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Analysis of the Juvenile Idiopathic Arthritis Immunization Schedule

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Background: *The connection between vaccination and autoimmune diseases (and rheumatic pathology in particular) is still a subject of discussions. When discussing the possibility of vaccinating rheumatic patients we should take into account the ultra high dangers that infectious diseases pose for such patients, including those that can be prevented by vaccination. We should also take into account the experience of using various vaccine types in rheumatic patients, which illustrates of their high safety profile.* ***Objective:*** *Our aim was to study the immunization schedule in children with juvenile idiopathic arthritis.* ***Methods:*** *The evaluation of vaccine history and other anamnestic data in juvenile idiopathic arthritis patients was based on individual medical records (individual child's card/preventive vaccination certificate), as well as questionnaires filled by mothers.* ***Results:*** *It has been determined that a significant proportion of children with vaccination schedule deviations are juvenile idiopathic arthritis patients. Almost one in four children with a confirmed rheumatic diagnosis has not been immunized against the major vaccine-preventable diseases. In one non-vaccinated group, there was a case of juvenile arthritis onset after recovering from measles. A small number of patient mothers connects the manifestation of rheumatic diseases with vaccination.* ***Conclusion:*** *Violations of vaccination status in JIA patients require corrections according to the results of clinical studies and the recommendations of international experts.*
Key words: *juvenile idiopathic arthritis, vaccination, safety vaccination, children.*

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RATIONALE

Juvenile idiopathic arthritis (JIA) - a disease of unknown etiology, lasting more than 6 weeks, developing in children aged under 16 years, in the absence of other diseases of the joints [1, 2]. JIA is the most common chronic rheumatic disease of childhood and is characterized by inflammation of the synovial membrane of joints, destruction of joint cartilage and bone tissue, and the development of a wide range of extra-articular manifestations [1]. The chronic, relentlessly progressive course of juvenile arthritis leads to a rapid development of invalidization of patients, their life quality reduction, and social and psychological maladjustment [1, 2].

The pathogenesis of JIA still remains poorly studied. However, it is known that JIA is an autoimmune disease with a polygenic type of inheritance [3-5]. Its development depends on hereditary and environmental factors, among which the most important are a viral or mixed bacterial and viral infection, joint injuries, insolation or hypothermia [6-8]. An increase in antibody titer to bacterial peptidoglycan indicates the bacterial infection role in the development of JIA [6]. There are also data on connection of JIA debut with mycoplasma, chlamydia and intestinal infection [1, 2]. In the scientific literature there are a large number of reports on associations of antigens histocompatibility with JIA as a whole and with individual forms and variants of the disease in particular [1, 2, 7]. Identified immunogenetic markers of high risk of JIA and protective histocompatibility antigens are found in patients with JIA less often than in the population [5, 6]. There are several hypotheses to explain the relationship of infectious agents and histocompatibility antigens with the development of rheumatic diseases. The most common is the hypothesis of antigenic mimicry [1, 8].

The aim of our study was to examine the vaccination status, characteristics of vaccination and other medical history in patients with JIA.

METHODS

Study design

A transverse (cross-sectional) continuous retrospective study of vaccination status of children with JIA, complemented by a prospective interview with mothers.

Eligibility criteria

The study included data on patients with a confirmed diagnosis of juvenile idiopathic arthritis.

Terms of the study

The study was performed on the basis of rheumatological department of Scientific Center of Children's Health (Moscow). The study included data of patients hospitalized during May-November 2015. Interviews with mothers were taken in the same time period.

Sources of data and the analyzed parameters

Anamnestic data were obtained from the individual stories of child development (f. 112-u), certificates of vaccinations (f. 156/u-93), medical histories, as well as from interviews with parents of patients by means of questionnaires. The following characteristics were evaluated: vaccination status (presence or absence of vaccination, accordance to the national calendar, extra-calendar vaccinations); tolerability of vaccination (the presence of post-vaccination reactions); time connection of vaccination with the manifestation of JIA (within 7 days after vaccination with an inactivated vaccine and 28 days after vaccination with a live vaccine); a time connection of the first symptoms of JIA with the impact of other factors (a common infectious morbidity, insolation, hypothermia, stress, repeated courses of antibiotics and/or antipyretic drugs).

STATISTICAL ANALYSIS

The sample size was not calculated previously. Quantitative data are presented as median (25th, 75th percentiles).

RESULTS

Sample characteristics

The study included data on 44 patients with a confirmed diagnosis of JIA aged 1.5 to 13 years, with a median of 6.7 (4.0, 9.0) years, there were 28 (64%) girls among them. Rheumatic diseases in children has developed at an average age of 3.1 (2.0, 6.0) years. Herewith, debut of the disease before the age of under 3 years was observed in 22 (50%) patients, in the pre-school age (4-6 years) — in 14 (32%) patiens, in the primary school age (7-9 years) — in 8 (18 %) patients, and in the age of 10 years and older — a single case.

Hereditary burdeness on rheumatic diseases has been established in 6 (14%) children. Concomitant allergic pathology (asthma, food allergies) was diagnosed in 18 (41%), chronic inflammatory pathologies (chronic gastroduodenitis, peptic ulcer, ulcerative colitis) — in 8 (18%). 16 (36%) parents pointed frequent respiratory infections in children. Among the undergone infectious diseases there were chickenpox (in 10; 23%), angina (in 8; 18%), measles (in 2, 5%), acute intestinal infections (in 4, 9%).

Key findings

All the children have been vaccinated at least once in the early neonatal period with BCG-m vaccine. Hereinafter, violations in vaccination schedule according to the national calendar of preventive vaccinations, such as the unfinished scheme of primary immunization series, and the lack of age required booster doses, were observed in 32/44 (73%) children. Among the reasons of non-compliance with immunization schedules, there were deliberate parental refusal of the preventive vaccination, concomitant intercurrent infection in children, and manifestation of the underlying disease. 18 (56%) children were vaccinated with deviations from the national calendar, before the manifestation of the underlying disease; in 14 (44%) children vaccinations were postponed due to the established rheumatic pathology.

One in five patients with JIA (*n* = 10; 23%) either has not been vaccinated in their lifetime (except the BCG m vaccinations, made in a maternity hospital), or received a single dose of inactivated vaccine (DPT or hepatitis B; **Figure 1**). When clarifying the violations of vaccination status, it was found that one in five patients with JIA (*n* = 10; 23%) have not been vaccinated against measles, rubella, parotitis, and the same number of patients have not been vaccinated against polio. 10 (23%) patients were not vaccinated against pertussis, diphtheria, tetanus, or have received only one dose of vaccine, and 12 (27%) were not vaccinated against hepatitis B.

Patients vaccinated according to the national calendar of preventive vaccination (*n* = 12) received preparations of Russian production (whole-cell pertussis-diphtheria-tetanus vaccine — DPT, live parotitis-measles vaccine, rubella vaccine). Additional — extra-calendar — vaccination against Hib was made in 4 (9%) children; 2 (5%) children have once received a flu vaccine.

Additional findings

When collecting anamnestic data, tolerability of vaccination analysis was carried out (**Fig. 2**). No serious post-vaccination complications (BCGitis, anaphylactic reactions, afebrile convulsions, collaptoid reaction), which would require exemption of the subsequent boost vaccine, were registered. Most of the children (42/44; 95%) got the first vaccination (BCG m) before the JIA manifestation. In all cases of BCG m vaccination in the early neonatal period, the post-vaccination period was physiological and was not conjugated with any complications, including any in the long term.

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Fig. 1. Characteristics of violations of vaccination schedule among hospitalized patients with JIA

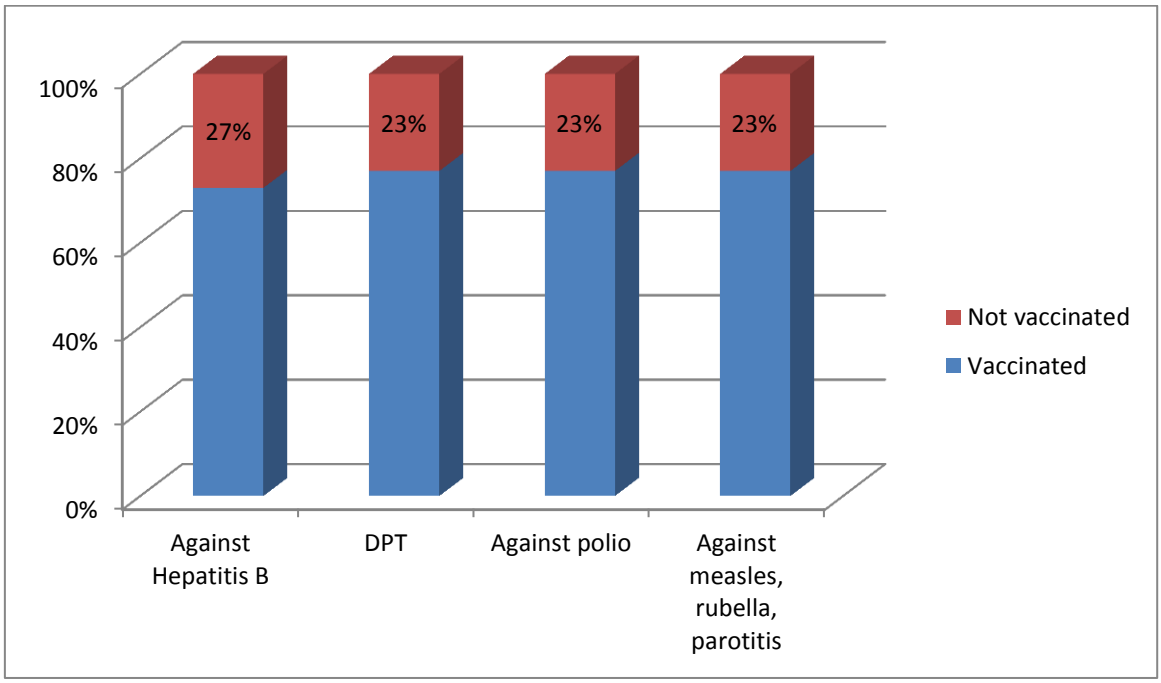


Fig. 2. The post-vaccination period curse

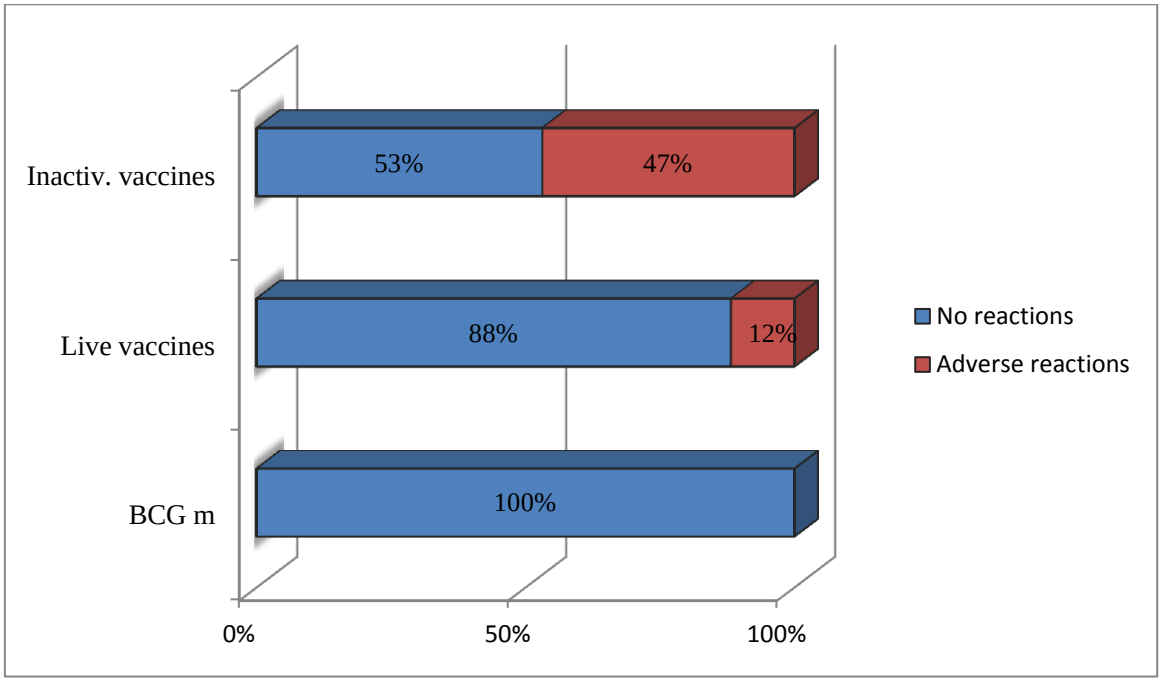
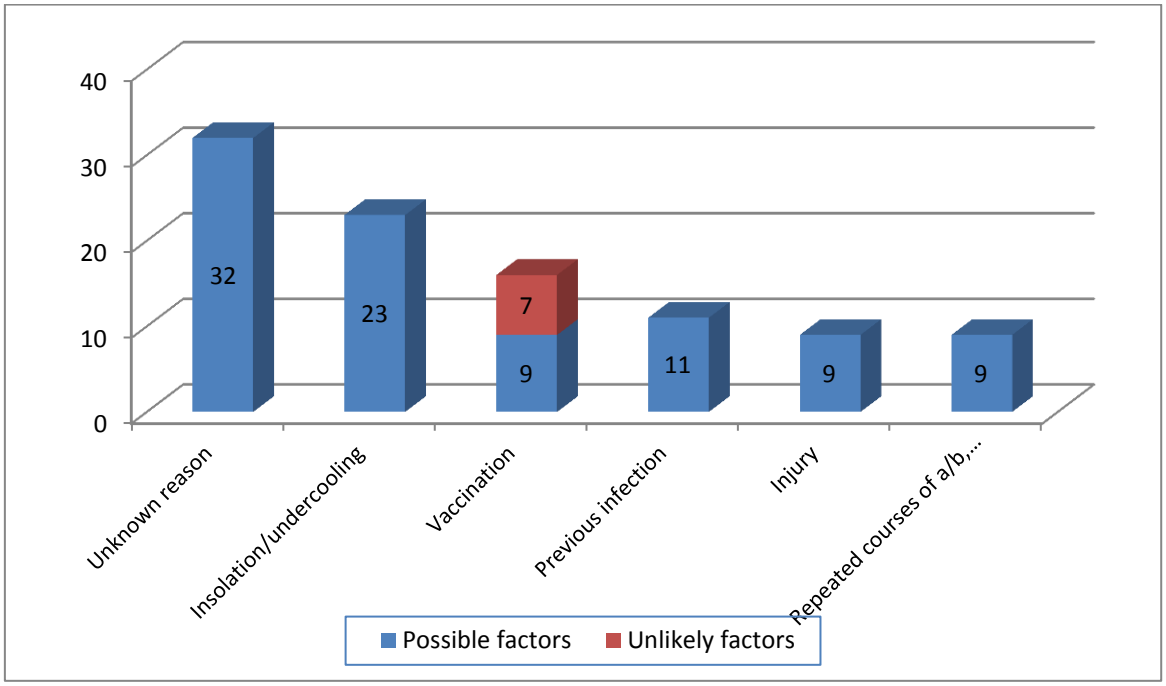


Fig. 3. Analysis of possible trigger factors of rheumatic disease development, according to the parents of patients, %



In 30 (88%) out of 34 children vaccinated with live vaccines (parotitis-measles, oral polio, rubella), the post-vaccination period was uneventful. In 4 (12%) from the same 34 vaccinated children, there was a brief moderately severe swelling of the joints, which was cupped off independently. On average, every second vaccination [20 of 42 children (48%)], with inactivated vaccines — whole-cell DPT combined with polio vaccine and a recombinant vaccine against hepatitis B) at least once was followed by the development of local or systemic reactions. All post-vaccination effects in vaccinated with inactivated vaccine patients were of mild and moderate severity, successfully ended during 3 days and did not require medical help.

Parents' interviews results

About 1/3 of the mothers (14/44; 32%) were unable to identify the factors that influenced the development of rheumatic disease (**Fig. 3**). 10 (23%) mothers pointed out a temporal connection with undercooling or excessive insolation. 7 (16%) parents considered vaccination as the triggering factor for the development of rheumatic diseases. Therefore only in 3 (7%) cases, the connection between the debut of JIA with vaccination seems possible: in 2 children for 7 days after the DPT vaccination and in 1 — in the post-vaccination period (up to 28 days) after vaccination against measles, rubella, parotitis. One mother regarded BCG m vaccination, made in the maternity hospital, as the cause of chronic disease at one year of age. In two cases, mothers could not specify with which vaccination the onset of the disease should be associated, and in what time interval after the vaccination the first symptoms of rheumatic disease appeared. Among other causes of JIA parents also indicated previous infections (5; 11%), and injuries of joints, repeated courses of antibacterial drugs and uncontrolled use of immunomodulators (4 cases, 9%).

18 (41%) adults confirmed the presence of temporal connection between previous infections with the rheumatic disease debut. Herewith it was found that in 1 patient, the JIA development was provoked within 1 month after a measles infection.

DISCUSSION

Summary of key findings

It is confirmed that the majority of patients with JIA have disrupted vaccination

schedule. Described deviations from the national immunization schedule were related both to the exemption of vaccination due to the set of the underlying disease, and to other causes prior to its occurrence.

Discussion of research results

The above characteristics of the patients in our study are confirmed with the results of the epidemiological studies carried out in different countries of the world, and pointing to the peak of the manifestation of JIA at the age of the first 3 years of life. [9]

The value of genetic factor in the etiology of rheumatic diseases is currently regarded as the leading. However, during the history taking from the parents of patients, most of them denied the hereditary burdeness for autoimmune diseases. We believe these data are unreliable, because, as a rule, young parents are not sufficiently aware of the various types of autoimmune diseases. In addition, according to the results of the family analysis, it was found that there are elevated levels of antibodies against its own tissues, and other abnormalities, indicating the propensity to autoimmune processes in children, even in the absence of the disease in their nearer relations [10].

From our point of view, it was important to find out the parents, whose children were later rheumatology department patients, attitude to previous vaccination, because until now there is an erroneous opinion that one of the primary reasons for the development of autoimmune diseases is vaccination among the population.

Connection between vaccination and the development of JIA

Although the possible connection between vaccination and autoimmune disease cannot be completely ruled out currently, but numerous epidemiological studies, including large-scale, ongoing for decades, do not support this hypothesis, and cast doubt on the degree of causality of immunization [11-13].

In June 2006, the Global Advisory Committee on Vaccine Safety (GACVS), established by the World Health Organization (WHO), addressed the issue of the connection between vaccination against hepatitis B and rheumatoid arthritis [12]. A thorough review of the literature containing references to cases of a possible association between hepatitis B and rheumatoid arthritis, as well as of the results of published studies, was carried out preliminarily. In the meeting's conclusion, published on the WHO website, it was stated that "the examined facts do not permit to make a convincing conclusion supporting a connection between hepatitis B vaccination and rheumatoid arthritis" [12]. In particular, they took into account the data of the largest study carried out in the USA (vaccine safety database project ― Vaccine Safety Datalink, VSD), which included a significant number of patients with rheumatoid arthritis, and only few of them have been previously vaccinated against hepatitis B [12, 14]. According to this data, any impact of vaccination against hepatitis B on the total incidence of rheumatoid arthritis can be considered marginal.

In extremely rare cases, vaccination can cause the development of Guillain-Barre syndrome, which has an autoimmune mechanism of development as a basis [12, 15]. In general, studies prove the absence of a causal relationship between vaccination and the formation of rheumatic diseases [13].

Given that the proportion of patients in our study were not vaccinated against socially significant severe infectious diseases, these children are not only at the group of high risk of contamination and complicated course of viral infections, but also are a danger in the form of the source of unfavorable epidemiological situation in the society.

Vaccination of patients with rheumatic diseases

In modern rheumatology, comorbid infections have significant influence on the course of rheumatic diseases, including JIA, and its outcomes [13-17]. The significance of the problem has increased substantially with the introduction in clinical practice of a new therapeutic option ―

genetically engineered biological preparations (GEBP), the effect of which is directed to various parts of the pathogenesis of autoimmune diseases [13, 18, 19]. Extensive clinical experience in the use of GEBP, accumulated in recent years, evidences of association between the use of this group of drugs and the risk of two or more chronic diseases. Each case requires the cancel of antirheumatic therapy, which in turn leads to an exacerbation of joint disease. In patients with rheumatoid arthritis, the incidence of comorbid infections is 1.5-2 times higher than in the population [18, 19]. In this regard, timely vaccination of this group of patients is seen as the only effective preventive measure.

Recommendations of the European League Against Rheumatism (EULAR) [18], the American College of Rheumatology (ACR) [20], and the Infectious Diseases Society of America (IDSA) [21] provide information on rules and procedures of vaccination of patients with rheumatic diseases. However, some clinicians still treat autoimmune diseases as contraindications for vaccination. A study carried out in France and the UK, showed a relatively low level of coverage with vaccination against influenza and pneumococcal disease of patients with rheumatoid disease — 28 and 37%, respectively [22]. According to the results of the international cross-sectional study, devoted to comorbid conditions in rheumatic diseases COMORA and included more than 4500 patients with JIA, vaccination figures were even lower — 25 and 17%, respectively [18].

Numerous data on the absence of negative impact of vaccination on the course of rheumatic disease is presented in the scientific literature [4, 6, 13]. On the contrary, the results of a significant number of clinical studies have shown the effectiveness and safety of vaccination aimed at preventing infectious diseases, significant in case of rheumatic pathologies [13, 16, 17]. Authors suggest the possibility of carrying out (if necessary) the immunization against the background of minimal doses of immunosuppressive therapy and non-steroidal anti-inflammatory drugs during remission of the disease lowest activity [4].

The analysis of post-vaccination period, evaluated by the parents of our patients, showed characteristics of the safety of immunizing agents that are comparable with the average. The frequency of adverse reactions in children with JIA is comparable to that in the general population of vaccinated children, which is confirmed by a number of clinical observations [23-25]. A similar study was carried out by our colleagues from Nizhny Novgorod in 2006 [26]. In 138 children with rheumatic diseases, which were at a cardiorheumatologist's clinical account, no connection of the disease with vaccination against hepatitis B has been established according to evaluation of immunization history data. In the majority of patients vaccinated before the disease manifestation, the post-vaccination period was uneventful; only in 1 case, the child had symptoms of juvenile rheumatoid arthritis in 2 weeks after the second vaccination. This work also shows that only in 2 children from 137, rheumatic disease manifested in 14 days after administration of measles vaccine, and in 1 patient out of 135 children with rheumatic disorders — immediately after re-vaccination with DPT and oral polio vaccine. In addition, the safety of vaccination, conducted in patients already diagnosed with a rheumatoid disease, was evaluated. In 21% of children vaccinated against measles, no exacerbations of articular syndrome were fixed.

In a study of A.A. Tarasova and M.P. Kostinov, the efficacy and safety of vaccination with pneumococcal polysaccharide vaccine of children with various forms of rheumatic diseases, were evaluated [27]. It was shown that specific immunization against pneumococcal infection of rheumatic patients is accompanied by synthesis of antibodies and does not cause deterioration of the disease.

Another study carried out in St. Petersburg, testifies the safety of vaccination against diphtheria and tetanus among patients with rheumatic diseases [28]. Post-vaccination period was uneventful in 77% (n = 60), and follow-up monitoring of vaccinated within 1-3 years have not shown either any deterioration in the underlying disease or increased incidence of respiratory pathology.

The safety of live attenuated vaccines in patients with rheumatoid diseases, such as measles vaccine, is demonstrated in a study of S.M. Harith [29]. The possibility of specific prophylaxis of varicella and yellow fever in these patients was confirmed in a study of C.A. Silva et al. from Brazil [30].

Limitations of the study

Limitations of the study should include a small sample of patients with JIA, the scope of which was limited by the low incidence of this disease. Unfortunately, the lack of guidance on post-vaccination reactions in the majority of medical records does not allow to evaluate objectively the temporal relationship of vaccination with manifestation of JIA. This indicates the need to improve the system of monitoring of post-vaccination reactions and complications, as well as to revisal of vaccination documentation samples.

CONCLUSION

It has been established that the predominant majority of patients with JIA requires correction of the disturbed vaccination schedule. It is necessary to include in the individual vaccination plan for such children additional vaccines against the most significant comorbid infections, such as pneumococcal and influenza, along with the universal immunization in accordance with the National calendar of preventive vaccinations. Vaccination should be planned at a minimum activity of autoimmune inflammatory process, prior to the appointment of monoclonal antibody therapy. If necessary, it is recommended to prescribe anti-inflammatory therapy for 10-15 days before vaccination and during 3 weeks after it for patients with unstable JIA remission. Immunization with attenuated vaccines against measles and chicken pox is not contraindicated; inactivated polio vaccine should be used instead of the oral polio vaccine.

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Not specified.

CONFLICT OF INTEREST

The authors declared they have no competing interests to disclose.

REFERENCES

1. Алексеева Е.И., Литвицкий П.Ф. *Ювенильный ревматоидный артрит. Этиология. Патогенез. Клиника. Алгоритмы диагностики и лечения. Руководство для врачей, преподавателей, научных сотрудников* / Под общей ред. А.А. Баранова. — М.; 2007. — С. 325–339. [Alexeeva EI, Litvitskii PF. *Yuvenil'nyi revmatoidnyi artrit. Etiologiya. Patogenez. Klinika. Algoritmy diagnostiki i lecheniya. Rukovodstvo dlya vrachei, prepodavatelei, nauchnykh sotrudnikov*. Ed by A.A. Baranov. Moscow; 2007. p. 325–339. (In Russ).]
2. Cassidy JT, Petty RE. *Juvenile idiopathic arthritis. Textbook of pediatric rheumatology*. 5th ed. Philadelphia: WB Saunders; 2005. p. 210–220.
3. Ogilvie EM, Khan A, Hubank M, et al. Specific gene expression profiles in systemic juvenile idiopathic arthritis. *Arthritis Rheum.* 2007;56(6):1954–1965. doi: 10.1002/art.22644.

4. Kuijk LM, Hoffman HL, Neven B, Frenkel J. *Episodic autoinflammatory disorders in children*. In: Cimas R, Lehman T, editors. *Handbook of systemic autoimmune disease*. Elsevier; 2008. V.6. p. 119–135.
5. Ling X, Park JL, Carroll T, et al. Plasma profiles in active systemic juvenile idiopathic arthritis: biomarkers and biological implications. *Proteomics*. 2010;10(24):4415–4430. doi: 10.1002/pmic.201000298.
6. Masters SL, Simon A, Aksentijevich I, Kastner DL. Horror autoinflammaticus: the molecular pathophysiology of autoinflammatory disease (*). *Annu Rev Immunol*. 2009;27:621–668. doi: 10.1146/annurev.immunol.25.022106.141627.
7. Mellins ED, Macaubas C, Grom AA. Pathogenesis of systemic juvenile idiopathic arthritis: some answers, more questions. *Nat Rev Rheumatol*. 2011;7(7):416–426. doi: 10.1038/nrrheum.2011.68.
8. Prakken B, Albani S, Martini A. Juvenile idiopathic arthritis. *Lancet*. 2011;377(9783):2138–2149. doi: 10.1016/S0140-6736(11)60244-4.
9. Oberle EJ, Harris JG, Verbsky JW. Polyarticular juvenile idiopathic arthritis - epidemiology and management approaches. *Clin Epidemiol*. 2014;6:379–393. doi: 10.2147/CLEP.S53168.
10. Ярилин А.А. *Основы иммунологии. Учебник*. — М.: Медицина; 1999. — 608 с. [Yarilin AA. *Osnovy immunologii. Uchebnik*. Moscow: Meditsina; 1999. 608 p. (In Russ).]
11. Костинов М.П., Тарасова А.А. *Вакцинопрофилактика пневмококковой инфекции и гриппа при аутоиммунных заболеваниях. Руководство для врачей*. — М.: МДВ; 2009. —252 с. [Kostinov MP, Tarasova AA. *Vaktsinoprofilaktika pnevmokokkovoi infektsii i grippa pri autoimmunnykh zabolevaniyakh. Rukovodstvo dlya vrachei*. Moscow: MDV; 2009. 252 p. (In Russ).]
12. Lee K, Hall AJ. *Executive summary of report on hepatitis B vaccine and putative associations with arthritis and chronic fatigue syndrome. Reports WHO*. London; 2008.
13. Белов Б.С., Наумцева М.С., Тарасова Г.М., Полянская М.В. Вакцинация в ревматологии: современные аспекты // *Научно-практическая ревматология.* — 2014. — Т.52. — №6. — С. 660–668. [Belov BS, Naumtseva MS, Tarasova GM, Polyanskaya MV. Vaccination in rheumatology: Current aspects. *Science-practical rheumatology*. 2014;52(6):660–668. (In Russ).]
14. Current awareness. *Pharmacoepidemiol Drug Saf*. 2001;10(5):467–482. doi: 10.1002/pds.550.
15. Maglione MA, Gidengil C, Das L, et al. *Safety of vaccines used for routine immunization in the United States. Evidence Report/Technology Assessment No. 215* [Internet]. (Prepared by the Southern California Evidence-based Practice Center under Contract No. 290-2007-

10062-I.) AHRQ Publication No. 14-E002-EF. Rockville, MD: Agency for Healthcare Research and Quality; 2014 [cited 2016 Jun 21]. Available from: http://effectivehealthcare.ahrq.gov/ehc/products/468/1930/vaccine-safety-report-140701.pdf.

16. Белов Б.С., Балабанова Р.М., Манукян С.Г., и др. *Коморбидные инфекции при ревматических заболеваниях / Тезисы доклада международной конференции ревматологов*. — Чимкент; 2006. — С. 17. [Belov BS, Balabanova RM, Manukyan SG, et al. *Komorbidnye infektsii pri revmaticheskikh zabolevaniyakh*. In: (Conference proceedings) *Tezisy doklada mezhdunarodnoi konferentsii revmatologov*. Chimkent; 2006. p. 17. (In Russ).]
17. Wolfe F, Mitchell DM, Sibley JT, et al. The mortality of rheumatoid arthritis. *Arthritis Rheum.* 1994;37(4):481–494. doi: 10.1002/art.1780370408.
18. Dougados M, Soubrier M, Antunez A, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). *Ann Rheum Dis.* 2014;73(1):62–68. doi: 10.1136/annrheumdis-2013-204223.
19. van Assen S, Agmon-Levin N, Elkayam O, et al. EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. *Ann Rheum Dis.* 2011;70(3):414–422. doi: 10.1136/ard.2010.137216.
20. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. *Arthritis Care Res (Hoboken).* 2012;64(5):625–639. doi: 10.1002/acr.21641.
21. Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis.* 2014;58(3):e44–100. doi: 10.1093/cid/cit684.
22. Lawson EF, Trupin L, Yelin EH, Yazdany J. Reasons for failure to receive pneumococcal and influenza vaccinations among immunosuppressed patients with systemic lupus erythematosus. *Semin Arthritis Rheum.* 2015;44(6):666–671. doi: 10.1016/j.semarthrit.2015.01.002.
23. Вакцины для профилактики коклюша (Позиция ВОЗ) // *Педиатрическая фармакология.* — 2008. — Т.5. — №1. — С. 91–94. [Vaccines for pertussis prevention (WHO position). (editorial) *Pediatric pharmacology*. 2008;5(1):91–94. (In Russ).]
24. Лакоткина Е.А., Харит С.М., Черняева Т.В., Брусов Н.К. *Поствакцинальные осложнения (клиника, диагностика, лечение, профилактика). Пособие для практического врача*. — СПб.; 2002. — 82 с. [Lakotkina EA, Kharit SM, Chernyaeva

TV, Brusov NK. *Postvaktsinal'nye oslozhneniya (klinika, diagnostika, lechenie, profilaktika). Posobie dlya prakticheskogo vracha*. St. Petersburg; 2002. 82 p. (In Russ).]

25. Institute of Medicine. *Adverse events associated with childhood vaccine*. Washington: National Academy Press; 1994. 65 p.
26. Тарасова А.А. *Состояние специфического иммунитета у детей с иммунопатологическими заболеваниями, вакцинированных в рамках календаря прививок, и клинико-иммунологический эффект бактериальной и гриппозной вакцин*: автореф. дис… докт. мед. наук. — Н. Новгород; 2006. — 46 с. [Tarasova AA. *Sostoyanie spetsificheskogo immuniteta u detei s immunopatologicheskimi zabolevaniyami, vaktsinirovannykh v ramkakh kalendarya privivok, i kliniko-immunologicheskii effekt bakterial'noi i grippoznoi vaktsin*. [dissertation abstract] N. Novgorod; 2006. 46 p. (In Russ).]
27. Тарасова А.А., Костинов М.П., Коровкина Т.И., и др. Иммунологическая эффективность и безопасность вакцинации против пневмококковой инфекции у детей с ревматическими заболеваниями // *Педиатрия. Журнал им. Г.Н.* Сперанского. — 2015. — Т.94. — №2. — С. 110–115. [Tarasova AA, Kostinov MP, Korovkina TI, et al. Immunological efficacy and safety of vaccination against pneumococcal infection in children with rheumatic diseases. *Pediatriia*. 2015;94(2):110–115. (In Russ).]
28. Кощеева Ю.В., Харит С.М., Калинина Н.М., и др. *Особенности поствакцинального противодифтерийного иммунитета у детей с ревматическими заболеваниями* / *Сб. материалов по конференции: «Дни иммунологии»*. — СПб.; 1999. — С. 67–68. [Koshcheeva YuV, Kharit SM, Kalinina NM, et al. *Osobennosti postvaktsinal'nogo protivodifteriinogo immuniteta u detei s revmaticheskimi zabolevaniyami*. In: (Conference proceedings) *Sb. materialov po konferentsii: «Dni immunologii»*. St. Petersburg; 1999. p. 67–68. (In Russ).]
29. Харит С.М. *Клинико-иммунологическая характеристика вакцинального процесса у детей с иммунопатологическими заболеваниями и поражением нервной системы*: автореф. дис. …докт. мед. наук. — СПб.; 2002. — 42 с. [Kharit SM. *Kliniko-immunologicheskaya kharakteristika vaktsinal'nogo protsessa u detei s immunopatologicheskimi zabolevaniyami i porazheniem nervnoi sistemy*. [dissertation abstract] St. Petersburg; 2002. 42 p. (In Russ).]
30. Silva CA, Terreri MT, Aikawa NE, et al. Pratica de vacinao em criancas com doencas reumaticas. *Rev Bras Reumatol.* 2010;50(4):351–361. doi: 10.1590/s0482-50042010000400002.