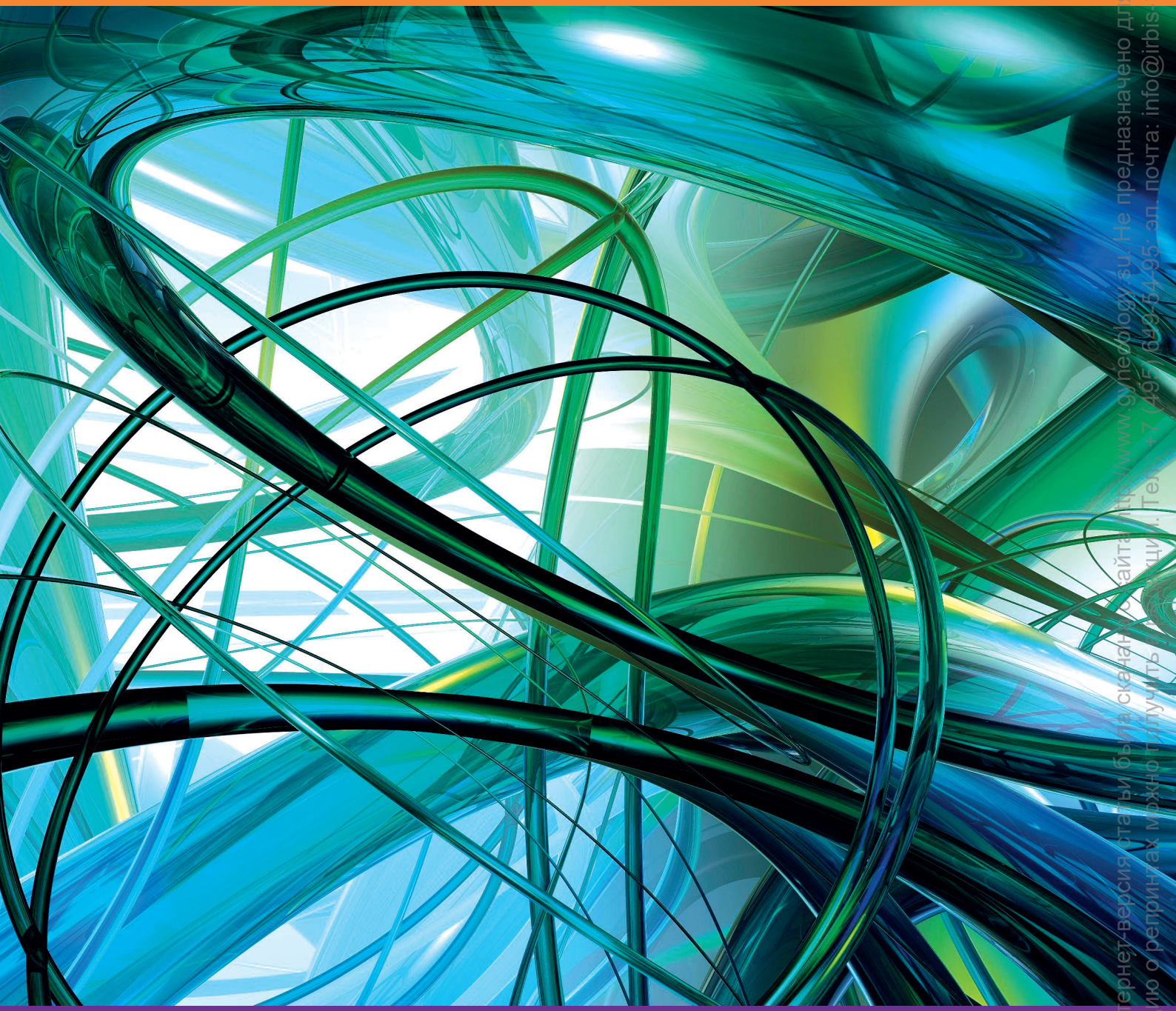
ISSN 2313-7347 (print)
ISSN 2500-3194 (online)

АКУШЕРСТВО ГИНЕКОЛОГИЯ РЕПРОДУКЦИЯ

Включен в перечень ведущих рецензируемых журналов и изданий ВАК

2022 • том 16 • № 2



OBSTETRICS, GYNECOLOGY AND REPRODUCTION

2022 Vol. 16 No 2

www.gynecology.su

ISSN 2313-7347 (print)
ISSN 2500-3194 (online)

https://doi.org/10.17749/2313-7347/ob.gyn.rep.2022.305

The role of platelets in antiviral immunity

Ekaterina V. Slukhanchuk[1,2], Viktoria O. Bitsadze[1], Jamilya Kh. Khizroeva[1], Antonina G. Solopova[1], Valentina I. Tsibizova[3], Fidan Yakubova[1], Cihan Ay[4], Jean-Christophe Gris[1,5], Alexander D. Makatsariya[1]

[1]Sechenov University; 2 bldg. 4, Bolshaya Pirogovskaya Str., Moscow 119991, Russia;

[2]Petrovsky National Research Centre of Surgery; 2 Abrikosovskiy Lane, Moscow 119991, Russia;

[3]Almazov National Medical Research Centre, Health Ministry of Russian Federation; 2 Akkuratova Str., Saint Petersburg 197341, Russia;

[4]University of Vienna; 1 Universitätsring, Vienna 1010, Austria;

[5]University of Montpellier; 163 Rue Auguste Broussonnet, Montpellier 34090, France

Corresponding author: *Ekaterina V. Slukhanchuk, e-mail: ekaterina@ginekologhirurg.ru*

Abstract

The main role of platelets is traditionally assigned to participation in hemostasis reactions. In recent years, the data have appeared on the non-hemostatic platelet-related role and their active participation in inflammatory reactions. These platelet functions are predetermined by their ability to activate and secrete various immunomodulatory cytokines and chemokines. In addition, activated platelets can directly interact with viral receptors. Recently, there has been growing the knowledge regarding platelet-related regulation of diverse cell types. The result of this interaction is, among others, the formation of platelet-leukocyte aggregates, the focusing of neutrophils at the sites of injury, and generation of a scaffold for developing extracellular traps. Thus, platelets are not only participants in coagulation processes, but also important players in the inflammatory process. This lecture details the issues of platelets controlling and modulating host response to viral infection, as well as potential targets for therapeutic intervention.

Keywords: platelets, hemostasis, inflammation, viral infection, cytokines, chemokines, COVID-19

For citation: Slukhanchuk E.V., Bitsadze V.O., Khizroeva J.Kh., Solopova A.G., Tsibizova V.I., Yakubova F., Ay C., Gris J.-C., Makatsariya A.D. The role of platelets in antiviral immunity. *Akusherstvo, Ginekologia i Reprodukcia = Obstetrics, Gynecology and Reproduction*. 2022;16(2):204–212. https://doi.org/10.17749/2313-7347/ob.gyn.rep.2022.305.

Роль тромбоцитов в противовирусном иммунитете

Е.В. Слуханчук[1,2], В.О. Бицадзе[1], Д.Х. Хизроева[1], А.Г. Солопова[1], В.И. Цибизова[3], Ф. Якубова[1], Д. Ай[4], Ж.-К. Гри[1,5], А.Д. Макацария[1]

[1]ФГАОУ ВО Первый Московский государственный медицинский университет имени И.М. Сеченова Министерства здравоохранения Российской Федерации (Сеченовский Университет); Россия, 119991 Москва, ул. Большая Пироговская, д. 2, стр. 4;

[2]ФГБНУ «Российский научный центр хирургии имени академика Б.В. Петровского»; Россия, 119991 Москва, Абрикосовский пер., д. 2;

[3]ФГБУ «Национальный медицинский исследовательский центр имени В.А. Алмазова» Министерства здравоохранения Российской Федерации; Россия, 197341 Санкт-Петербург, ул. Аккуратова, д. 2;

[4]Венский университет; Австрия, 1010 Вена, Universitätsring, д. 1;

[5]Университет Монпелье; Франция, 34090 Монпелье, ул. Огюста Бруссоне, д. 163

Для контактов: *Екатерина Викторовна Слуханчук, e-mail: ekaterina@ginekologhirurg.ru*

Резюме

Основная роль тромбоцитов традиционно отводится участию в реакциях гемостаза. В последние годы появились данные о негемостатической роли тромбоцитов и их активном участии в реакциях воспаления. Эти функции тромбоцитов предопре-

2022 • Vol. 16 • № 2
Obstetrics, Gynecology and Reproduction

делены их способностью к активации и секреции различных иммуномодулирующих цитокинов и хемокинов. Кроме этого, активированные тромбоциты могут напрямую взаимодействовать с вирусными рецепторами. Знания о регуляции различных типов клеток тромбоцитами в последние годы растут. Результатом этого взаимодействия является в том числе образование тромбоцитарно-лейкоцитарных агрегатов, фокусирование нейтрофилов в местах повреждения и создание каркаса для образования внеклеточных ловушек. Таким образом, тромбоциты являются не только участниками процессов коагуляции, но и важными игроками воспалительного процесса. В этой лекции подробно освещены вопросы тромбоцитарного контроля и модуляции ответа на вирусную инфекцию, а также возможные мишени для терапевтического воздействия.

Ключевые слова: тромбоциты, гемостаз, воспаление, вирусная инфекция, цитокины, хемокины, COVID-19

Для цитирования: Слуханчук Е.В., Бицадзе В.О., Хизроева Д.Х., Солопова А.Г., Цибизова В.И., Якубова Ф., Ай Д., Гри Ж.-К., Макацария А.Д. Роль тромбоцитов в противовирусном иммунитете. *Акушерство, Гинекология и Репродукция.* 2022;16(2):204–212. https://doi.org/10.17749/2313-7347/ob.gyn.rep.2022.305.

Platelet biology / Биология тромбоцитов

Platelets are small non-nucleated cells derived from megakaryocytes that play a crucial role in primary hemostasis. Megakaryocyte fragmentation is regulated by thrombopoietin receptor binding [1]. Any platelet contains no nucleus, however being enriched in mitochondrial DNA as well as RNA the latter accounting for protein synthesis [2]. About 750 billion platelets circulate in the human body, and about 200 billion new cells are formed daily in the bone marrow [3] and lungs [4]. Platelets circulate for 10 days to be subsequently utilized in the liver and spleen. While aging platelets gradually lose membrane-bound sialic acid and reduce thrombopoietin accumulation.

In recent years, there have been emerged increasing evidence regarding the role of platelets in pathological processes such as autoimmune reactions [5], tumor growth [6], and infectious processes [7]. Small molecules, nucleic acids, lipid mediators, and proteins are stored in diverse platelet organelles – alpha granules, dense granules, and lysosomal vesicles [8]. Upon activation, platelets rapidly change shape and release into the extracellular environment such factors either soluble or encapsulated in bioactive microvesicles [9]. The ability of platelets to participate in immune responses is executed due to release of various pro-inflammatory and bioactive molecules stored in their granules. Released mediators attract and modulate the activity of circulating leukocytes [10]. Platelets also act as independent immune effector cells [11]. Megakaryocytes and platelets express several immune-associated molecules and receptors, including Fc-receptors [12], complement receptors [13], chemokine receptors [14], and some toll-like receptors (TLRs) [15].

Platelets and immune response / Тромбоциты и иммунный ответ

Platelets contain various membrane receptors such as TLRs capable of detecting PAMPs (pathogen-associated molecular patterns) and DAMPs (damage-associated molecular patterns) [16]. In addition to direct binding to pathogens, platelets are involved in pathogen elimination by coordinating activity of immune cells such as neutrophils, which bind to activated platelets via P-selectin glycoprotein ligand-1 (PSGL-1, CD162) and migrate to inflammatory sites [17]. Similar interaction leads to formation of neutrophilic vesicles filled with arachidonic acid, which are rapidly internalized by platelets via macrophage-1 antigen (Mac-1). Being internalized, arachidonic acid is converted to thromboxane A2 (TXA2). Then, platelet-derived TXA2 activates neutrophils by upregulating ICAM-1 (intercellular adhesion molecule 1) expression followed by enhanced migration, and extravasation [18].

Serotonin plays an essential role in neutrophil adhesion. Platelets are the main source of peripheral serotonin [19]. Platelets cover a large area at the site of endothelial injury; migrating neutrophils use the platelet scaffold to attach and migrate to the site of inflammation [20].

The interaction between platelets and neutrophils has been shown to attract monocytes to the site of inflammation via CD40–CD40L dependent mechanism [21]. Platelets also attract monocytes via platelet-derived CCL5 (chemokine (C-C motif) ligand 5) and neutrophil-derived HNP1 (human neutrophil peptide 1, alpha-defensin) heteromers [22]. Moreover, activated platelets release the contents of alpha granules containing mediators such as adenosine diphosphate (ADP). The binding of ADP to P2Y receptors [23] results in rapid translocation of P-selectin to the plasma membrane, thereby enhancing recruitment of neutrophils, monocytes, and lymphocytes to the injury site [24]. Platelet-released HMGB1 protein (high-mobility group protein B1) is also involved in attracting immune cells [25]. Recent *in vitro* data indicate that CXCL4 (also known as PF4, platelet factor 4), a critical

chemokine secreted by activated platelets, may be involved in monocyte migration by binding to the CCR1 receptor (C-C chemokine receptor type 1) [26].

Platelets not only attract immune cells to the site of inflammation but also actively move towards site of damage. Motile platelets are capable of active adhesion to the endothelium assisted by ADP and TXA2. In addition, platelets trap infectious agents and increase phagocyte activity [27]. Bacteria activate platelets, enhancing their interaction with neutrophils, which leads to enhanced phagocytosis [28]. Platelet-deprived model demonstrated that mice were prone to bacteremia caused by *Staphylococcus aureus* [29]. Thrombin-activated platelets also appear to enhance the uptake and destruction of Gram-positive bacteria by dendritic cells, macrophages, and neutrophils [30]. Platelets can form aggregates with erythrocytes infected with malarial plasmodia and destroy the pathogen [31].

Platelet microvesicles containing nucleic acids, proteins, lipids, and other molecular constituents also derived from megakaryocytes play an essential role in immune responses. Microvesicles containing microRNAs can modulate mRNA transcription in macrophages, reprogramming them for a phagocytic phenotype [32].

Platelets and regulation of immune cell functioning / Тромбоциты и регуляция работы иммунных клеток

Cytokines and chemokines underlie immune cell generation, growth, differentiation and functioning. The adhesion of monocytes to platelets during inflammation leads to nuclear translocation of the transcription factor NF-κB (nuclear factor kappa B) followed by upregulated monocytic expression of CCL2 and IL-8 (interleukin-8). Platelet CCL5 activates the release of monocyte pro-inflammatory chemokines as well as P-selectin-dependent interaction [33]. The chemokine CXCL4 (chemokine (C-X-C motif) ligand 4) plays an important role in systemic inflammatory response. During inflammation, platelet Rac-1 (Ras-related C3 botulinum toxin substrate 1) pathway is engaged to release CXCL4 that recruits neutrophils, followed by tissue damage, also resulting in elevated level of CCL5, CXCL1, and CXCL2. Experimental CXCL4 suppression reduces the concentration of pro-inflammatory markers and improves general condition of laboratory animals [34]. Platelets are the source of CD40L (CD154) markedly affecting leukocytes. In systemic lupus erythematosus (SLE), platelets were shown to be activated by immune complexes followed by aggregation with monocytes and dendritic cells. The latter increased release of IFN-α (interferon alfa) via CD40/CD40L-axis. Platelet depletion in mouse SLE models improved the disease course, whereas platelet transfusion exacerbated it [35]. The neutrophil-platelet interaction via CD40 is regulated by the positive feedback loop so that the leukocyte release of superoxide and reactive oxygen species becomes elevated along with platelet stimulated CD40L secretion [36].

Another important regulatory cytokine is IL-1β being mainly produced by leukocytes in the human body. Platelets may elevate expression of this leukocyte cytokine, whereas P-selectin level was shown to be associated with higher concentrations of IL-1β and IL-6 after *ex vivo* stimulation [37]. During viral infection, platelets release microvesicles filled with IL-1β resulting from NLRP3 (NOD-, LRR- and pyrin domain-containing protein 3) activation by reactive oxygen species [38].

In addition to platelet-related pro-inflammatory effect on immune cells, platelets also exhibit anti-inflammatory effects due to direct interaction or release of various factors. In particular, platelets and their derivatives were experimentally shown to reduce level of pro-inflammatory cytokines such as TNF-α (tumor necrosis factor-α) and IL-6. Depletion of the platelet pool resulted in increased mortality and multiple organ failure in murine models of septic shock, and conversely, platelet inoculation attenuated the generalized hyperimmune response [39]. Another study demonstrated platelets added to mononuclear cell culture were able to suppress IL-6 and TNF-α production and elevated IL-10 production after stimulation with PAMPs of various origins [40].

Platelets and neutrophil extracellular traps / Тромбоциты и внеклеточные ловушки нейтрофилов

Neutrophil extracellular traps (NETs) consist of extracellular DNA as well as cytoplasmic and nuclear proteins released into the extracellular space by neutrophils upon activation [41]. After the very discovery of this process, platelets were shown to play a fundamental role in the formation of such structures in sepsis by sensing TLR4 ligands and triggering neutrophil adhesion [42]. Later, it was unveiled that such interaction depends on the αLβ2 integrin LFA-1 (lymphocyte function-associated antigen 1, CD11a/CD18) [43]. Platelet microvesicles enriched in HMGB1 also stimulate neutrophils for NETs production

2022 • Vol. 16 • № 2
Obstetrics, Gynecology and Reproduction

[44]. Along with interaction between platelet GPIb (glycoprotein Ib) and neutrophil CD18, release of vWF (von Willebrand factor) and CXCL4 also promotes netosis. At the same time, intensity of netosis is accounted for by TXA2 production and, accordingly, can be suppressed by acting acetylsalicylic acid and prostacyclin [45].

Platelets and viruses / Тромбоциты и вирусы

Antiviral immunity is traditionally associated with the work of leukocytes. However, in various viral infections, including Dengue virus [46], HIV (human immunodeficiency virus), influenza virus [47], and SARS-CoV-2 [48], an increase in platelet activity has been also noted. The main antiviral platelet-related effect is mediated by sequestration of viral particles that limits viral spread. In HIV patients, platelets were proved to bind to and endocytose HIV virions contributing to clearance of viral particles from the circulation [49]. During platelet activation, α-granules are delivered to the cell surface and externalized, thereby releasing a wide range of bioactive molecules, including PF4 (also called the chemokine CXCL4). In addition to being an essential agent in leukocyte chemotaxis, PF4 exerts a direct antiviral activity [50]. Platelets also secrete antimicrobial proteins such as PD1–PD4 (programmed cell death proteins 1–4) exhibiting antiviral against cowpox virus [51]. Recent studies have shown that platelets contain virus-specific immunoglobulin G (IgG) that can potentially neutralize cytomegalovirus (CMV) and influenza A virus both *in vitro* and *in vivo* [52]. IgG is localized in α-granules [53]. Megakaryocytes can engulf IgG molecules to be stored in α-granules for subsequent secretion by mature platelets. However, platelet-released vs. serum IgG antibodies is more effective in virus neutralization [52].

Platelets are also capable of directing the local immune response to infectious agents. Cytomegalovirus is recognized by platelet TLR2, leading to platelet degranulation, leukocyte chemotaxis, as well as platelet aggregation with neutrophils, monocytes, B cells, T cells, and dendritic cells [54]. Such platelet-leukocyte interactions allows platelets to present viral antigens on the major histocompatibility complex class I molecule to leukocytes [55] and provide stimulatory signals to antigen-presenting cells [56]. Similar events were also noted in Dengue fever [57].

Viruses evolved mechanisms to evade platelet recognition as a part of platelet-mediated antiviral immunity. Viruses interact with platelet surface receptors. In particular, Dengue virus and HIV bind to platelet surface lectin receptors and DC-SIGN (dendritic cell-specific intercellular adhesion molecule-3-grabbing nonintegrin) [58]. Such interactions lead to internalization of viral particles, so that viruses such as HIV, CMV, and hepatitis C virus (HCV) can continue to replicate both inside megakaryocytes and platelets [58]. Along with using platelets for replication, some viruses may be carried inside circulating platelets to avoid immune detection as it was shown for influenza virus [59] and HIV, which form latent viral reservoirs. The hepatitis C virus is believed to use circulating platelets for transport to the liver, where interactions between platelets and hepatocytes prolong HCV persistence [60].

Thrombocytopenia in viral infection / Тромбоцитопения при вирусной инфекции

Thrombocytopenia is a common symptom observed in severe viral infections. The mechanisms for its development are as follows:

1) neuraminidase activity of the influenza virus and herpes simplex virus (HSV) shortens platelet lifespan, ensuring their rapid clearance in the liver and spleen [61];

2) neuraminidase activity alters megakaryocyte ploidy, as well as future platelet morphology and size [62];

3) herpes simplex viruses, affecting thrombopoietin activity reduce megakaryocyte colony formation [63] as well as relevant cell survival and differentiation [64];

4) impaired megakaryocyte differentiation also occurs due to changes in cytokine expression in the bone marrow, particularly during infection with Dengue virus [65];

5) upon infection with Dengue virus, HIV, etc., it is noted to alter megakaryocyte development, platelet activation, accompanied by mitochondrial dysfunction, decreased cellular integrity and increased apoptosis [66, 67].

Impaired platelet aggregation and activation in viral infection / Нарушения процессов агрегации и активации тромбоцитов при вирусной инфекции

Viral infection also affects platelet function [68].

1. Coxsackie B virus (CVB) binds to and enters platelets via the Coxsackie adrenoreceptor. CVB is unable to replicate inside platelets, but may modulate activity and enhance P-selectin release and phosphatidylserine-related effects, which together promote platelet-leukocyte interactions, leading to platelet destruction and thrombocytopenia [69].

2. The cowpox virus also invades platelets [68]. *In vitro* studies showed decreased platelet aggregation and subsequently increased release of serotonin after infection. *In vivo* studies demonstrated that infection with the cowpox virus resulted in increased intravascular coagulation [70] associated with enhanced platelet response. This discrepancy may indicate that the cowpox virus may affect endothelial function critical for regulating platelet function *in vivo* [71].

3. Increased platelet activation during influenza infection is partly due to the release of monocyte cytokines, which further activate platelets [72].

4. The immune response to infection with hepatitis C, HIV, CMV, HSV, and coronaviruses includes production of neutralizing antibodies against viral glycoproteins. Glycoprotein-specific antibodies cross-react with platelet integrins, leading to the development of antibody-dependent thrombocytopenia [73].

5. By damaging the endothelium, viruses indirectly affect platelet functioning. For instance, Dengue virus infects endothelial cells promoting endothelial activation, endothelial-platelet interactions, and increased vascular permeability [38, 74]. Impaired integrity of blood vessels infected with the virus promotes platelet activation and may underlie one of the mechanisms for increased platelet clearance.

6. Patients with chronic viral infection such as that caused by HIV require continuous suppression of viral replication. Studies showed that some antiretroviral drugs increase the risk of myocardial infarction [75] due to elevated platelet activation and aggregation [76]. Moreover, antiretroviral therapy may be further affect endothelial functions [77].

Thus, both viral infection and antiviral drugs can affect platelet activation.

Platelets and SARS-CoV-2 / Тромбоциты и SARS-CoV-2

Activation of inflammation and coagulation combined with the activation of multiple immune cells at the site of the infection was coined an “immunothrombosis” that was first described in 2013 by B. Engelmann and S. Massberg [78].

COVID-19 is a viral infection with a polymorphic clinical picture determined by the amplitude of immunothrombosis and degree of tissue damage. Studies conducted suggest that coagulopathy in COVID-19 combines local platelet consumption in the lungs, disseminated intravascular coagulation, and thrombotic microangiopathy.

Severe lung inflammation and obstructive pulmonary microvascular immunothrombosis in COVID-19 patients lead to pulmonary thrombosis/thromboembolism, underlying multiple organ failure, and mortality [79].

SARS-CoV-2 mRNA was found in platelets collected from patients with COVID-19 [80]. It is not entirely clear whether SARS-CoV-2 enters platelets via receptor-mediated endocytosis. SARS-CoV-2 enters host cells by binding to the angiotensin-converting enzyme 2 (ACE2) receptor [81]. Some studies have shown that neither mRNA nor protein ACE2 were found in platelets [82]. Other studies reported platelet ACE2 expression that promoted direct platelet activation by SARS-CoV-2 [83]. This discrepancy may be due to difference in preparation protocol used for washed platelets or genetic differences between patient cohorts.

Platelet activation is one of the arms in COVID-19 pathophysiology. In particular, patients with COVID-19 have abnormal platelet morphology, with large, hyperchromic, and vacuolated platelets [84]. A study found that patients with COVID-19 vs. control subjects had increased platelet activity [85]. Higher number of platelet-monocytic and platelet-granulocyte aggregates indicative of increased systemic platelet activation was observed in patients with COVID-19-associated pneumonia [86]. Platelets during COVID-19 contribute to increased concentration of fibrinogen, von Willebrand factor, and factor XII, which contributes to enhanced XII-dependent coagulation [86]. Platelets from patients with severe COVID-19 induce tissue factor expression *in vivo* [66].

Various circulating biomarkers such as fibrin/fibrinogen, D-dimer, P-selectin, von Willebrand factor multimers, soluble thrombomodulin, and tissue factor are of special interest. The basis to consider them as biomarkers is related to cognate receptors and signaling pathways in endothelial cells, platelets, monocytes, and erythrocytes. An open question remains is whether hemostasis may be directly virally affected or whether hemostatic activation occurs secondary to the inflammatory response.

Currently, no consensus on platelet ACE2 expression has been reached yet. Does SARS-CoV-2 bind directly to platelets via ACE2, or are there alternative pathways? Studies in this field may uncover mechanisms of hypercoagulability in cytokine storm. Management of the cytokine storm in severe COVID-19 may include antiplatelet therapy [87]. Acetylsalicylic acid has been shown to reduce the need for mechanical ventilation, the rate of admission to the intensive care unit, and in-hospital mortality in patients hospitalized with COVID-19 [88]. A deeper insight into contribution of

platelets to antiviral immunity will increase therapeutic effectiveness of viral infections (**Fig. 1**).

Conclusion / Заключение

Previously recognized as a part of the hemostasis system, in recent years platelets acquired another understanding owing to findings that allowed to put them together with most critical players in the immune response.

Platelets are participants in anti-infective immunity, pathogenesis of autoimmune and chronic inflammatory diseases. The growing interest in platelets is also related to the fact that they may be a new target for developing anti-inflammatory therapy with promising results.

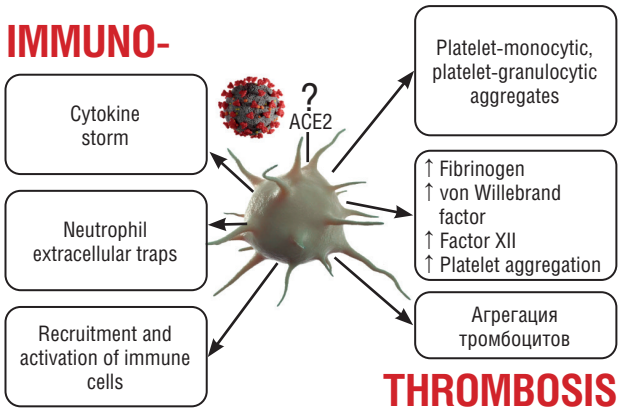


Figure 1. Platelets and COVID-19 [drawn by authors].

Note: *ACE2 – angiotensin-converting enzyme 2 receptors on platelet.*

Рисунок 1. Тромбоциты и COVID-19 [рисунок авторов].

Примечание: *ACE2 – рецептор ангиотензинпревращающего фермента 2 на тромбоците.*

ARTICLE INFORMATION	ИНФОРМАЦИЯ О СТАТЬЕ
Received: 15.03.2022. **Revision received:** 10.04.2022.	**Поступила:** 15.03.2022. **В доработанном виде:** 10.04.2022.
Accepted: 21.04.2022. **Published:** 30.04.2022.	**Принята к печати:** 21.04.2022. **Опубликована:** 30.04.2022.
Author's contribution	**Вклад авторов**
All authors contributed equally to the article.	Все авторы внести равный вклад в написание и подготовку рукописи.
All authors have read and approved the final version of the manuscript.	Все авторы прочитали и утвердили окончательный вариант рукописи.
Conflict of interests	**Конфликт интересов**
The authors declare no conflict of interests.	Авторы заявляют об отсутствии конфликта интересов.
Funding	**Финансирование**
The work was funded by RFBR, project number 20-04-60274.	Работа выполнена при финансовой поддержке РФФИ в рамках научного проекта РФФИ №20-04-60274.
Provenance and peer review	**Происхождение статьи и рецензирование**
Not commissioned; externally peer reviewed.	Журнал не заказывал статью; внешнее рецензирование.

References / Литература:

1. Li R., Hoffmeister K.M., Falet H. Glycans and the platelet life cycle. *Platelets*. 2016;27(6):505–11. https://doi.org/10.3109/09537104.2016.1171304.
2. Garcia-Souza L.F., Oliveira M.F. Mitochondria: biological roles in platelet physiology and pathology. *Int J Biochem Cell Biol*. 2014;50:156–60. https://doi.org/10.1016/j.biocel.2014.02.015.
3. Junt T., Schulze H., Chen Z. et al. Dynamic visualization of thrombopoiesis within bone marrow. *Science*. 2007;317(5845):1767–70. https://doi.org/10.1126/science.1146304.
4. Lefrançais E., Ortiz-Muñoz G., Caudrillier A. et al. The lung is a site of platelet biogenesis and a reservoir for haematopoietic progenitors. *Nature*. 2017;544(7648):105–9. https://doi.org/10.1038/nature21706.
5. Liu X., Gorzelanny C., Schneider S.W. Platelets in skin autoimmune diseases. *Front Immunol*. 2019;10:1453. https://doi.org/10.3389/fimmu.2019.01453.
6. Haemmerle M., Stone R.L., Menter D.G. et al. The platelet lifeline to cancer: challenges and opportunities. *Cancer Cell*. 2018;33(6):965–83. https://doi.org/10.1016/j.ccell.2018.03.002.
7. Middleton E., Rondina M.T. Platelets in infectious disease. *Hematology*. 2016;2016(1):256–61. https://doi.org/10.1182/asheducation-2016.1.256.
8. Sharda A., Flaumenhaft R. The life cycle of platelet granules. *F1000Research*. 2018;7:236. https://doi.org/10.12688/f1000research.13283.1.
9. Kuravi S.J., Harrison P., Rainger G.E., Nash G.B. Ability of platelet-derived extracellular vesicles to promote neutrophil-endothelial cell interactions. *Inflammation*. 2019;42(1):290–305. https://doi.org/10.1007/s10753-018-0893-5.
10. Ribeiro L.S., Migliari Branco L., Franklin B.S. Regulation of innate immune responses by platelets. *Front Immunol*. 2019;10:1320. https://doi.org/10.3389/fimmu.2019.01320.
11. Liu J., van Sommeren S., Huang H. et al. Association analyses identify 38 susceptibility loci for inflammatory bowel disease and highlight shared genetic risk across populations. *Nat Genet*. 2015;47(979):86. https://doi.org/10.1038/ng.3359.
12. Riaz A.H., Tasma B.E., Woodman M.E. et al. Human platelets efficiently kill IgG-opsonized E. coli. *FEMS Immunol Med Microbiol*. 2012;65(1):78–83. https://doi.org/10.1111/j.1574-695X.2012.00945.x.
13. Martel C., Cointe S., Maurice P. et al. Requirements for membrane attack complex formation and anaphylatoxins binding to collagen-activated platelets. *PLoS One*. 2011;6(4):e18812. https://doi.org/10.1371/journal.pone.0018812.
14. Clemetson K.J., Clemetson J.M., Proudfoot A.E. et al. Functional expression of CCR1, CCR3, CCR4, and CXCR4 chemokine receptors on human platelets. *Blood*. 2000;96(13):4046–54.
15. D'Atri L.P., Etulain J., Rivadeneyra L. et al. Expression and functionality of Toll-like receptor 3 in the megakaryocytic lineage. *J Thromb Haemost*. 2015;13(5):839–50. https://doi.org/10.1111/jth.12842.

16. Hamzeh-Cognasse H., Berthelot P., Tardy B. et al. Platelet toll-like receptors are crucial sensors of infectious danger moieties. *Platelets*. 2018;29(6):533–40. https://doi.org/10.1080/09537104.2018.1445842.
17. Sreeramkumar V., Adrover J.M., Ballesteros I. et al. Neutrophils scan for activated platelets to initiate inflammation. *Science*. 2014;346(6214):1234–8. https://doi.org/10.1126/science.1256478.
18. Rossaint J., Kühne K., Skupski J. et al. Directed transport of neutrophil-derived extracellular vesicles enables platelet-mediated innate immune response. *Nat Commun*. 2016;7:13464. https://doi.org/10.1038/ncomms13464.
19. Duerschmied D., Suidan G.L., Demers M. et al. Platelet serotonin promotes the recruitment of neutrophils to sites of acute inflammation in mice. *Blood*. 2013;121(6):1008–15. https://doi.org/10.1182/blood-2012-06-437392.
20. Slaba I., Wang J., Kolaczkowska E. et al. Imaging the dynamic platelet-neutrophil response in sterile liver injury and repair in mice. *Hepatology*. 2015;62(5):1593–605. https://doi.org/10.1002/hep.28003.
21. Zuchtriegel G., Uhl B., Puhr-Westerheide D. et al. Platelets guide leukocytes to their sites of extravasation. *PLoS Biol*. 2016;14(5):e1002459. https://doi.org/10.1371/journal.pbio.1002459.
22. Alard J-.E., Ortega-Gomez A., Wichapong K. et al. Recruitment of classical monocytes can be inhibited by disturbing heteromers of neutrophil HNP1 and platelet CCL5. *Sci Transl Med*. 2015;7(317):317ra196. https://doi.org/10.1126/scitranslmed.aad5330.
23. Léon C., Ravanat C., Freund M. et al. Differential involvement of the P2Y1 and P2Y12 receptors in platelet procoagulant activity. *Arterioscler Thromb Vasc Biol*. 2003;23(10):1941–7. https://doi.org/10.1161/01.ATV.0000092127.16125.E6.
24. Liverani E., Rico M.C., Yaratha L. et al. LPS-induced systemic inflammation is more severe in P2Y12 null mice. *J Leukoc Biol*. 2014;95(2):313–23. https://doi.org/10.1189/jlb.1012518.
25. Vogel S., Bodenstein R., Chen Q. et al. Platelet-derived HMGB1 is a critical mediator of thrombosis. *J Clin Invest*. 2015;125(12):4638–54. https://doi.org/10.1172/JCI81660.
26. Fox J.M., Kausar F., Day A. et al. CXCL4/Platelet Factor 4 is an agonist of CCR1 and drives human monocyte migration. *Sci Rep*. 2018;8(1):9466. https://doi.org/10.1038/s41598-018-27710-9.
27. Gaertner F., Ahmad Z., Rosenberger G. et al. Migrating platelets are mechano-scavengers that collect and bundle bacteria. *Cell*. 2017;171(6):1368–1382.e23. https://doi.org/10.1016/j.cell.2017.11.001.
28. Assinger A., Laky M., Schabbauer G. et al. Efficient phagocytosis of periodontopathogens by neutrophils requires plasma factors, platelets and TLR2. *J Thromb Haemost*. 2011;9(4):799–809. https://doi.org/10.1111/j.1538-7836.2011.04193.x.
29. Wuescher L.M., Takashima A., Worth R.G. A novel conditional platelet depletion mouse model reveals the importance of platelets in protection against Staphylococcus aureus bacteremia. *J Thromb Haemost*. 2015;13(2):303–13. https://doi.org/10.1111/jth.12795.
30. Hurley S.M., Kahn F., Nordenfelt P. et al. Platelet-dependent neutrophil function is dysregulated by M protein from Streptococcus pyogenes. *Infect Immun*. 2015;83(9):3515–25. https://doi.org/10.1128/IAI.00508-15.
31. Kho S., Barber B.E., Johar E. et al. Platelets kill circulating parasites of all major Plasmodium species in human malaria. *Blood*. 2018;132(12):1332–44. https://doi.org/10.1182/blood-2018-05-849307.
32. Laffont B., Corduan A., Rousseau M. et al. Platelet microparticles reprogram macrophage gene expression and function. *Thromb Haemost*. 2016;115(2):311–23. https://doi.org/10.1160/TH15-05-0389.
33. Weyrich A.S., Elstad M.R., McEver R.P. et al. Activated platelets signal chemokine synthesis by human monocytes. *J Clin Invest*. 1996;97(6):1525–34. https://doi.org/10.1172/JCI118575.
34. Hwaiz R., Rahman M., Syk I. et al. Rac1-dependent secretion of platelet-derived CCL5 regulates neutrophil recruitment via activation of alveolar macrophages in septic lung injury. *J Leukoc Biol*. 2015;97(5):975–84. https://doi.org/10.1189/jlb.4A1214-603R.
35. Duffau P., Seneschal J., Nicco C. et al. Platelet CD154 potentiates interferon-α secretion by plasmacytoid dendritic cells in systemic lupus erythematosus. *Sci Transl Med*. 2010;2(47):47ra63. https://doi.org/10.1126/scitranslmed.3001001.
36. Vanichakarn P., Blair P., Wu C. et al. Neutrophil CD40 enhances platelet-mediated inflammation. *Thromb Res*. 2008;122(3):346–58. https://doi.org/10.1016/j.thromres.2007.12.019.
37. Tunjungputri R.N., Li Y., de Groot P.G. et al. The inter-relationship of platelets with interleukin-1β-mediated inflammation in humans. *Thromb Haemost*. 2018;118(12):2112–25. https://doi.org/10.1055/s-0038-1675603.
38. Hottz E.D., Lopes J.F., Freitas C. et al. Platelets mediate increased endothelium permeability in dengue through NLRP3-inflammasome activation. *Blood*. 2013;122(20):3405–14. https://doi.org/10.1182/blood-2013-05-504449.
39. Xiang B., Zhang G., Guo L. et al. Platelets protect from septic shock by inhibiting macrophage-dependent inflammation via the cyclooxygenase 1 signalling pathway. *Nat Commun*. 2013;4:2657. https://doi.org/10.1038/ncomms3657.
40. Hally K.E., La Flamme A.C., Harding S.A., Larsen P.D. Platelets regulate leucocyte responses to Toll-like receptor stimulation. *Clin Transl Immunology*. 2018;7(7):e1036. https://doi.org/10.1002/cti2.1036.
41. Ascherio A., Munger K.L. Environmental risk factors for multiple sclerosis. Part I: the role of infection. *Ann Neurol*. 2007;61(4):288–99. https://doi.org/10.1002/ana.21117.
42. Clark S.R., Ma A.C., Tavener S.A. et al. Platelet TLR4 activates neutrophil extracellular traps to ensnare bacteria in septic blood. *Nat Med*. 2007;13(4):463–9. https://doi.org/10.1038/nm1565.
43. McDonald B., Urrutia R., Yipp B.G. et al. Intravascular neutrophil extracellular traps capture bacteria from the bloodstream during sepsis. *Cell Host Microbe*. 2012;12(3):324–33. https://doi.org/10.1016/j.chom.2012.06.011.
44. Zhou H., Deng M., Liu Y. et al. Platelet HMGB1 is required for efficient bacterial clearance in intra-abdominal bacterial sepsis in mice. *Blood Adv*. 2018;2(6):638–48. https://doi.org/10.1182/bloodadvances.2017011817.
45. Carestia A., Kaufman T., Schattner M. Platelets: new bricks in the building of neutrophil extracellular traps. *Front Immunol*. 2016;7:271. https://doi.org/10.3389/fimmu.2016.00271.
46. Ojha A., Nandi D., Batra H. et al. Platelet activation determines the severity of thrombocytopenia in dengue infection. *Sci Rep*. 2017;7:41697. https://doi.org/10.1038/srep41697.
47. Mayne E., Funderburg N.T., Sieg S.F. et al. Increased platelet and microparticle activation in HIV infection: upregulation of P-selectin and tissue factor expression. *J Acquir Immune Defic Syndr*. 2012;59(4):340–6. https://doi.org/10.1097/QAI.0b013e3182439355.
48. Ackermann M., Verleden S.E., Kuehnel M. et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. *N Engl J Med*. 2020;383(2):120–8. https://doi.org/10.1056/NEJMoa2015432.
49. Banerjee M., Huang Y., Joshi S. et al. Platelets endocytose viral particles and are activated via TLR (toll-like receptor) signaling. *Arterioscl Thromb Vasc Biol*. 2020;40(7):1635–50. https://doi.org/10.1161/ATVBAHA.120.314180.
50. Parker Z.F., Rux A.H., Riblett A.M. et al. Platelet factor 4 inhibits and enhances HIV-1 infection in a concentration-dependent manner by modulating viral attachment. *AIDS Res Hum Retroviruses*. 2016;32(7):705–17. https://doi.org/10.1089/AID.2015.0344.
51. Mohan K.V., Rao S.S., Atreya C.D. Antiviral activity of selected antimicrobial peptides against vaccinia virus. *Antiviral Res*. 2010;86(3):306–11. https://doi.org/10.1016/j.antiviral.2010.03.012.
52. Schrottmaier W.C., Salzmann M., Badrnya S. et al. Platelets mediate serological memory to neutralize viruses in vitro and in vivo. *Blood Adv*. 2020;4(16):3971–6. https://doi.org/10.1182/bloodadvances.2020001786.
53. George J.N., Saucerman S., Levine S.P. et al. Immunoglobulin G is a platelet alpha granule-secreted protein. *J Clin Invest*. 1985;76(5):2020–5. https://doi.org/10.1172/JCI112203.
54. Assinger A., Kral J.B., Yaiw K.C. et al. Human Cytomegalovirus–platelet interaction triggers toll-like receptor 2–dependent proinflammatory and proangiogenic responses. *Arterioscler Thromb Vasc Biol*. 2014;34(4):801–9. https://doi.org/10.1161/ATVBAHA.114.303287.
55. Chapman L.M., Aggrey A.A., Field D.J. et al. Platelets present antigen in the context of MHC class I. *J Immunol*. 2012;189(2):916–23. https://doi.org/10.4049/jimmunol.1200580.
56. Czapiga M., Kirk A.D., Lekstrom-Himes J. Platelets deliver costimulatory signals to antigen-presenting cells: a potential bridge between injury and immune activation. *Exp Hematol*. 2004;32(2):135–9. https://doi.org/10.1016/j.exphem.2003.11.004.
57. Barbosa-Lima G., Hottz E.D., de Assis E.F. et al. Dengue virus-activated

platelets modulate monocyte immunometabolic response through lipid droplet biogenesis and cytokine signaling. *J Leukoc Biol*. 2020;108(4):1293–306. https://doi.org/10.1002/JLB.4MA0620-658R.
58. Chaipan C., Soilleux E.J., Simpson P. et al. DC-SIGN and CLEC-2 mediate human immunodeficiency virus type 1 capture by platelets. *J Virol*. 2006;80(18):8951–60. https://doi.org/10.1128/JVI.00136-06.
59. Terada H., Baldini M., Ebbe S., Madoff M.A. Interaction of influenza virus with blood platelets. *Blood*. 1966;28(2):213–28.
60. Zahn A., Jennings N., Ouwehand W.H., Allain J.-P. Hepatitis C virus interacts with human platelet glycoprotein VI. *J Gen Virol*. 2006;87(Pt 8):2243–51. https://doi.org/10.1099/vir.0.81826-0.
61. Sørensen A.L., Rumjantseva V., Nayeb-Hashemi S. et al. Role of sialic acid for platelet life span: exposure of β-galactose results in the rapid clearance of platelets from the circulation by asialoglycoprotein receptor–expressing liver macrophages and hepatocytes. *Blood*. 2009;114(8):1645–54. https://doi.org/10.1182/blood-2009-01-199414.
62. Stenberg P.E., Levin J., Baker G. et al. Neuraminidase-induced thrombocytopenia in mice: Effects on thrombopoiesis. *J Cell Physiol*. 1991;147(1):7–16. https://doi.org/10.1002/jcp.1041470103.
63. Isomura H., Yoshida M., Namba H. et al. Suppressive effects of human herpesvirus-6 on thrombopoietin-inducible megakaryocytic colony formation in vitro. *J Gen Virol*. 2000;81(Pt 3):663–73. https://doi.org/10.1099/0022-1317-81-3-663.
64. Gonelli A., Mirandola P., Grill V. et al. Human herpesvirus 7 infection impairs the survival/differentiation of megakaryocytic cells. *Haematologica*. 2002;87(11):1223–5.
65. Zapata J.C., Cox D., Salvato M.S. The role of platelets in the pathogenesis of viral hemorrhagic fevers. *PLoS Negl Trop Dis*. 2014;8(6):e2858. https://doi.org/10.1371/journal.pntd.0002858.
66. Hottz E.D., Oliveira M.F., Nunes P.C. et al. Dengue induces platelet activation, mitochondrial dysfunction and cell death through mechanisms that involve DC-SIGN and caspases. *J Thromb Haemost*. 2013;11(5):951–62. https://doi.org/10.1111/jth.12178.
67. Pastori D., Esposito A., Carnevale R. et al. HIV-1 induces in vivo platelet activation by enhancing platelet NOX2 activity. *J Infect*. 2015;70(6):651–8. https://doi.org/10.1016/j.jinf.2015.01.005.
68. Bik T., Sarov I., Livne A. Interaction between vaccinia virus and human blood platelets. *Blood*. 1982;59(3):482–7.
69. Negrotto S., de Giusti J.C., Rivadeneyra L. et al. Platelets interact with coxsackieviruses B and have a critical role in the pathogenesis of virus-induced myocarditis. *J Thromb Haemost*. 2015;13(2):271–82. https://doi.org/10.1111/jth.12782.
70. Sottnek H.M., Campbell W.G., Cassel W.A. The pathogenesis of Vaccinia virus toxicity. II. An electron microscopic study. *Lab Invest*. 1975;33(5):522–32.
71. Moore C., Tymvios C., Michael E. Functional regulation of vascular and platelet activity during thrombosis by nitric oxide and endothelial nitric oxide synthase. *Thromb Haemost*. 2010;104(2):342–9. https://doi.org/10.1160/TH09-11-0764.
72. Bouwman J., Visseren F., Bosch M. et al. Procoagulant and inflammatory response of virus-infected monocytes. *Eur J Clin Iinvest*. 2002;32(10):759–66. https://doi.org/10.1046/j.1365-2362.2002.01041.x.
73. Goeijenbier M., van Wissen M., van De Weg C. et al. Review: Viral infections and mechanisms of thrombosis and bleeding. *J Med Virol*. 2012;84(10):1680–96. https://doi.org/10.1002/jmv.23354.
74. Gavrilovskaya I.N., Gorbunova E.E., Mackow E.R. Pathogenic hantaviruses direct the adherence of quiescent platelets to infected endothelial cells. *J Virol*. 2010;84(9):4832–9. https://doi.org/10.1128/JVI.02405-09.
75. Sabin C.A., Reiss P., Ryom L. et al. Is there continued evidence for an association between abacavir usage and myocardial infarction risk in individuals with HIV? A cohort collaboration. *BMC Med*. 2016;14:61. https://doi.org/10.1186/s12916-016-0588-4.
76. Taylor K.A., Smyth E., Rauzi F. et al. Pharmacological impact of antiretroviral therapy on platelet function to investigate human immunodeficiency virus-associated cardiovascular risk. *Br J Pharmacol*. 2019;176(7):879–89. https://doi.org/10.1111/bph.14589.
77. Khawaja A.A., Taylor K.A., Lovell A.O. et al. HIV antivirals affect endothelial activation and endothelial-platelet crosstalk. *Circ Res*. 2020;127(11):1365–80. https://doi.org/10.1161/CIRCRESAHA.119.316477.
78. Engelmann B., Massberg S. Thrombosis as an intravascular effector of innate immunity. *Nat Rev Immunol*. 2013;13(1):34–45. https://doi.org/10.1038/nri3345.
79. Gu S.X., Tyagi T., Jain K. et al. Thrombocytopathy and endotheliopathy: crucial contributors to COVID-19 thromboinflammation. *Nat Rev Cardiol*. 2021;18(3):194–209. https://doi.org/10.1038/s41569-020-00469-1.
80. Campbell R.A., Boilard E., Rondina M.T. Is there a role for the ACE2 receptor in SARS-CoV-2 interactions with platelets? *J Thromb Haemost*. 2021;19(1):46–50. https://doi.org/10.1111/jth.15156.
81. Hoffmann M., Kleine-Weber H., Schroeder S. et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*. 2020;181(2):271–80.e8. https://doi.org/10.1016/j.cell.2020.02.052.
82. Manne B.K., Denorme F., Middleton E.A. et al. Platelet gene expression and function in patients with COVID-19. *Blood*. 2020;136(11):1317–29. https://doi.org/10.1182/blood.2020007214.
83. Zhang S., Liu Y., Wang X. et al. SARS-CoV-2 binds platelet ACE2 to enhance thrombosis in COVID-19. *J Hematol Oncol*. 2020;13:120. https://doi.org/10.1186/s13045-020-00954-7.
84. Zini G., Bellesi S., Ramundo F., d'Onofrio G. Morphological anomalies of circulating blood cells in COVID-19. *Am J Hematol*. 2020;95(7):870–2. https://doi.org/10.1002/ajh.25824.
85. Zaid Y., Guessous F., Puhm F. et al. Platelet reactivity to thrombin differs between patients with COVID-19 and those with ARDS unrelated to COVID-19. *Blood Adv*. 2021;5(3):635–9. https://doi.org/10.1182/bloodadvances.2020003513.
86. Taus F., Salvagno G., Canè S. et al. Platelets promote thromboinflammation in SARS-CoV-2 pneumonia. *Arterioscl Thromb Vasc Biol*. 2020;40(12):2975–89. https://doi.org/10.1161/ATVBAHA.120.315175.
87. Mehta P., McAuley D.F., Brown M. et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020;395(10229):1033–4. https://doi.org/10.1016/S0140-6736(20)30628-0.
88. Chow J.H., Khanna A.K., Kethireddy S. et al. Aspirin use is associated with decreased mechanical ventilation, intensive care unit admission, and in-hospital mortality in hospitalized patients with coronavirus disease 2019. *Anesth Analg*. 2021;132(4):930–41. https://doi.org/10.1213/ANE.0000000000005292.

About the authors:

Ekaterina V. Slukhanchuk – MD, PhD, Associate Professor, Department of Obstetrics and Gynecology, Filatov Clinical Institute of Children's Health, Sechenov University, Moscow Russia; Obstetrician-Gynecologist, Department of Abdominal Surgery and Oncology 2, Petrovsky National Research Centre of Surgery, Moscow, Russia. E-mail: ekaterina@ginekologhirurg.ru. ORCID: https://orcid.org/0000-0001-7441-2778.

Victoria O. Bitsadze – MD, Dr Sci Med, Professor of RAS, Professor, Department of Obstetrics and Gynecology, Filatov Clinical Institute of Children's Health, Sechenov University, Moscow, Russia. ORCID: https://orcid.org/0000-0001-8404-1042. Scopus Author ID: 6506003478. Researcher ID: F-8409-2017.

Jamilya Kh. Khizroeva – MD, Dr Sci Med, Professor, Department of Obstetrics and Gynecology, Filatov Clinical Institute of Children's Health, Sechenov University, Moscow, Russia. ORCID: https://orcid.org/0000-0002-0725-9686. Scopus Author ID: 57194547147. Researcher ID: F-8384-2017.

Antonina G. Solopova – MD, Dr Sci Med, Professor, Department of Obstetrics and Gynecology, Filatov Clinical Institute of Children's Health, Sechenov University, Moscow, Russia. ORCID: https://orcid.org/0000-0002-7456-2386. Scopus Author ID: 6505479504. Researcher ID: Q-1385-2015.

Valentina I. Tsibizova – MD, PhD, Obstetrician-Gynecologist, Research Laboratory of Operative Gynecology, Institute of Perinatology and Pediatrics; Physician, Department of Functional and Ultrasound Diagnostics, Almazov National Medical Research Centre, Saint Petersburg, Russia. ORCID: https://orcid.org/0000-0001-5888-0774.

Fidan Yakubova – MD, Clinical Resident, Department of Obstetrics and Gynecology, Filatov Clinical Institute of Children's Health, Sechenov University, Moscow, Russia. ORCID: https://orcid.org/0000-0002-8882-1588.

Cihan Ay – MD, PhD, Professor, Department of Medicine I, Clinical Division of Haematology and Haemostaseology, Medical University of Vienna, Vienna, Austria. ORCID: https://orcid.org/0000-0003-2607-9717. Scopus Author ID: 55356863800.
Jean-Christophe Gris – MD, Dr Sci Med, Professor, Department of Obstetrics and Gynecology, Filatov Clinical Institute of Children's Health, Sechenov University, Moscow, Russia; University of Montpellier, Montpellier, France. ORCID: https://orcid.org/0000-0002-9899-9910. Researcher ID: AAA-2923-2019.
Alexander D. Makatsariya – MD, Dr Sci Med, Academician of RAS, Professor, Head of the Department of Obstetrics and Gynecology, Filatov Clinical Institute of Chil-dren's Health, Sechenov University, Moscow, Russia. ORCID: https://orcid.org/0000-0001-7415-4633. Scopus Author ID: 57222220144. Researcher ID: M-5660-2016.

Сведения об авторах:
Слуханчук Екатерина Викторовна – к.м.н., доцент кафедры акушерства и гинекологии Клинического института детского здоровья имени Н.Ф. Филатова ФГАОУ ВО Первый Московский государственный медицинский университет имени И.М. Сеченова Министерства здравоохранения Российской Федерации (Сеченовский Университет), Москва, Россия; врач акушер-гинеколог отделения абдоминальной хирургии и онкологии 2, ФГБНУ «Российский научный центр хирургии имени академика Б.В. Петровского», Москва, Россия. E-mail: ekaterina@ginekologhirurg.ru. ORCID: https://orcid.org/0000-0001-7441-2778.
Бицадзе Виктория Омаровна – д.м.н., профессор РАН, профессор кафедры акушерства и гинекологии Клинического института детского здоровья имени Н.Ф. Филатова ФГАОУ ВО Первый Московский государственный медицинский университет имени И.М. Сеченова Министерства здравоохранения Российской Федерации (Сеченовский Университет), Москва, Россия. ORCID: https://orcid.org/0000-0001-8404-1042. Scopus Author ID: 6506003478. Researcher ID: F-8409-2017.
Хизроева Джамиля Хизриевна – д.м.н., профессор кафедры акушерства и гинекологии Клинического института детского здоровья имени Н.Ф. Филатова ФГАОУ ВО Первый Московский государственный медицинский университет имени И.М. Сеченова Министерства здравоохранения Российской Федерации (Сеченовский университет), Москва, Россия. ORCID: https://orcid.org/0000-0002-0725-9686. Scopus Author ID: 57194547147. Researcher ID: F-8384-2017.
Солопова Антонина Григорьевна – д.м.н., профессор кафедры акушерства и гинекологии Клинического института детского здоровья имени Н.Ф. Филатова ФГАОУ ВО Первый Московский государственный медицинский университет имени И.М. Сеченова Министерства здравоохранения Российской Федерации (Сеченовский Университет), Москва, Россия. ORCID: https://orcid.org/0000-0002-7456-2386. Scopus Author ID: 6505479504. Researcher ID: Q-1385-2015.
Цибизова Валентина Ивановна – к.м.н., врач акушер-гинеколог НИЛ оперативной гинекологии Института перинатологии и педиатрии, врач отделения функциональной ультразвуковой диагностики ФГБУ «Национальный медицинский исследовательский центр имени В.А. Алмазова» Министерства здравоохранения Российской Федерации, Санкт-Петербург, Россия. ORCID: https://orcid.org/0000-0001-5888-0774.
Якубова Фидан – клинический ординатор кафедры акушерства и гинекологии Клинического института детского здоровья имени Н.Ф. Филатова ФГАОУ ВО Первый Московский государственный медицинский университет имени И.М.Сеченова Министерства здравоохранения Российской Федерации (Сеченовский Университет), Москва, Россия. ORCID: https://orcid.org/0000-0002-8882-1588.
Ай Джихан – д.м.н., профессор, клиническое подразделение гематологии и гемостазиологии, медицинское отделение I, Венский университет, Вена, Австрия. ORCID: https://orcid.org/0000-0003-2607-9717. Scopus Author ID: 55356863800.
Гри Жан-Кристоф – д.м.н., профессор кафедры акушерства и гинекологии Клинического института детского здоровья имени Н.Ф. Филатова ФГАОУ ВО Первый Московский государственный медицинский университет имени И.М. Сеченова Министерства здравоохранения Российской Федерации (Сеченовский университет), Москва, Россия; профессор гематологии, университет Монпелье, Монпелье, Франция. ORCID: https://orcid.org/0000-0002-9899-9910. Researcher ID: AAA-2923-2019.
Макацария Александр Давидович – д.м.н., профессор, академик РАН, зав. кафедрой акушерства и гинекологии Клинического института детского здоровья имени Н.Ф. Филатова ФГАОУ ВО Первый Московский государственный медицинский университет имени И.М. Сеченова Министерства здравоохранения Российской Федерации (Сеченовский Университет), Москва, Россия. ORCID: https://orcid.org/0000-0001-7415-4633. Scopus Author ID: 57222220144. Researcher ID: M-5660-2016.