, every fifth child with atopic dermatitis has *Staphylococcus aureus*.

In the control group this percentage was 6.6%. As for the presence of *Staphylococcus aureus*, there was a statistical significance ( $p < 0.01$ ) between the examined and the control groups.

The total summary rating for all the positive stool cultures is significantly higher in children with atopic dermatitis ( $p < 0.001$ ), especially in three-year old children born in 2005 ( $p < 0.001$ ).

Bjorksten et al. prove the presence of *Staphylococcus aureus* in the alimentary tract of two-year-old children manifesting features of allergy [3]. The analysis of the author's own studies confirms these findings.

Professional literature presents an extensive role of *Staphylococcus aureus* as a pathogen colonizing atopic dermal changes [1,11]. Authors of numerous studies stress the role of the bacterium as a superantigen responsible for a direct activation as many as 20% lymphocytes [12,17,19]. *Staphylococcus aureus* significantly more often appears in the alimentary tract of children with atopic dermatitis than in children of the same age who do not manifest features of allergy. This fact implies that children with atopic dermatitis are prone to develop infections whose source is this pathogen. These infections are not only skin infections but they also affect other systems.

The results of the author's own research imply that the presence of *Staphylococcus aureus* in the alimentary tract brings about atopic dermal changes. As a superantigen, it can activate lymphocytes regulating GALT system towards the secretion of cytokines characteristic for Th2 allergy profile. Further research is however needed.

Fungi of *Candida* strain also appear in the group of children with atopic dermatitis.

Patients in examined and control groups developed other infectious diseases almost equally often. The diseases included a three-day fever, urinary tract infections, purulent conjunctivitis, varicella. The difference was visible only in the case of acute otitis media. 10 children with atopic dermatitis suffered from it, which made up 8.6% of the whole group of patients. In the control group there were two cases of otitis media (1.5%). The difference was statistically significant ( $p < 0.01$ ).

The author's results of the research correspond to the ones obtained by Scandinavian researchers, who proved the relationship between atopic dermatitis and frequent incidence of otitis media [5].

Children with atopic dermatitis also suffered more often from fever of unknown origin.

Bearing in mind all findings which show that antibiotic therapy in the first year of life entails the risk of incidence of allergic diseases, a decision to examine all the children who belonged to the examined group was taken [20].

According to the medical documentation multiple antibiotic therapy was used more often in children with atopic dermatitis and the difference was statistically significant ( $p < 0.001$ ).

The percentage of children who were not administered antibiotic therapy in the first 12 months of life was significantly higher in the control group ( $p < 0.001$ ). It should be

emphasized that in the control group which included infants born in 2008, the percentage was 90%. Infrequent administration of antibiotics in the control group indicates a general tendency to apply antibiotics as rarely as possible, especially in infancy. All over the world antibiotic therapy is being administered less and less frequently [2,18].

## CONCLUSIONS

Children with atopic dermatitis are more prone to infectious diseases. Their course is more chronic; they more often require antibiotic therapy. Such children are also hospitalized more frequently since it is more difficult to set a diagnosis and then apply treatment outside hospital care. They also suffer from chronic diarrhea and their stool contains *Staphylococcus aureus*.

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