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DYNAMICS OF FORMATION OF ANTIBODIES TO SARS-CoV-2 AFTER CORONAVIRUS INFECTION IN CHILDREN

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ДИНАМИКА ОБРАЗОВАНИЯ АНТИТЕЛ К SARS-CoV-2 ПОСЛЕ ПЕРЕНЕСЕННОЙ КОРОНАВИРУСНОЙ ИНФЕКЦИИ У ДЕТЕЙ

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Objective. To estimate the level of antibodies to SARS-CoV-2-IgM and SARS-CoV-2-IgG in children with COVID-19 in acute period and during 1 year period of follow-up after coronavirus infection.
Materials and methods. Blood samples for the presence of IgM and IgG antibodies to SARS-CoV-2 were analyzed in 119 children aged 11.0 [10.1; 11.2] with COVID-19 in the acute period (29.4 % asymptomatic, 51.3 % mild and 19.3 % moderate), and SARS–CoV-2-IgG in the dynamics of the follow-up after 1 (*n*=55), 6 (*n*=33) and 12 (*n*=32) months from the moment of discharge from the hospital in a prospective cohort study. The levels of SARS-CoV-2 surface glycoprotein S, including the receptor-binding domain – RBD were measured at different time by using enzyme-linked immunosorbent assay.
Results. The level of IgM positive rate for SARS-CoV-2 was initially negative in 86.6 % of children with COVID-19. The original seroconversion (on admission to the hospital) was 38.7 % and it increased to 96.7 % in 1 month and to 100 % in 12 months of observation. There were no statistically significant differences in IgG persistence depending on the age and course of COVID-19.
Conclusions. The new coronavirus infection causes a long-term response of IgG antibodies to SARS-CoV-2 which persists for one year of observation and increases by 12 months after the infection regardless of the severity of COVID-19.
Key words. COVID-19, new coronavirus infection, SARS-CoV-2, IgG and IgM antibodies, children.

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Цель. Оценить уровень антител SARS-CoV-2-IgM и SARS-CoV-2-IgG у детей с COVID-19 в острый период и на протяжении одного года наблюдения после перенесенной коронавирусной инфекции.

Материалы и методы. В проспективном когортном исследовании проанализированы образцы крови на наличие антител класса IgM и IgG к SARS-CoV-2 от 119 детей в возрасте 11 [10,1; 11,2] лет с COVID-19 в остром периоде (29,4 % бессимптомная, 51,3 % – легкая и 19,3 % среднетяжелая форма), а также определены SARS-CoV-2-IgG в динамике наблюдения за пациентами через один ($n = 55$), 6 ($n = 33$) и 12 ($n = 32$) месяцев от момента выписки из стационара. Уровни поверхностного гликопротеина S SARS-CoV-2, включая рецептор-связывающий домен – RBD, измерялись в различные моменты времени с помощью иммуноферментного анализа.

Результаты. Уровень коэффициента позитивности IgM на SARS-CoV-2 изначально оказался отрицательным у 86,6 % детей с COVID-19. Исходная (на момент поступления в стационар) сероконверсия составила 38,7 %, которая увеличилась до 96,7 % через месяц и до 100 % через 12 месяцев соответствующего последующего наблюдения. Не обнаружено статистически значимых различий в отношении персистенции IgG в зависимости от возраста и степени тяжести COVID-19.

Выводы. Коронавирусная инфекция вызывает длительный ответ антител класса IgG к SARS-CoV-2, который сохраняется на протяжении года наблюдения и усиливается к 12 месяцам после инфекции независимо от степени тяжести COVID-19.

Ключевые слова. COVID-19, коронавирусная инфекция, SARS-CoV-2, антитела IgG и IgM, дети.

INTRODUCTION

The novel human coronavirus SARS-CoV-2 is highly contagious, and the disease it causes, COVID-19, can lead to significant morbidity and mortality in some patients [1]. In children, SARS-CoV-2 infection is asymptomatic or mild; however, children are susceptible to severe COVID-19 manifestations and the associated post-infectious multisystem inflammatory syndrome [2]. Moreover, the severity of COVID-19 is associated with the host's immune response against SARS-CoV-2, and children and adolescents with mild or asymptomatic coronavirus infection can produce a strong and persistent antibody response [3].

Laboratory methods for diagnosing SARS-CoV-2 are based on the detection of viral RNA in patient secretions using the polymerase chain reaction (PCR) method and of antibodies (immunoglobulins M and G) in blood serum [4].

The immune response against SARS-CoV-2 plays a critical role in determining clinical outcome in adults and children [5]. Immunity to SARS-CoV-2 induced by natural infection may be mediated by a combination of humoral and cellular immunity [6]. A study comparing children to adults revealed different immune profiles during coronavirus infection, indicating less severe outcomes in pediatric patients [7].

Immune protective factors against SARS-CoV-2 have not been identified, although neutralizing antibodies are increasingly recognized as major mediators of protection [8].

Studies of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome showed that virus-specific antibodies were detected in 80 %–100 % of patients 2 weeks after symptom onset [9; 10].

Most adults with coronavirus infection produce an IgG response that can persist for at least 12 months [11]. Recovered seropositive adults have up to 89 % protection against reinfection with the same strain [12]. In contrast, the proportion of children infected with

SARS-CoV-2 with seroconvertion is unknown, particularly among patients with asymptomatic or mild COVID-19. Furthermore, children may have distinct immune responses that modulate clinical severity [7]. Additionally, preexisting antibodies to seasonal human coronaviruses may contribute to some level of protection against SARS-CoV-2 in children [13]. Several innate and adaptive immune response aspects in children are not yet fully characterized owing to the limited number of studies in this population. The humoral response to SARS-CoV-2 remains poorly understood, whereas the immunological response to vaccines is well described in clinical trials, the characteristics and persistence of seroconversion are unclear, and follow-up data on IgG levels after COVID-19 are limited.

This study aimed to assess the level of SARS-CoV-2-IgM and SARS-CoV-2-IgG in pediatric patients with COVID-19 in the acute period and during 1-year follow-up after coronavirus infection.

MATERIALS AND METHODS

The prospective cohort study involved 119 children with COVID-19 from the City Clinical Hospital No. 1 of Chita, which at the time of the work was the single hospital accepting patients with coronavirus infection in the Trans-Baikal Territory.

Government authorities have taken preventive measures and given recommendations for the hospitalization of all pediatric patients with COVID-19, including asymptomatic forms to maintain social distance between people and prevent the spread of the SARS-CoV-2 virus.

Inclusion criteria were age 0–17 years, positive result for SARS-CoV-2, and parent/child consent to participate in the study. Non-inclusion criteria were children aged >17 years, negative test result for SARS-CoV-2, and refusal of parents (legal representatives) or children to participate in the study.

The diagnosis of COVID-19 is based on the criteria according to the methodological recommendations “Aspects of clinical manifestations and treatment of the disease caused by a new coronavirus infection (COVID-19) in pediatric patients” (version 1 dated April 24, 2020).

Demographic data, information about positive PCR tests for SARS-COV-2, medical history, comorbidities, and heredity were obtained from the electronic database of medical records.

All cases were confirmed by PCR using nasal and oropharyngeal swabs. During the study period, children and adolescents were not vaccinated against COVID-19. No reinfections were recorded during the follow-up period.

The severity of coronavirus infection was classified as asymptomatic but with a positive test for SARS-CoV-2 in 35 (29.4 %) pediatric patients (group I), as mild in 61 (51.3 %) pediatric patients (group II), and moderate in 23 (19.3 %) patients (group III). The median age of the pediatric patients was 11 (10.1; 11.2) years old; 53.8 % of those examined were boys. Additionally, children were distributed by age (subgroup 1, 0–6 years (n = 21); subgroup 2, 7–17 years (n = 98)).

To analyze the intensity of humoral immunity after coronavirus infection, SARS-

CoV-2-IgG was determined by monitoring patients 1 month (n = 55), 6 months (n = 33), and 12 (n = 32) months after discharge from the hospital.

Blood samples were collected within 48 hours of hospitalization from all 119 pediatric patients and tested for the presence of IgM and IgG antibodies to the surface glycoprotein S of SARS-CoV-2, including the receptor-binding domain (RBD) in the blood serum. The study was conducted using an enzyme immunoassay with a set of reagents SARS-CoV-2-IgM-ELISA-BEST and SARS-CoV-2-IgG-ELISA-BEST (Vector-Best, Novosibirsk region) according to manufacturer instructions. Antibody levels were expressed in S/CO (Signal/Cut-off) as signal/critical value: positive, results higher than 1.1 S/CO; questionable, those higher than 0.8 S/CO and lower than 1.1 S/CO; and negative, results lower than 0.8 S/CO.

Written voluntary informed consent to participate in the study was obtained from participants aged >15 years or from parents (legal representatives) of pediatric patients aged <15 years.

The study was approved by the local ethics committee of the Chita State Medical Academy (protocol no. 101; April 15, 2020) and was conducted in accordance with the Declaration of Helsinki.

Statistical processing of the research results was performed using IBM SPSS Statistics Version 25.0 software (International Business Machines Corporation, USA). The normality of distribution was tested using the Kolmogorov–Smirnov test. Quantitative variables were presented as median (Me) and interquartile range (Q_1; Q_3) and categorical variables as absolute values and percentages (%). The assessment of variations in the levels of the studied markers in the blood serum between two independent groups was performed using the Mann–Whitney test (U). Intergroup differences in one quantitative sign for comparisons of three or more independent groups were analyzed using the Kruskal–Wallis rank analysis of variance (H). The significant differences in pairwise comparisons between dependent samples were assessed using the Wilcoxon test. $P < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

Serological testing for SARS-CoV-2 upon hospital admission demonstrated a lack of IgM antibody response in pediatric patients with COVID-19 in majority (86.6 %) of cases (Table 1).

Positive test results for IgM antibodies to the surface glycoprotein S (Spike) of SARS-CoV-2 in the blood serum were detected in 6.7 % of patients with confirmed SARS-CoV-2 infection, whereas 4.3 % of them were asymptomatic and 4.9 % and 11.4 % of patients had a mild and moderate form of the disease, respectively.

The seroprevalence (positive IgG antibodies to SARS-CoV-2) at the time of hospitalization was 38.7 %. Additionally, 56.3 % of patients with positive PCR for SARS-CoV-2 did not have IgG antibodies, and questionable results were recorded in 5 % of pediatric patients. It was revealed that 34.8 % of patients in group 1, 40.9 % of patients in group 2, and 37.1 % of pediatric patients in group 3 tested positive for SARS-CoV-2-IgG.

Table 1

Level of positivity rate of SARS-CoV-2-IgM and SARS-CoV-2-IgG depending on the severity of COVID-19 in pediatric patients of different ages upon admission

COVID-19 severity	IgM PC* level, *n*/ %			IgG PC level, *n*/ %		
	Negative < 0.8 S/CO	Questionable ≥ 0.8 and < 1.1 S/CO	Positive > 1.1 S/CO	Negative < 0.8 S/CO	Questionable ≥ 0.8 and < 1.1 S/CO	Positive > 1.1 S/CO
Asymptomatic, *n* = 23	19/82.6	3/13	1/4.3	15/65.2	0/0	8/34.8
Mild, *n* = 61	54/88.5	4/6.6	3/4.9	35/57.4	1/1.6	25/40.9
Moderate, *n* = 35	30/85.7	1/2.9	4/11.4	17/48.6	5/14.3	13/37.1
Total, *n* = 119	103/86.6	8/6.7	8/6.7	67/56.3	6/5.0	46/38.7

Note: *, level of positivity coefficient (PC).

The median level of SARS-CoV-2-IgM in asymptomatic coronavirus infection was 0.37 [0.35; 0.55] S/CO and corresponded to the values for mild (0.27 [0.27; 0.56] S/CO; $p = 0.533$) and moderate (0.28 [0.27; 0.73] S/CO; $p = 0.661$) severity of COVID-19. The asymptomatic course of SARS-COV-2 infection was characterized by a serum IgG concentration of 0.41 [0.39; 2.86] and did not differ from the indicators for mild (0.49 [0.37, 2.99] S/CO; $p = 0.439$) and moderate (0.75 [1.76, 3.14] S/ CO; $p = 0.551$) forms. No statistical difference was found in the IgM and IgG levels between patients of groups II and III ($p = 0.734$ and $p = 0.894$ S/CO, respectively).

Table 2 presents the antibody titers used depending on the coronavirus infection severity in pediatric patients of different ages. The study results showed an increase in the titer of IgG antibodies to SARS-CoV-2 in patients aged 0–6 years with moderate COVID-19 compared to that in asymptomatic patients and those with mild forms of the disease, whereas no significant differences were noted in the levels of antibodies of the IgM and IgG classes depending on the age of the pediatric patients and disease severity ($p > 0.05$). Because no significant differences were observed in IgM and IgG levels between pediatric patients of different ages, further dynamic follow-up of the study groups was performed among pediatric patients aged 0–17 years.

Median level of SARS-CoV-2-IgG during dynamic follow-up 1 month after coronavirus infection was 9.55 [8.15; 10.90], which is significantly higher by 12 times than similar data in the acute period (0.81 [0.79, 3.74]; $p = 0.000$). By month 6 from the date of discharge from the hospital, the IgG level to SARS-CoV-2 was 10.38 [8.97; 10.25], which is significantly higher than that in the initial study (0.92 [0.87, 2.48]; $p = 0.000$).

The proportion of seropositive patients (IgG to SARS-CoV-2) reached its maximum (100 %) values of 10.12 [8.63; 10.34] when determined after 12 months, compared to the results obtained 1 month and 6 months after coronavirus infection (96.4 % and 96.9 %, respectively; Table 3).

Table 2

Antibody titers upon admission depending on the severity of coronavirus infection in pediatric patients of different ages

Ig (S/CO)	Study group						Test statistics		
	I, $n = 23$		II, $n = 61$		III, $n = 35$				
	0–6 years, $n = 7$	7–17 years, $n = 16$	0–6 years, $n = 7$	7–17 years, $n = 54$	0–6 years, $n = 7$	7–17 years, $n = 28$	Kruskal–Wallis, $df = 3$	Mann–Whitney	
								Intragroup comparison	Comparison of subgroups studied
	1	2	3	4	5	6			
IgM	0.49 [0.40; 0.65]	0.30 [0.30; 0.55]	0.27 [0.,27; 0.54]	0.27 [0.27; 0.58]	0.50 [0.50; 1.28]	0.28 [0.28; 0.67]	$U = 3.45$; $p = 0.632$	$U_{1-2} = 43.5$, $p_{1-2} = 0.402$; $U_{3-4} = 185.5$, $p_{3-4} = 0.937$; $U_{5-6} = 65.0$, $p_{5-6} = 0.172$	$U_{1-3} = 20.0$, $p_{1-3} = 0.562$; $U_{1-5} = 21.5$, $p_{1-5} = 0.701$; $U_{3-5} = 18.0$, $p_{3-5} = 0.404$; $U_{2-4} = 427.5$, $p_{2-4} = 0.950$; $U_{2-6} = 216.0$, $p_{2-6} = 0.845$; $U_{4-6} = 739.0$, $p_{4-6} = 0.868$
IgG	0.44 [0.44; 4.08]	0.37 [0.36; 2.85]	0.31 [0.30; 1.68]	0.49 [0.49; 3.23]	3.30 [3.20; 8.35]	0.69 [0.67; 2.13]	$U = 3.90$; $p = 0.564$	$U_{1-2} = 46.5$, $p_{1-2} = 0.524$; $U_{3-4} = 151.5$, $p_{3-4} = 0.396$; $U_{5-6} = 62.5$, $p_{5-6} = 0.143$	$U_{1-3} = 20.0$, $p_{1-3} = 0.564$; $U_{1-5} = 16.0$, $p_{1-5} = 0.277$; $U_{3-5} = 15.0$, $p_{3-5} = 0.225$; $U_{2-4} = 363.0$, $p_{2-4} = 0.334$; $U_{2-6} = 211.5$, $p_{2-6} = 0.760$; $U_{4-6} = 696.0$, $p_{4-6} = 0.557$

Table 3

Dynamics of SARS-CoV-2-IgG antibody titer in pediatric patients after COVID-19

Post-COVID term	IgG PC level, n/%		
	Negative < 0.8 S/CO	Questionable ≥0.8 and < 1.1 S/CO	Positive > 1.1 S/CO
1 month, $n = 55$	2/3.6	0/0	53/96.4
6 months, $n = 33$	1/3,0	0/0	32/96.9
12 months, $n = 32$	0/0	0/0	32/100.0

Serological testing for COVID-19 demonstrated IgG seroconversion in all pediatric patients after 12-month follow-up, including asymptomatic patients, and in the acute period of the disease, SARS-CoV-2-IgG was recorded in 38.7 %.

IgM provides the first line of defense in viral infections, whereas IgG production lags behind IgM and is responsible for long-term immunity and memory [14]. According to a previous report on SARS in 2003, IgM was detected in the blood of patients 3–6 days after disease onset, and IgG could be detected 8 days after the onset of infection [15]. Other studies [16; 17] on seropositivity for antibodies to SARS-CoV-2 in pediatric patients reported lower rates than those detected in this study. Thus, in a meta-analysis, Rostami et al. revealed that the prevalence of antibodies to SARS-CoV-2 in the population aged <19 years was 2.3 % [16]. According to the Spanish national registry, seropositivity for SARS-CoV-2 was registered in 12.5 % of adults and 7.7 % of children [17]. The present study showed that the level of anti-SARS-CoV-2-IgG at the time of hospitalization is already relatively high (38.7 %), which is consistent with a previous study that found an early and high level of IgG response against SARS-CoV-2 [18]. The high incidence of positive IgG in the early stage of SARS-CoV-2 infection may be due to the fact that some patients with COVID-19 are asymptomatic in the first days after infection [19]. A study showed that in 97.5 % of people, symptoms appear within 11.5 days [20]. The recorded date of disease onset may be later than the date of infection because of the asymptomatic course, which explains the high level of IgG during week 1 of illness [21].

The long-term immune response of SARS-CoV-2, demonstrated during the dynamic follow-up of pediatric patients who had coronavirus infection in our study, coincides with that of the coronavirus associated with SARS-CoV [22]. The researchers reported that IgG antibodies were continuously detected for 2 years in patients who recovered from SARS-CoV [23].

Additionally, previous studies confirm our findings of high IgG positivity rate for SARS-CoV-2 [21; 24; 25]. Thus, IgG antibody titers remained elevated against protein S and RBD in 96 % and 99 % of cases, respectively [24]. In 95.3 % of patients included in the study by Li, IgG against SARS-CoV-2 was detected 5 weeks after symptom onset [21]. Iyer et al. examined 343 patients and showed that IgG persisted for 90 days after symptom onset [25]. Moreover, Zhu et al. reported that over 60 % of adults remained IgG positive 7 months after symptom onset, regardless of COVID-19 severity [26]. In the study by Whitcombe, 96 % of patients had anti-S protein IgG levels above baseline 4–8 months after infection [24]. In children in the Irkutsk Region, after recovery from a confirmed new coronavirus infection, antibodies were detected in 66.1 % of cases and persisted for up to 10–15 months to the nucleocapsid and up to 15–18 months to the RBD of SARS-CoV-2 [27]. An assessment of IgG levels to SARS-CoV-2 after COVID-19 in pediatric patients demonstrated that the highest antibody levels persisted for 2–4 months after the illness [28].

Thus, longer follow-up of pediatric patients infected with SARS-CoV-2 is crucial to establish the duration of humoral protection in this population. Further research is required to elucidate the role of long-term humoral responses in pediatric patients following SARS-CoV-2 infection and their relationship with protection against recurrent infections.

Tracking dynamic changes in SARS-CoV-2-IgG can provide additional information for diagnosing, monitoring, and predicting COVID-19 and developing new vaccines.

Conclusions

In 6.7 % of pediatric patients with coronavirus infection at the time of hospitalization, positive levels of the positivity coefficient of IgM antibodies to SARS-CoV-2 were detected, whereas the overall seroconversion rate was 38.7 %. Children who have had COVID-19, starting from month 1 after discharge from the hospital, demonstrated increased SARS-CoV-2-IgG antibody titer. Most pediatric patients with SARS-CoV-2 infection remain serologically positive 6 months after infection. IgG antibodies to SARS-CoV-2 persist up to 12 months after infection, regardless of the severity of COVID-19.

References

1. *Guan W.J., Ni Z.Y., Hu Y., Liang W.H., Ou C.Q., He J.X., Liu L., Shan H., Lei C.L., Hui D.S.C., Du B., Li L.J., Zeng G., Yuen K.Y., Chen R.C., Tang C.L., Wang T., Chen P.Y., Xiang J., Li S.Y., Wang J.L., Liang Z.J., Peng Y.X., Wei L., Liu Y., Hu Y.H., Peng P., Wang J.M., Liu J.Y., Chen Z., Li G., Zheng Z.J., Qiu S.Q., Luo J., Ye C.J., Zhu S.Y., Zhong N.S.; China Medical Treatment Expert Group for COVID-19.* Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020; 382 (18): 1708–1720. DOI: 10.1056/NEJMoa2002032

2. *Ravichandran S., Tang J., Grubbs G., Lee Y., Pourhashemi S., Hussaini L., Lapp S.A., Jerris R.C., Singh V., Chahroudi A., Anderson E.J., Rostad C.A., Khurana S.* SARS-CoV-2 immune repertoire in MIS-C and pediatric COVID-19. Nat Immunol. 2021; 22 (11): 1452–1464. DOI: 10.1038/s41590-021-01051-8

3. *Garrido C., Hurst J.H., Lorang C.G., Aquino J.N., Rodriguez J., Pfeiffer T.S., Singh T., Semmes E.C., Lugo D.J., Rotta A.T., Turner N.A., Burke T.W., McClain M.T., Petzold E.A., Permar S.R., Moody M.A., Woods C.W., Kelly M.S., Fouda G.G.* Asymptomatic or mild symptomatic SARS-CoV-2 infection elicits durable neutralizing antibody responses in children and adolescents. JCI Insight. 2021; 6 (17): e150909. DOI: 10.1172/jci.insight.150909

4. *Mou D., Feng H., Cao R., Weng X., Zhao L., Yang L., Jin R., Chen W.* Profile of specific antibodies to the SARS-CoV-2. J Med Microbiol. 2021; 70 (3): 001335. DOI: 10.1099/jmm.0.001335

5. *Petrara M.R., Bonfante F., Costenaro P., Cantarutti A., Carmona F., Ruffoni E., Di Chiara C., Zanchetta M., Barzon L., Donà D., Da Dalt L., Bortolami A., Pagliari M., Plebani M., Rossi P., Cotugno N., Palma P., Giaquinto C., De Rossi A.* Asymptomatic and Mild SARS-CoV-2 Infections Elicit Lower Immune Activation and Higher Specific Neutralizing Antibodies in Children Than in Adults. Front Immunol. 2021; 12: 741796. DOI: 10.3389/ fimmu.2021.741796

6. *Le Bert N., Tan A.T., Kunasegaran K., Tham C.Y.L., Hafezi M., Chia A., Chng M.H.Y., Lin M., Tan N., Linster M., Chia W.N., Chen M.I., Wang L.F., Ooi E.E., Kalimuddin S., Tambyah P.A., Low J.G., Tan Y.J., Bertoletti A.* SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls. Nature. 2020; 584 (7821): 457–462. DOI: 10.1038/s41586-020-2550-z

7. *Weisberg S.P., Connors T.J., Zhu Y., Baldwin M.R., Lin W.H., Wontakal S., Szabo P.A., Wells S.B., Dogra P., Gray J., Idzikowski E., Stelitano D., Bovier F.T., Davis-Porada J., Matsumoto R., Poon M.M.L., Chait M., Mathieu C., Horvat B., Decimo D., Hudson K.E., Zotti F.D., Bitan Z.C., La Carpia F., Ferrara S.A., Mace E., Milner J., Moscona A., Hod E., Porotto M., Farber D.L.* Distinct antibody responses to SARS-CoV-2 in children and adults across the COVID-19 clinical spectrum. Nat Immunol. 2021; 22 (1): 25–31. DOI: 10.1038/s41590-020-00826-9

8. *Krammer F.* A correlate of protection for SARS-CoV-2 vaccines is urgently needed. Nat Med. 2021; 27 (7): 1147–1148. DOI: 10.1038/s41591-021-01432-4

9. *Hsueh P.R., Huang L.M., Chen P.J., Kao C.L. & Yang P.C.* Chronological evolution of IgM, IgA, IgG and neutralisation antibodies after infection with SARS-associated coronavirus. Clin. Microbiol. Infect. 2004; 10: 1062–1066.

10. *Park W.B., Perera R.A., Choe P.G., Lau E.H., Choi S.J., Chun, J.Y., Oh M.D.* Kinetics of Serologic Responses to MERS Coronavirus Infection in Humans, South Korea. Emerging Infectious Diseases. 2015; 21 (12): 2186–2189. DOI: 10.3201/eid2112.151421. (2015)

11. *Feng C., Shi J., Fan Q., Wang Y., Huang H., Chen F., Tang G., Li Y., Li P., Li J., Cui J., Guo L., Chen S., Jiang M., Feng L., Chen L., Lei C., Ke C., Deng X., Hu F., Tang X., Li F.* Protective humoral and cellular immune responses to SARS-CoV-2 persist up to 1 year after recovery. Nat Commun. 2021; 12 (1): 4984. DOI: 10.1038/s41467-021-25312-0

12. *Lumley S.F., O'Donnell D., Stoesser N.E., Matthews P.C., Howarth A., Hatch S.B., Marsden B.D., Cox S., James T., Warren F., Peck L.J., Ritter T.G., de Toledo Z., Warren L., Axten D., Cornall R.J., Jones E.Y., Stuart D.I., Screaton G., Ebner D., Hoosdally S., Chand M., Crook D.W., O'Donnell A.M., Conlon C.P., Pouwels K.B., Walker A.S., Peto T.E.A., Hopkins S., Walker T.M., Jeffery K., Eyre D.W.* Oxford University Hospitals Staff Testing Group. Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers. N Engl J Med. 2021; 384 (6): 533–540. DOI: 10.1056/NEJMoa2034545

13. *Ng K.W., Faulkner N., Cornish G.H., Rosa A., Harvey R., Hussain S., Ulferts R., Earl C., Wrobel A.G., Benton D.J., Roustan C., Bolland W., Thompson R., Agua-Doce A., Hobson P., Heaney J., Rickman H., Paraskevopoulou S., Houlihan C.F., Thomson K., Sanchez E., Shin G.Y., Spyer M.J., Joshi D., O'Reilly N., Walker P.A., Kjaer S., Riddell A., Moore C., Jebson B.R., Wilkinson M., Marshall L.R., Rosser E.C., Radziszewska A., Peckham H., Ciurtin C., Wedderburn L.R., Beale R., Swanton C., Gandhi S., Stockinger B., McCauley J., Gamblin S.J., McCoy LE., Cherepanov P., Nastouli E., Kassiotis G.* Preexisting and de novo humoral immunity to SARS-CoV-2 in humans. Science. 2020; 370 (6522): 1339–1343. DOI: 10.1126/science.abe1107

14. *Li Z., Yi Y., Luo X., Xiong N., Liu Y., Li S., Sun R., Wang Y., Hu B., Chen W., Zhang Y., Wang J., Huang B., Lin Y., Yang J., Cai W., Wang X., Cheng J., Chen Z., Sun K., Pan W., Zhan Z., Chen L., Ye F.* Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 in-

fection diagnosis. J Med Virol. 2020; 92 (9): 1518–1524. DOI: 10.1002/jmv.25727

15. *di Mauro G., Scavone C., Rafaniello C., Rossi F., Capuano A.* SARS-Cov-2 infection: Response of human immune system and possible implications for the rapid test and treatment. Int Immunopharmacol. 2020; 84: 106519. DOI: 10.1016/j.intimp.2020.106519

16. *Rostami A., Sepidarkish M., Leeflang M.M.G., Riahi S.M., Nourollahpour Shiadeh M., Esfandyari S., Mokdad A.H., Hotez P.J., Gasser R.B.* SARS-CoV-2 seroprevalence worldwide: a systematic review and meta-analysis. Clin Microbiol Infect. 2021; 27 (3): 331–340. DOI: 10.1016/j.cmi.2020.10.020

17. *Pollán M., Pérez-Gómez B., Pastor-Barriuso R., Oteo J., Hernán M.A., Pérez-Olmeda M., Sanmartín J.L., Fernández-García A., Cruz I., Fernández de Larrea N., Molina M., Rodríguez-Cabrera F., Martín M., Merino-Amador P., León Paniagua J., Muñoz-Montalvo J.F., Blanco F., Yotti R.; ENE-COVID Study Group.* Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. Lancet 2020; 396 (10250): 535–544. DOI: 10.1016/S0140-6736(20)31483-5

18. *Xu X., Sun J., Nie S., Li H., Kong Y., Liang M., Hou J., Huang X., Li D., Ma T., Peng J., Gao S., Shao Y., Zhu H., Lau J.Y., Wang G., Xie C., Jiang L., Huang A., Yang Z., Zhang K., Hou F.F.* Seroprevalence of immunoglobulin M and G antibodies against SARS-CoV-2 in China. Nat Med. 2020; 26 (8): 1193–1195. DOI: 10.1038/s41591-020-0949-6

19. *Long Q.X., Tang X.J., Shi Q.L., Li Q., Deng H.J., Yuan J., Hu J.L., Xu W., Zhang Y., Lv F.J., Su K., Zhang F., Gong J., Wu B., Liu X.M., Li J.J., Qiu J.F., Chen J., Huang A.L.* Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. Nat Med. 2020; 26 (8): 1200–1204. DOI: 10.1038/s41591-020-0965-6

20. *Wiersinga W.J., Rhodes A., Cheng A.C., Peacock S.J. & Prescott H.C.* Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. J. Am. Med. Assoc. 2020; 324: 782–793.

21. *Li K., Huang B., Wu M., Zhong A., Li L., Cai Y., Wang Z., Wu L., Zhu M., Li J., Wang Z., Wu W., Li W., Bosco B., Gan Z., Qiao Q., Wu J., Wang Q., Wang S., Xia X.* Dynamic changes in anti-SARS-CoV-2 antibodies during SARS-CoV-2 infection and recovery from COVID-19. Nat Commun. 2020; 11 (1): 6044. DOI: 10.1038/s41467-020-19943-y

22. *Jiang S., Hillyer C., Du L.* Neutralizing antibodies against SARS-CoV-2 and other human coronaviruses. Trends Immunol 2020; 41: 355–359. DOI: 10.1016/j.it.2020.03.007

23. *Cao W.C., Liu W., Zhang P.H., Zhang F., Richardus J.H.* Disappearance of antibodies to SARS-associated coronavirus after recovery. N Engl J Med 2007; 357: 1162–1163. DOI: 10.1056/NEJMc070348

24. *Whitcombe A.L., McGregor R., Craigie A., James A., Charlewood R., Lorenz N., Dickson J.M., Sheen C.R., Koch B., Fox-Lewis S., McAuliffe G., Roberts S.A., Morpeth S.C., Taylor S., Webb R.H., Jack S., Upton A., Ussher J.E., Moreland N.J.* Comprehensive analysis of SARS-CoV-2 antibody dynamics in New Zealand. Clin Transl Immunology. 2021; 10 (3): e1261. DOI: 10.1002/cti2.1261

25. *Iyer A.S., Jones F.K., Nodoushani A., Kelly M., Becker M., Slater D., Mills R., Teng E., Kamruzzaman M., Garcia-Beltran W.F., Astudillo M., Yang D., Miller T.E., Oliver E.,*

Fischinger S., Atyeo C., Iafrate A.J., Calderwood S.B., Lauer S.A., Yu J., Li Z., Feldman J., Hauser B.M., Caradonna T.M., Branda J.A., Turbett S.E., LaRocque R.C., Mellon G., Barouch D.H., Schmidt A.G., Azman A.S., Alter G., Ryan E.T., Harris J.B., Charles R.C. Persistence and decay of human antibody responses to the receptor binding domain of SARS-CoV-2 spike protein in COVID-19 patients. Sci Immunol 2020; 5: eabe0367. DOI: 10.1126/sciimmunol.abe0367

26. *Zhu L., Xu X., Zhu B., Guo X., Xu K., Song C., Fu J., Yu H., Kong X., Peng J., Huang H., Zou X., Ding Y., Bao C., Zhu F., Hu Z., Wu M., Shen H.* Kinetics of SARS-CoV-2 Specific and Neutralizing Antibodies over Seven Months after Symptom Onset in COVID-19 Patients. Microbiol Spectr. 2021; 9 (2): e0059021. DOI: 10.1128/Spectrum.00590-21

27. *Bryukhova D.D., Dubrovina V.I., Kiseleva N.O., Pyatidesyatnikova A.B., Korytov K.M., Balakhonov S.V.* Assessment of indicators of specific humoral immune against COVID-19 in children during the distribution of a new coronavirus infection in the Irkutsk region (2020–2021). *Acta biomedical scientifica* 2023; 8 (1): 239–246. DOI: 10.29413/ABS.2023-8.1.24 (in Russian).

28. *Evseeva G.P., Lazareva M.A., Vlasova M.A., Nagovitsyna E.B., Suprun S.V., Telepneva R.S., Knizhnikova E.V., Galyant O.I., Lebed'ko O.A.* Assessment of the level of immune layer to SARS-CoV-2 in children under conditions of novel coronavirus infection COVID-19. *Bûlleten' fiziologii i patologii dyhaniâ = Bulletin Physiology and Pathology of Respiration* 2023; (88): 59–68. DOI: 10.36604/1998-5029-2023-88-59-68 (in Russian).

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