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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

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გამოიცემა თბილისის სახელმწიფო სამედიცინო უნივერსიტეტთან
თანამშრომლობითა და მისი პატრონაჟით

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

ТБИЛИСИ - НЬЮ-ЙОРК

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board and The International Academy of Sciences, Education, Industry and Arts (U.S.A.) since 1994. **GMN** carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

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GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией и Международной академией наук, образования, искусств и естествознания (IASEIA) США с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения.

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GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

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тел.: 995(32) 254 24 91, 5(55) 75 65 99
Fax: +995(32) 253 70 58, e-mail: ninomikaber@geomednews.com; nikopir@geomednews.com

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CONTACT ADDRESS IN TBILISI

GMN Editorial Board
7 Asatiani Street, 4th Floor
Tbilisi, Georgia 0177

Phone: 995 (32) 254-24-91
995 (32) 253-70-58
Fax: 995 (32) 253-70-58

CONTACT ADDRESS IN NEW YORK

NINITEX INTERNATIONAL, INC.
3 PINE DRIVE SOUTH
ROSLYN, NY 11576 U.S.A.

Phone: +1 (917) 327-7732

WEBSITE
www.geomednews.org

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При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

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2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

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ავტორთა საყურადღებოდ!

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1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

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6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

Содержание:

REACTIVE ARTHRITIS IN CHILDREN (REVIEW)

Tugelbayeva A., Ivanova R., Goremykina M., Rymbayeva T., Toktabayeva B.

NCJSC «Semey Medical University», Semey, Kazakhstan

Reactive arthritis (ReA) is an inflammatory arthritis related to the subset of seronegative spondyloarthropathies which manifests 1 to 4 weeks after an intestinal, urogenital, or nasopharyngeal infections. The absence of pathogenic microorganisms in the joint fluid or in the synovial membrane distinguishes it from infectious arthritis, also called septic arthritis. ReA is the most common among rheumatic diseases in children and adolescents and represents a systemic clinical manifestation of the above mentioned infections [18].

Additionally, ReA is included into the subset of juvenile spondyloarthropathies (JSpA) that refers to a group of related rheumatic diseases characterized by involvement of peripheral large joints, axial joints, and enthesitis that begin in the early years of life (before reaching the age of 16). The nomenclature and concept of spondyloarthropathies has changed over the past few decades. Though there is no any specific classification of juvenile spondyloarthropathies, diseases related to the nomenclature of spondyloarthropathies in young patients involve: the seronegative enthesitis and arthropathy, juvenile ankylosing spondylitis, reactive arthritis and inflammatory bowel disease-associated arthritis [47].

Depending on the entrance gate, ReA infections are classified into the following three groups: 1) postenterocolitic (enterogenic/intestinal); 2) urogenital (urogenic); 3) arthritis with nasopharyngeal infection that is preceded by the acute infections of the upper respiratory tract such as an acute respiratory disease, angina, pharyngitis, or bronchitis. Some authors refer to the latter as “post-respiratory ReA (priReA)” [2-4,18].

Furthermore, it should be noted that joint disorders are less common among children compared to adults. But, the course of the disease is different and more complicated in children. Recently, there is an increase in the number of preschool children suffering from reactive arthritis [12].

Joint lesions with clinically similar manifestations in certain cases can be the sign of other more serious, often systemic rheumatic diseases [15]. The appropriate treatment does not necessarily bring about a cure of the arthritis. On many occasions it can progress to a chronic condition, thereby increasing the likelihood of juvenile idiopathic arthritis, osteoarthritis, and other severe immunoagressive diseases [12,48,60]. According to some authors, chronic and recurring arthritis or spondylitis occurs in almost 15-30% of patients [42].

Despite the fact that the interest towards ReA has been lost over the past 10 years, this disease still remains a serious issue in rheumatology and requires an early and individual treatment [24].

In this regard, patients who are diagnosed with reactive arthritis should continue to be monitored regularly by a rheumatologist to maintain control and prevent long-term complications.

Epidemiology. The epidemiological data for ReA varies across the world. The factors behind this diversity involve different approaches to performing the diagnostic process and a variety of clinical presentations, the lack of specific laboratory biomarkers, different geographical locations that predispose to multiple pathogens, different genetic backgrounds, different grades of infection, and recently identified changes in the intestinal microbiome [31,34,46].

The scarcity of epidemiological data and prevalence studies is due to the heterogeneity of the disease manifestations and lack of definitive diagnostic criteria, respectively [59]. In Scandinavia, where most studies were conducted, the incidence is around 0.6 to 27 per 100,000 inhabitants [36].

ReA typically affects young adults of working age. Though children also suffer from ReA, its prevalence among children is lower [38,49,63]. The incidence of ReA varies considerably in Europe. It ranges from 0.9 to 9.3 per 100,000 inhabitants depending on the study [36,37,58]. The recent study shows an increase in annual incidence of ReA following intestinal infection [63]; however, the incidence rates range from 1% to 15% across studies due to different research designs [51]. Since intestinal infections are common in developing countries, the incidence of ReA in such countries is higher in comparison to developed countries [35].

In a research conducted by Brinster et al., the clinical presentation and microbiological context of ReA in Canada appears without considerable difference over the period of 30 years [24]. According to the systematic review by Horton et al. in which authors analyze the ReA following intestinal infections, arthritis is recorded in 9 cases out of 1000 for Campylobacter and 12 out of 1000 for Salmonella and Shigella [39]. The incidence of reactive arthritis after Clostridia infection among children constitutes 1.4%, while its incidence following Chlamydia infection varies from 4% to 8%. The relative risk of ReA in women is 1.5 times higher than in men. Besides, the frequency of ReA in adults is 2.5 times higher compared to children [19]. According to certain data, the frequency of ReA with urogenital etiology constitutes 2: 1 in favour of males, with nasopharyngeal etiology is 3:1 in favour of males, whereas in arthritis with enteral etiology it is the same among both sexes [45]. A recent systematic review by Ajene et al. demonstrates that the incidence of Campylobacter-associated arthritis ranges from 8% to 16% with a median of 8% among adults compared to 0% to 6% with a median of 3% among children. Salmonella-associated arthritis ranges from 1% to 24% with a median of 11% among adults compared to 0% to 12% with a median of 5% among children. Shigella-associated ReA ranges from 7% to 12% among adults and from 0% to 7% with a median of 3.5% among children [19].

If we observe the season of onset for causative bacterial agents, we notice that: reactive arthritis caused by bacteria from urinary tract is present throughout the year. Reactive arthritis caused by bacterial agents from enteral tract is more frequent during the summer season, whereas reactive arthritis caused by nasopharyngeal agents is more present during the winter season [45].

The results of a bicentre retrospective analysis of features and outcomes of ReA show that the incidence of ReA in two cohorts of patients diagnosed between 1986 and 1996 as well as between 2002 and 2012 was similar. But, currently ReA more frequently leads to spondyloarthritis [29]. Other authors came to the similar conclusion that ReA tends to progress into the chronic disorders and definitely requires closer attention [24].

Pathophysiology. ReA is a very complex pathological process that reflects the dynamic interface between the triggers of the disease and genetic predisposition. In fact, the development of ReA depends on four main factors – the etiological agents that

caused it, cytokines, the participation of a genetic factor (HLA-B27) and the gut microbiota [63].

Etiological factor. Some bacteria are known to trigger the reactive arthritis. They can enter the joints through the intestine or by urogenital route [31,55]. Moreover, it has been proven that the synovial fluid may contain bacterial antigens, and the persistence of these elements can cause the progress of acute ReA to chronic arthritis [63]. Recent studies show that the synovial fluid of patients with ReA contains immunogenic products such as bacterial DNA, antigenic proteins, lipopolymers, and saccharides [46].

In case of ReA being transmitted by urogenital route, *Chlamydia trachomatis* is the most common cause, followed by *Ureaplasma urealyticum* and other less common microbes [31]. The constant persistence of bacterial components of *Chlamydia trachomatis* induces a chronic inflammatory state [33]. This fact also explains the ability of *Chlamydia* to inhibit the formation of phagosomes and lysosomes which allows *Chlamydia* to persist in cells [26,63].

The bacterial antigens are transferred from the primary centre to the synovial membrane, which causes the activation of T-lymphocytes and, as a result, leads to the rapid release of inflammatory cytokines, resulting in synovial inflammation [46,63].

Factor of cytokines. Previous studies have demonstrated that levels of inflammatory cytokines such as tumor necrosis factor alpha (TNF-α) and interferon gamma (IFN-γ) were reduced in acute ReA [22,62]. In contrast, the level of TNF-α increases in chronic ReA which allows assuming that this cytokine plays a dual role at various stages of the pathogenesis of this disease [64]. Researchers have found that the imbalance of cytokines and their concentrations depends on the duration of ReA [10].

The comparison of cytokine level in coprofiltrates and serum showed that the acute ReA is associated with a high level of TNF-α in coprofiltrates, and the chronic ReA is correlated with increasing values of interleukin-6 (IL-6) and interleukin–10 (IL-10) [17]. Probably, the determination of serum interleukin-10 (IL-10) concentration is useful for assessing and monitoring the activity of the inflammatory process in ReA [13]. Katsikas et al. provide data on the pathogenetic role of pro-inflammatory cytokines, especially TNF-α, in the pathogenesis of juvenile spondyloarthropathies. Besides, authors suggest that interleukin-1 (IL-1), interleukin-6 (IL-6) and interleukin-17 (IL-17) also play a significant pathogenetic role in these diseases [47].

A few studies aimed at determining the connections between the cytokine gene polymorphisms and the development of ReA (as the one conducted in Mexico to analyze the links with TNF-α polymorphisms) showed that TNF-α polymorphism (-308) is associated with a predisposition to undifferentiated spondyloarthritis, but at the same time, the association of ReA with TNF-α gene polymorphisms was not found since the sample size did not allow to assess the association [61].

One of the first studies revealed that the IL-10 gene promoter is associated with the development of ReA, i.e. high IL-10 production in the joints of patients may be genetically determined. This hypothesis requires further verification [41]. The results of studies among siblings and twins point out that the proportion of susceptibility to spondyloarthritis (SpA) is not determined by HLA genes, but rather by the level of secretion of TNF-α and IL-10 cytokines which affect their production and the course of SpA. The balance is regulated at the genetic level and depends on genetic polymorphisms of interleukin genes [54]. There are studies in which IL-17 levels were elevated in synovial fluid in patients with *Chlamydia*-induced ReA [64].

Several research focused on the study of patients with ReA following typhoid fever have shown that *Salmonella adventitia* proteins can stimulate the synovial immune cells to produce IL-17 or IL-23 [27]. Various cytokine genes polymorphisms have been described including polymorphisms in monocytes, TNF-α (-238), and TNFR polymorphisms. The exact pathogenesis of the Th1/Th2 imbalance has not been clarified. However, it is likely that genetic factors are involved [58].

Cytokine imbalance in ReA has been the subject of numerous scientific studies for many years; however, the results are quite contradictory. Therefore, the analysis of the correlation between the cytokine gene polymorphisms and their level of production in patients with ReA can be recommended for further molecular genetic studies which are one of the priority areas in rheumatology currently.

Genetic factor. The association of HLA-B27 with ReA is well known, but its involvement in the pathogenesis is still not fully investigated. The studies have shown that HLA-B27 is present in 50-80% of patients with ReA and 90% of patients with ankylosing spondylitis (AS) [21,46,49,52,63]. For example, it is assumed that HLA-B*2703 increases the risk of a typical clinical triad of ReA [30]. Besides, it is known that the persistence of pathogens in organism, especially *Chlamydia* and *Salmonella*, can be caused by HLA-B27 [32,43]. HLA-B27 expression enhances bacterial replication and thereby reduces the threshold of endoplasmic reticulum (ER) induction, so that *Salmonella* can induce an unfolded protein response. According to numerous studies, HLA-B27 is laid down more slowly than other types of HLA when ER is assembled, which leads to the accumulation of a homologous HLA-B27 dimer and b2-microglobulin in the synovial membrane, finally resulting in the activation of the inflammatory process [20,28].

Current research suggests a number of theories, including the theory of molecular mimicry between a gene and a pathogen. It has been proven that there is a similarity between the amino acid sequences in HLA-B27 and *Yersinia* or *Shigella* proteins, which leads to cross-reactivity, tolerance, and hence triggers an immuno-inflammatory response [28,57,64].

Gut microbiota. The intestinal microbiome and its role in the pathogenesis of arthritis has been gaining attention in recent years [64]. In fact, new research is focused on identifying the associations between the microbiome and spondyloarthritis, as well as other inflammatory arthritis [31].

The important information obtained claims that changes in microbiota can lead to aberrant immune responses of the intestinal flora, intestinal dysbiosis, inflammation, and, therefore, to spondyloarthritis [55]. Inflammatory bowel disease, psoriasis, and SpA are all characterized by intestinal dysbiosis. Though all diseases display a decrease in bacterial diversity in intestinal microbiota, this does not happen in ReA [46,64].

A similar conclusion has been drawn by researchers who compared two groups - patients with ReA and patients after an intestinal infection which did not develop into arthritis; that is, significant differences in the diversity of intestinal microbiota were not found [46]. It is stated that the prevalence of enteropathogens is high in patients with ReA and post-infectious peripheral spondyloarthritis. In addition, those patients have a reduced concentration of gut commensals [31,46]. Severe violations of intestinal microbiocenosis are observed in patients with acute and recurrent course, while the degree of dysbiosis is mainly moderate in patients with a prolonged course [12].

It is important to note that all children (100%) with acute ReA have violations of the intestinal microbiocenosis, though there

are considerable differences among children. 62.5% had II degree, and 37.5% had I degree of dysbiosis [16]. Clinical and microbiological studies in children with reactive and infectious arthritis have shown that dysbiotic disorders of the intestinal microbiota along with previously known factors are an important risk factor for the development of arthritis. Connective tissue dysplasia can serve as a factor for the development of reactive arthritis [8].

Thus, further in-depth study of pathogenetic factors, such as the level of certain cytokines and genetic polymorphisms in ReA, and the role of dysplasia in the development of ReA is very promising.

Clinical manifestations of ReA. It is well known that ReA and SpA belong to the same group of spondyloarthropathies [64]. In fact, Kaarela et al. showed that chronic ReA and AS have common clinical manifestations, such as sacroiliitis, peripheral arthritis and iritis [40,52].

The most common clinical presentation of ReA is its acute form. In some patients the disease resolves spontaneously within the first six months, while in others (10 to 30%) it tends to progress into the chronic ReA [25].

Oligoarthritis is the most frequent manifestation of ReA. Oligoarticular type is the most common in 70% of women and 73% of men. Monoarticular is characteristic to 13% of female patients and 14% of male patients, and polyarticular type is detected in 14% females and 10% males among adults [44].

The presence of asymmetric mono or oligoarthritis of the lower extremities is a typical manifestation of joint syndrome in children. In certain cases, the disease can also manifest as an arthritis in small joints [3,12,36]. Approximately 4% of children have polyarticular joint syndrome which is accompanied by limited functioning of joints and impaired self-care due to severe pain syndrome [7]. The analysis of the number of affected joints depending on the age group illustrates the predominance of monoarticular type of joint damage in preschool children, while oligoarthritis is more common in the middle and older age groups. Regardless of age and gender, the joints of the lower extremities are more often affected [6,11]. The joint syndrome is characterized by arthralgias without obvious inflammatory changes in the joint area and impaired functioning as well as by morning stiffness of short duration in majority of children [5,7]. It is also characterized by an asymmetric lesion of the interphalangeal and metatarsophalangeal joints and periarticular tissues of the hands and feet with expressed swelling of the fingers, soreness, hyperemia of the skin and the formation of the so-called “sausage-shaped deformity” which is observed in 5-10% of children [7,11]. Enthesitis is an inflammation of the enthesis. It represents the site of attachment of a tendon, ligament, fascia or capsule to the bone. The lesion seen in the lower extremities such as Achilles tendinitis or plantar fasciitis is a common condition in enthesitis [55]. Frequent heel pain, stiffness, reduced mobility in the cervical and lumbar spine, as well as in the ileosacral joints are noted in boys over the age of 6 who are carriers of HLA-B27 [1]. Such patients are at risk of developing juvenile spondyloarthritis [9].

Typically, skin lesions occur in a prolonged course. These symptoms include skin lesions in the form of keratoderma of the palms and soles, plaque psoriasis of the skin on face, torso and limbs. Onychodystrophy (nail dyschromia, brittleness, roughness, tuberosity) develops as a result of prolonged arthritis, which is often interpreted as a mycotic lesion [58].

Along with the joint syndrome, the symptoms of the gastrointestinal tract, urinary tract and visual organs disorders in the form of dyspepsia, bowel problems, dysuric phenomena and conjunctivitis are described in children with ReA [12]. The manifestations of the gastrointestinal infection caused by *Salmonella enteritidis* or *Salmonella typhimurium* are diarrhea and fever. The symptoms may be relatively mild. *Salmonella* can affect bones and joints, so it is important to exclude septic arthritis or osteomyelitis caused by these microorganisms. Leukopenia may be present in the early period of infection. In case of reactive arthritis, the joint syndrome develops at 1-3 weeks after an acute intestinal infection [55]. Intestinal infection caused by *Campilobacter jejuni* is accompanied by febrile body temperature, abdominal pain, vomiting, and moderate diarrhea. Clinical manifestations of the intestinal infection caused by *Yersinia enterocolitica* vary depending on the age of the child. Diarrhea often prevails in children under the age of 5. Tension and pain in the lower right quadrant of the abdomen are dominant in children aged 5 to 14 [53]. Acute gastroenteritis is followed by arthritis within 1 to 2 weeks. In children at an older age, the clinical presentation may resemble the manifestations of terminal ileitis or mesenteric lymphadenitis which are similar to the signs of appendicitis [50,53]. Intestinal infections caused by *Shigella* usually occur in a more acute form characterised by the presence of blood in the stool and high fever [55].

Thus, regardless of the etiological agent, the clinical presentation of arthritis proceeds in the same way. For instance, lesions of the joints of the lower extremities prevail in all age groups among adult patients [44].

Burdened premorbid background were the majority of children with ReA: 85% had frequent respiratory diseases, 64% had chronic focus of infection (adenoids, tonsillar hyperplasia, chronic tonsillitis, dental caries), 20% had exudative diathesis in a medical history, 25% had residual rickets features, and 6% of patients had a trauma preceding ReA [5,14].

Diagnostic criteria. There is no consensus on the validated diagnostic criteria for ReA to date. Mainly, it is a clinical diagnosis based on a thorough analysis of a medical history, physical examination, and a combination of microbiological criteria [29,55]. The microbiological profile of potential triggers depends on the detection method. Direct evidence of infection is hard to obtain, since the microorganism is not present in the focus of infection when arthritis occurs. As for indirect assessments, mainly serological tests, they have limitations [24].

Currently, the diagnostic criteria combining the recommendations of the American College of Rheumatology (ACR) and the Berlin Criteria (1999) which were adopted during the fourth international seminar on ReA are used.

The criteria are divided into main and additional ones. The main criteria include: 1. the presence of arthritis, asymmetric, mono or oligoarthritis, lesion of the joints of the lower extremities; 2. preceding infection accompanied by enteritis (manifested with diarrhea lasting at least 1 day which occurs within 3 days to 6 weeks after getting arthritis) or by urethritis (manifested with dysuria or urethral or vaginal discharge lasting at least 1 day which occurs within 3 days to 6 weeks before getting arthritis). Additional criteria include at least one of the following signs: 1. the presence of an initiating infection which is indicated by a positive urine culture, a smear from the cervix/urethra, a positive bacteriological stool examination for arthritic intestinal infections; 2. the presence of persistent synovial infection confirmed using immunohistology or PCR for *Chlamydia*. A reliable diagnosis of ReA is made if the patient meets both main criteria and one additional. A probable diagnosis of ReA

is made if the patient satisfies both main criteria or if s/he fulfils one main and one or more additional criteria [23,56].

Conclusion. Despite the progress being achieved towards understanding ReA, there are still many controversial issues in pediatrics in various directions. A comprehensive analysis of the literature from the past ten years have shown that insufficient attention was paid to this topic in pediatrics. To date, the studies of ReA among children in foreign sources are significantly less compared to the number of similar studies among adults.

Unfortunately, the available research on prognostic factors as well as analysis of the disease outcomes was focused only on adults, though everything that happens in adults is often laid down in childhood. Therefore, it is crucial to prevent the development of serious rheumatic diseases in childhood, especially in the presence of certain genetic predispositions and risk factors.

The study of ReA in children with a detailed analysis of clinical manifestations and constitutional symptoms can help not only in the diagnosis of a specific case, but also in the justification of complex adequate treatment of such patients, thereby reducing the frequency of adverse outcomes.

It is also important to develop an algorithm of subsequent personalized pediatric observation of children who suffered from ReA because the progress of ReA to chronic disease or other forms of spondyloarthritis requires rheumatological treatment, and in some cases can lead to disability in working age.

This information requires further fundamental research and verification of assumptions.

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SUMMARY

REACTIVE ARTHRITIS IN CHILDREN (REVIEW)

Tugelbayeva A., Ivanova R., Goremykina M., Rymbayeva T., Toktabayeva B.

NCJSC «Semey Medical University», Kazakhstan

Reactive arthritis is an aseptic inflammatory arthritis that is associated with intestinal, urogenital, and nasopharyngeal infections, and represents a systemic clinical presentation of these infections. Reactive arthritis among children still remains an issue in pediatric rheumatology. The variety of the clinical manifestations makes it difficult to diagnose and detect reactive arthritis. Moreover, there is a risk that reactive arthritis without a proper treatment can lead to chronic destructive joint diseases. As the articles' analysis has shown, this topic in pediatrics has been neglected over the past 10 years. Thus, the paper presents data on the epidemiology, pathophysiology, clinical presentation and diagnosis of this disease, as well as recommendations for further studies.

Keywords: reactive arthritis, children, epidemiology, pathophysiology, clinical presentation.

РЕЗЮМЕ

РЕАКТИВНЫЕ АРТРИТЫ У ДЕТЕЙ (ОБЗОР)

Тугелбаева А.М., Иванова Р.Л., Горемыкина М.В., Рымбаева Т.Х., Токтабаева Б.Ж.

НАО «Медицинский университет Семей», Казахстан

Реактивный артрит – асептическое воспалительное заболевание суставов, ассоциируется с кишечной, урогенной, носоглоточной инфекцией и является ее системным клиническим проявлением. Реактивный артрит у детей по сей день является актуальной проблемой детской ревматологии, так как из-за разнообразия клинических проявлений установить диагноз весьма сложно. На основании анализа ретроспективной и текущей научной литературы по указанному вопросу за последние 10 лет представлены сведения об эпидемиологии, патофизиологии, клинической картине и диагностике заболевания и возможные перспективы в лечении данной патологии у детей. Авторы статьи рекомендуют разработать алгоритм последующего персонализированного педиатрического наблюдения за детьми, страдающими реактивным артритом.

რეზიუმე

რეაქტიული ართრიტები ბავშვებში (მიმოხილვა)

ა.ტუგელბაევა, რ.ივანოვა, მ.გორემიკინა, თ.რიმბაევა, ბ.ტოკტაბაევა

არაკომერციული სააქციო საზოგადოება "სემეის სამედიცინო უნივერსიტეტი", ყაზახეთი

რეაქტიული ართრიტი წარმოადგენს სახსრების ასეპტიკური ანთებით დაავადებას, რომელიც ასოცირდება ნაწლავურ, უროგენულ, ნაზოფარინგეალურ ინფექციასთან და წარმოადგენს ამ ინფექციის სისტემურ კლინიკურ გამოვლინებას. რეაქტიული ართრიტი ბავშვებში სადღეისოდაც წარმოადგენს პედიატრული რევმატოლოგიის აქტუალურ პრობლემას მისი კლინიკური გამოვლინებების მრავალფეროვნების და დიაგნოზის დასმის სიძნელის გამო. საკითხის ირგვლივ გაანალიზებულია რეტროსპექტული და თანამედროვე სამეცნიერო ლიტერატურა ბოლო 10 წლის მანძილზე, რის შედეგადაც მიმოხილვაში მოცემულია ინფორმაცია ბავშვებში ამ პათოლოგიის ეპიდემიოლოგიის, პათოფიზიოლოგიის, კლინიკური დიაგნოზის და მკურნალობის შესაძლო პერსპექტივების შესახებ. ავტორების მიერ რეკომენდებულია რეაქტიული ართრიტით დაავადებული ბავშვების შემდგომი პერსონალიზებული პედიატრიული მეთვალყურეობის ალგორითმის შემუშავება.