Genij Ortopedii. 2022. Vol. 28, no. 2. P. 189-193.

Original article

https://doi.org/10.18019/1028-4427-2022-28-2-189-193

Monitoring of the most common gram-positive microflora and its antibiotic sensitivity in persons with chronic osteomyelitis over a three-year period

Irina V. Shipitsyna[1]✉, Elena V. Osipova[2]

[1, 2] Ilizarov National Medical Research Centre for Traumatology and Orthopedics, Kurgan, Russian Federation

[1] ivschimik@mail.ru
[2] E-V-OsipovA@mail.ru

Abstract

Purpose To study the most common gram-positive microflora and its antibiotic sensitivity in chronic osteomyelitis over a three-year period. **Materials and methods** The microbiological study included 5,226 clinical isolates of gram-positive microorganisms belonging to 6 taxa (*S. aureus, S. epidermidis, S. saprophyticus, Enterococcus sp., Streptococcus sp., Corynebacterium sp.*), detected in the period from 2017 to 2019 in primary cultures from wounds and fistulas of 5,116 patients with chronic osteomyelitis who were treated in the purulent department of our bone infection clinic. **Results and its discussion** According to our study, *S. aureus* strains are most common g gram-positive microflora in chronic osteomyelitis, taking the first place in terms of occurrence over a three-year period. The rate of isolation of methicillin-resistant strains of *S. aureus* (MRSA) over three years was 17.3 ± 1.9 %. In 2019, the occurrence of *S. epidermidis* strains increased by 28 % compared to 2017, while the number of isolated MRSE remained within 57.2 ± 1.8 %. The analysis of antibiotic patterns showed a tendency to an increase in the number of multi-resistant strains of *Staphylococcus sp*. Monitoring of the gram-positive microflora in chronic osteomyelitis revealed an insignificant isolation of the bacteria of the genus *Enterococcus* and *Streptococcus* (9–10 % of cases). The most effective against *Enterococcus* strains were glycopeptides and aminopenicillins, the least effective against strains of Enterococcus were quinolones and aminoglycosides. The most effective drugs against *Streptococcus sp*. were levofloxacin and clindamycin. The occurrence of bacteria of the genus *Corynebacterium sp*. was within 3–4 %. The least effective drugs against *Corynebacterium sp*. were clindamycin, gentamicin, and ciprofloxacin. The strains were susceptible to tetracycline drugs, penicillins, macrolides and rifampicin. **Conclusions** Considering that gram-positive microorganisms are primary pathogens in the etiology of chronic osteomyelitis, microbiological monitoring of the leading pathogens of the disease and their resistance enables to identify ineffective antibacterial drugs, optimize treatment, and thereby reduce the rate of poor outcomes in the management of the disease.

Keywords: chronic osteomyelitis, antibiotics, resistance, gram-positive microflora

For citation: Shipitsyna I.V., Osipova E.V. Monitoring of the most common gram-positive microflora and its antibiotic sensitivity in persons with chronic osteomyelitis over a three-year period. *Genij Ortopedii*, 2022, vol. 28, no 2, pp. 189-193. https://doi.org/10.18019/1028-4427-2022-28-2-189-193

INTRODUCTION

Despite the achievements of contemporary medicine, the problem of treating chronic osteomyelitis remains relevant [1–8]. In the etiological structure of chronic osteomyelitis, gram-positive microflora has been occupying a leading position for many years. The most common genus is represented by strains of *Staphylococcus aureus* [2, 3, 6–11]. Coagulase-negative staphylococci are also actively involved in the infection process in persons who undergo joint arthroplasty [2, 6–14]. The role of bacterial associations and prevalence of mixed cultures, represented by both gram-negative and gram-positive microorganisms, has increased in the pathogenesis of the inflammatory process in chronic osteomyelitis, [2, 7–16]. Over the past few years, the number of isolated methicillin-resistant *Staphylococcus sp*. strains characterized by resistance to beta-lactam antibiotics has grown. It has led to a renewed interest in the use of macrolides, lincosamides, and streptogramins [17–21]. At the same time, the percentage of multi-resistant staphylococci has been growing. It results in the ineffectiveness of empirical antibiotic therapy and, as a consequence, worsens the prognosis of the disease and prolongs hospitalization. Therefore, to control the effectiveness of prescribed drugs and to timely adjust the protocol of antibiotic therapy is a necessity aimed at containing the emergence of non-susceptible strains. Annual monitoring could assist in the fulfillment of this task.

Purpose To study the spectrum of the most common gram-positive microflora and its antibiotic sensitivity in patients with chronic osteomyelitis over a three-year period.

MATERIAL AND METHODS

This microbiological study included 5,226 clinical isolates of gram-positive microorganisms belonging to 6 taxa (*S. aureus, S. epidermidis, S. saprophyticus, Enterococcus sp., Streptococcus sp., Corynebacterium sp.*), detected in primary cultures from wounds and fistulas of 5,116 patients, who were treated in the infection department of the Federal State Budgetary Institution Ilizarov NMRC for TO of the Ministry of

© Shipitsyna I.V., Osipova E.V., 2022

Health of Russia within the period from 2017 to 2019. The criterion for the inclusion of a clinical isolate in the study is the contamination during bacteriological inoculation of 104 or more colony-forming units (CFU) per 1 ml.

Isolation of pure cultures was performed by routine methods or using a Walkaway-40 plus bacteriological analyzer (Siemens, USA). Determination of the sensitivity of microorganisms to drugs used in the clinical settings was carried out with gram-positive panels PBPC 20 (WalkAway-40 Plus, Siemens).

Statistical processing of the results was performed using the data analysis software AtteStat, version 13.0. The arithmetic mean and its standard error (M ± m) were calculated.

RESULTS

In 2017, the number of clinical gram-positive bacteria isolates from patients' wounds and fistulas was 1669 that beloned to 6 taxa: 1096 *Staphylococcus aureus* strains, 349 – *Staphylococcus epidermidis*, 14 – *Staphylococcus saprophyticus*, 127 – *Enterococcus sp*., 25 – *Streptococcus sp*., 58 – *Corynebacterium sp*. The number of MRS (methicillin-resistant staphylococci) was 398 strains, among them 191 – MRSA (methicillin-resistant *S. aureus*), 205 – MRSE (methicillin-resistant *S. epidermidis*), 2 – MRSS (methicillin-resistant *S. saprophyticus*).

In 2018, bacterial cultures showed 1682 clinical isolates of gram-positive bacteria, including 994 strains of *S. aureus*, 370 – *S. epidermidis*, 39 – *S. saprophyticus*, 166 – *Enterococcus sp*., 43 – *Streptococcus sp*., 70 – *Corynebacterium sp*. There were 397 isolates of MRS: 184 strains of MRSA, 208 – MRSE, 5 – MRSS.

In 2019, there were 1875 isolates including 1147 strains of *S. aureus*, 448 – *S. epidermidis*, 32 – *S. saprophyticus*, 162 – *Enterococcus sp*., 44 – *Streptococcus sp*., 42 – *Corynebacterium sp*. The total number of MRS was 447 strains (185 – MRSA, 254 – MRSE, 8 – MRSS).

The rates of gram-positive bacteria isolation in chronic osteomyelitis over a three-year period are presented in Table 1.

The analysis of antibiotic sensitivity of the bacteria of the genus *Staphylococcus* within the period from 2017 to 2019 shows high rates of multi-resistant strains among methicillin-resistant staphylococci (Table 2).

The number of aminoglycoside-resistant MSSE strains decreased by 60 %, MRSE – by 18.5 %, MRSA – by 18.2 %, MRSS – by 15.5 %. In 2018 and 2019, gentamicin was effective against 100 % of MSSS isolates studied. With regard to MSSA, the number of resistant strains remained within 3 % for three years.

Clindamycin was the least effective against MRSS, MRSE and MRSA strains (in 2019 the number of resistant isolates was 100 %, 66 % and 58 %, respectively).

Among the second generation of quinolones, ciprofloxacin showed the least activity against MRSA, MRSS, and MRSE. The drug showed the highest activity against 100 % of MSSS strains and 94 % against MSSA strains.

Table 1

Rates of gram-positive bacteria isolation in chronic osteomyelitis over a three-year period, %

Microorganism	2017	2018	2019
S. aureus	65.7	59.1	61.2
S. epidermidis	20.9	21.9	23.9
S. saprophyticus	0.8	2.3	1.9
Enterococcus sp.	7.6	9.9	8.6
Streptococcus sp.	1.5	2.6	2.3
Corynebacterium sp.	3.5	4.2	2.2

Table 2

Number of resistant strains of genus *Staphylococcus*, %

Drug name	Year	MSSA	MRSA	MSSS	MRSS	MSSE	MRSE
Gentamicin	2017	3	71	8	100	22	77
	2018	3	62	0	50	9	53
	2019	3	60	0	75	9	63
Clindamycin	2017	9	61	31	100	14	57
	2018	5	57	21	17	16	36
	2019	5	58	8	100	10	66
Cefoxitin	2017	0	100	0	100	0	100
	2018	0	100	0	100	0	100
	2019	0	100	0	100	0	100
Ciprofloxacin	2017	5	85	0	100	18	72
	2018	6	79	0	50	17	61
	2019	6	83	0	75	19	66
Erythromycin	2017	14	66	39	100	27	75
	2018	7	41	26	83	30	73
	2019	12	62	12	75	31	75

Erythromycin showed weak activity against MRSS and MRSE (75 % of resistant isolates, respectively).

With respect to bacteria of the genus *Enterococcus sp*., the most effective drugs were vancomycin (there were no insensitive strains) and ampicillin (the number of resistant strains was within 31.4 ± 3.9 %). Ciprofloxacin showed the least activity (the number of resistant strains increased by 20 % compared to 2017) and gentamicin (50.9 ± 4.9 % of resistant strains) (Table 3).

Bacteria of the genus *Streptococcus sp*. had good sensitivity to antibiotics. Thus, the most effective drugs were levofloxacin and clindamycin (Table 4).

The least effective drugs against strains of *Corynebacterium sp*. were clindamycin, gentamicin, and ciprofloxacin (Table 5). The number of strains that were resistant to rifampicin decreased by 59.2 % against the findings in 2017.

Table 3

Number of resistant strains of genus *Enterococcus*, %

Year	Ampicillin	Penicillin	Vancomycin	Gentamicin	Levofloxacin	Ciprofloxacin
2017	31.7	60.1	0	55.2	54.0	57.1
2018	34.2	38.1	0	45.7	47.2	74.6
2019	28.3	26.3	0	52.0	63.3	71.4

Table 4

Number of resistant strains of genus *Streptococcus sp*., %

Year	Levofloxacin	Penicillin	Erythromycin	Clindamycin
2017	23.5	15.0	25.0	30.1
2018	26.3	23.0	28.6	28.6
2019	13.1	20.2	29.4	16.7

Table 5

Number of resistant strains of genus *Corynebacterium sp*., %

Year	Tetracycline	Erythromycin	Penicillin	Rifanpicin	Clindamycin	Gentamicin	Ciprofloxacin
2017	31.7	50.1	30.1	25.0	67.9	54.0	57.1
2018	34.2	48.2	28.4	14.6	72.3	61.9	54.3
2019	28.3	34.2	24.3	10.2	71.4	66.3	65.6

DISCUSSION

The study revealed that among the most common gram-positive microflora in chronic osteomyelitis, the first place in terms of incidence of occurrence over a three-year period is occupied by strains of *S. aureus*. The rate of meticyllin resistant strains of S. aureus over a three-year period was 17.3 ± 1.9 %.

In 2019, the rate of incidence of *S. epidermidis* strains increased by 28 % compared to 2017. The number of isolated MRSEs remained within 57.2 ± 1.8 %. In the conditions of reduced immunoreactivity of the organism affected byn osteomyelitis, staphylococci can produce a huge number of pathogenicity factors (polysaccharide capsule, surface proteins, carotenoids, catalase, toxins, exotoxins, etc.) and actively display their virulent properties that cause the chronic course of the inflammatory process [2, 16, 25, 26]. Furthermore, strains of *S. aureus* and *S. epidermidis* may be involved in the formation of multilevel biofilms resulting in the ineffectiveness of standard antibiotic therapy [22–28]. The analysis of antibioticograms shows the tendency towards an increase in the number of multi-resistant strains.

The monitoring of the most common gram-positive microflora in chronic osteomyelitis showed an insignificant rate of isolation of bacteria of the genus *Enterococcus* and *Streptococcus* (9–10 % of cases). The most effective against the *Enterococcus* strains were glycopeptides and aminopenicillins, the least effective were quinolones and aminoglycosides. A number of studies have shown that bacteria of the genus *Enterococcus* may induce an inflammatory reaction as part of an association with other bacteria, but subsequently they do not affect the course of the process [3, 10].

It is not uncommon for the coryneform group of bacteria to cause various diseases, including osteomyelitis [29–30]. In our study, the detection of bacteria of the genus *Corynebacterium sp*. was within 3–4 %. Its strains were most sensitive to tetracycline drugs, penicillins, macrolides and rifampicin.

CONCLUSIONS

The monitoring of the most common gram-positive microflora and its antibiotic sensitivity over a three-year period in the individuals with osteomyelitis has shown the prevalence of *S. aureus* and an increased incidence of *S. epidermidis*. The number of gentamicin-resistant staphylococci decreased. Methicillin-resistant strains of *S. aureus* and *S. epidermidis* were characterized by multi-resistance to standard antibacterial drugs.

Due to the fact that gram-positive microorganisms are primary pathogens in the etiology of chronic osteomyelitis, the microbiological monitoring of the most common pathogens and their resistance enables to identify ineffective antibacterial drugs, optimize treatment and, thereby, reduce the rate of poor treatment outcomes.

REFERENCES

1. Mironov S.P., Tsiskarashvili A.V., Gorbatiuk D.S. Chronic post-traumatic osteomyelitis as a problem of contemporary traumatology and orthopedics (literature review). *Genij Ortopedii*, 2019, vol. 25, no 4, pp. 610-621. DOI 10.18019/1028-4427-2019-25-4-610-621.
2. Sakovich N.V., Andreev A.A., Mikulich E.V., Ostroushko A.P., Zviagin V.G. Sovremennye aspekty etiologii, diagnostiki i lecheniia osteomielita [Modern aspects of the etiology, diagnosis and treatment of osteomyelitis]. *Vestnik Eksperimentalnoi i Klinicheskoi Khirurgii*, 2018, vol. 11, no. 1, pp. 70-79. (in Russian)
3. Jerzy K., Francis H. Chronic Osteomyelitis – Bacterial Flora, Antibiotic Sensitivity and Treatment Challenges. *Open Orthop. J.*, 2018, vol. 12, pp. 153-163. DOI: 10.2174/1874325001812010153.
4. Ma X., Han S., Ma J., Chen X., Bai W., Yan W., Wang K. Epidemiology, microbiology and therapeutic consequences of chronic osteomyelitis in northern China: A retrospective analysis of 255 patients. *Sci. Rep*., 2018, vol. 8, no. 1, pp. 14895. DOI: 10.1038/s41598-018-33106-6.
5. Kremers H.M., Nwojo M.E., Ransom J.E., Wood-Wentz C.M., Melton L.J. 3rd, Huddleston P.M. 3rd. Trends in the epidemiology of osteomyelitis: a population-based study, 1969 to 2009. *J. Bone Joint Surg. Am*., 2015, vol. 97, no. 10, pp. 837-845. DOI: 10.2106/JBJS.N.01350.
6. Leonova S.N., Rekhov A.V., Kameka A.L. Bakteriologicheskoe issledovanie ranevogo otdeliaemogo u patsientov s lokalnoi i rasprostranennoi formoi khronicheskogo osteomielita. *Acta Biomedica Scientifica*, 2016, vol. 1, no. 4, pp. 91-94. (in Russian)
7. Kliushin N.M., Liulin S.V., Shipitsyna I.V., Kochnev E.Ia. Analysis of the results of bacteriological study of wounds in patients with implant-associated spinal infection. *Genij Ortopedii*, 2019, T. 25, No 3, pp. 355-359. DOI 10.18019/1028-4427-2019-25-3-355-359.
8. Burnashov S.I., Shipitsyna I.V., Osipova E.V. Mikroflora operatsionnykh ran i svishchei u patsientov s khronicheskim osteomielitom bolshebertsovoi kosti do rekonstruktivnogo lecheniia, pri retsidive infektsii [Microflora of surgical wounds and fistulas in patients with chronic osteomyelitis of the tibia before reconstructive treatment, with recurrence of infection]. *Klinicheskaia Laboratornaia Diagnostika*, 2019, vol. 64, no. 10, pp. 627-631. (in Russian) DOI: 10.18821/0869-2084-2019-64-10-627-631.
9. Terekhova R.P., Mitish V.A., Paskhalova Iu.S., Skladan G.E., Prudnikova S.A., Blatun L.A. Vozbuditeli osteomielita dlinnykh kostei i ikh rezistentnost [Causative agents of osteomyelitis of long bones and their resistance]. *Rany i Ranevye Infektsii*, 2016, vol. 3, no. 2, pp. 24-30. (in Russian)
10. Zimmerli W., Trampuz A., Ochsner P.E. Prosthetic-joint infections. *N. Engl. J. Med*., 2004, vol. 351, no. 16, pp. 1645-1654. DOI: 10.1056/NEJMra040181.
11. Otto M. Coagulase-negative staphylococci as reservoirs of genes facilitating MRSA infection: Staphylococcal commensal species such as Staphylococcus epidermidis are being recognized as important sources of genes promoting MRSA colonization and virulence. *Bioessays*, 2013, vol. 35, no. 1, pp. 4-11. DOI: 10.1002/bies.201200112.
12. Triffault-Fillit C., Ferry T., Laurent F., Pradat P., Dupieux C., Conrad A., Becker A., Lustig S., Fessy M.H., Chidiac C., Valour F.; Lyon BJI Study Group. Microbiologic epidemiology depending on time to occurrence of prosthetic joint infection: a prospective cohort study. *Clin. Microbiol. Infect*., 2019, vol. 25, no. 3, pp. 353-358. DOI: 10.1016/j.cmi.2018.04.035.
13. Bozhkova S.A., Kasimova A.R., Tikhilov R.M., Poliakova E.M., Rukina A.N., Shabanova V.V., Liventsov V.N. Neblagopriiatnye tendentsii v etiologii ortopedicheskoi infektsii: rezultaty 6-letnego monitoringa struktury i rezistentnosti vedushchikh vozbuditelei [Unfavorable trends in the etiology of orthopedic infection: results of a 6-year monitoring of the structure and resistance of the leading pathogens]. *Travmatologiia i ortopediia Rossii*. 2018. t. 24, № 4. s. 20-31. (in Russian) DOI: 10.21823/2311-2905-2018-24-4-20-31.
14. Marcano-Lozada M., Molero-Leon S. 7 Years of Experience in Osteomyelitis Management in Caracas, Venezuela. *Cohesive J. Microbiol. Infect. Dis*., 2018, vol. 2, no. 1, pp. 1-9. DOI: 10.31031/CJMI.2018.02.000530.
15. Dakher Z.R. Analiz assotsiatsii mikroorganizmov pri osteomielite trubchatykh kostei [Analysis of associations of microorganisms in osteomyelitis of tubular bones]. *Integrativnye Tendentsii v Meditsine i Obrazovanii*, 2016, vol. 4, pp. 30-31. (in Russian)
16. Shipitsyna I.V., Osipova E.V. Bioplenkoobrazuiushchaia sposobnost vydelennykh iz ran bolnykh khronicheskim osteomielitom shtammov Staphylococcus aureus i Pseudomonas aeruginosa i ikh assotsiatsii, poluchennykh in vitro [Biofilm-forming ability of strains of Staphylococcus aureus and Pseudomonas aeruginosa isolated from wounds of patients with chronic osteomyelitis and their associations obtained in vitro]. *Uspekhi Sovremennogo Estestvoznaniia*, 2014, no. 11-3, pp. 18-21. (in Russian)
17. Mitrofanov V.N., Gordinskaia N.A. Fenotip antibiotikorezistentnosti vozbuditelei periproteznoi infektsii kak osnova vybora ratsionalnogo antimikrobnogo lecheniia [Phenotype of antibiotic resistance of causative agents of periprosthetic infection as the basis for choosing rational antimicrobial treatment]. *Meditsinskii Almanakh*, 2017, no. 4 (49), pp. 72-75. (in Russian)
18. Benito N., Franco M., Ribera A., Soriano A., Rodriguez-Pardo D., Sorlí L., Fresco G., Fernández-Sampedro M., Dolores Del Toro M., Guío L., Sánchez-Rivas E., Bahamonde A., Riera M., Esteban J., Baraia-Etxaburu J.M., Martínez-Alvarez J., Jover-Sáenz A., Dueñas C., Ramos A., Sobrino B., Euba G., Morata L., Pigrau C., Coll P., Mur I., Ariza J.; REIPI (Spanish Network for Research in Infectious Disease) Group for the Study of Prosthetic Joint Infections. Time trends in the aetiology of prosthetic joint infections: a multicentre cohort study. *Clin. Microbiol. Infect*., 2016, vol. 22, no. 8, pp. 732.e1-732e8. DOI: 10.1016/j.cmi.2016.05.004.
19. Olearo F., Albrich W.C., Vernaz N., Harbarth S., Kronenberg A.; Swiss Centre For Antibiotic Resistance Anresis. Staphylococcus aureus and methicillin resistance in Switzerland: regional differences and trends from 2004 to 2014. *Swiss Med. Wkly*, 2016, vol. 146, pp. w14339. DOI: 10.4414/smw.2016.14339.
20. Petukhov V.I., Bulavkin V.P., Okulich V.K., Plotnikov F.V. Ratsionalnoe ispolzovanie antibiotikov v lechenii posttravmaticheskogo osteomielita s uchetom dinamiki izmeneniia rezistentnosti [Rational use of antibiotics in the treatment of post-traumatic osteomyelitis, taking into account the dynamics of changes in resistance]. *Novosti Khirurgii*, 2012, vol. 20, no. 1, pp. 71-79. (in Russian)
21. Bulavkin V.P., Okulich V.K., Konopelko E.A. Antibakterialnaia terapiia khronicheskogo osteomielita dlinnykh trubchatykh kostei [Antibacterial therapy of chronic osteomyelitis of long tubular bones]. *Immunopatologiia, Allergologiia, Infektologiia*, 2000, no. 3, pp. 48-53. (in Russian)

22. Kornienko M.A., Kopyltsov V.N., Shevliagina N.V., Didenko L.V., Liubasovskaia L.A., Priputnevich T.V., Ilina E.N. Sposobnost stafilokokkov razlichnykh vidov k obrazovaniiu bioplenok i ikh vozdeistvie na kletki cheloveka [The ability of staphylococci of various species to form biofilms and their effect on human cells]. *Molekuliarnaia Genetika, Mikrobiologiia i Virusologiia*, 2016, no. 1, pp. 18-25. (in Russian) DOI: 10.18821/0208-0613-2016-34-1-18-25.
23. Shlepotina N.M., Plotkin L.L., Belov V.V. Mikrobiologicheskoe i klinicheskoe znachenie bioplenochnykh infektsii (obzor literatury) [Microbiological and clinical significance of biofilm infections (literature review)]. *Uralskii Meditsinskii Zhurnal*, 2014, no. 4 (118), pp. 106-112. (in Russian)
24. Chebotar I.V., Maianskii A.N., Maianskii N.A. Matriks mikrobnykh bioplenok [Matrix of microbial biofilms]. *Klinicheskaia Mikrobiologiia i Antimikrobnaia Khimioterapiia*, 2016, vol. 18, no. 1, pp. 9-19. (in Russian)
25. Plata K., Rosato A.E., Wegrzyn G. Staphylococcus aureus as an infectious agent: overview of biochemistry and molecular genetics of its pathogenicity. *Acta Biochim. Pol*., 2009, vol. 56, no. 4, pp. 597-612.
26. Otto M. Molecular basis of Staphylococcus epidermidis infections. *Semin. Immunopathol*., 2012, vol. 34, no. 2, pp. 201-214. DOI: 10.1007/s00281-011-0296-2.
27. Bondarenko V.M., Bekhalo V.A., Sysoliatina E.V., Nagurskaia E.V. Immunobiologicheskie osobennosti bakterialnykh kletok meditsinskikh bioplenok [Immunobiological features of bacterial cells in medical biofilms]. *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii*, 2010, no. 4, pp. 97-105. (in Russian)
28. Stepanović S., Vuković D., Jezek P., Pavlović M., Svabic-Vlahović M. Influence of dynamic conditions on biofilm formation by staphylococci. *Eur. J. Clin. Microbiol. Infect. Dis*., 2001, vol. 20, no. 7, pp. 502-504. DOI: 10.1007/s100960100534.
29. Kraeva L.A., Tseneva G.Ia. Izmenenie chuvstvitelnosti k antibiotikam u mikroorganizmov roda Corynebacterium v Sankt-Peterburge i Leningradskoi oblasti [Changes in sensitivity to antibiotics in microorganisms of the genus Corynebacterium in St. Petersburg and the Leningrad Region]. *Zdorove Naseleniia i Sreda Obitaniia*, 2011, no. 2 (215), pp. 25-27. (in Russian)
30. Kharseeva G.G., Voronina N.A. Faktory patogennosti Corynebacterium non diphtheriae [Pathogenicity factors of Corynebacterium non diphtheriae]. *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii*, 2016, no. 3, pp. 97-104. (in Russian)

The article was submitted 11.11.2020; approved after reviewing 27.05.2021; accepted for publication 26.01.2022.

Information about the authors:

1. Irina V. Shipitsyna – Candidate of Biological Sciences, ivschimik@mail.ru, http://orcid.org/0000-0003-2012-3115;
2. Elena V. Osipova – Candidate of Biological Sciences, E-V-OsipovA@mail.ru, http://orcid.org/0000-0003-2408-4352.