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New SARS-CoV-2 Omicron subvariant. Is XBB.1.5 associated with an increase in COVID-19 morbidity?

Nowy subwariant omikronu. Czy XBB.1.5 jest powiązany ze wzrostem zachorowalności na COVID-19?

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Abstract

As a result of genetic changes and mutations of SARS-CoV-2, new variants emerge that have different properties compared to the original strains of the virus, which is a challenge for public health. XBB.1.5, also known as Kraken, is a subvariant of Omicron, and it is the most infectious and transmissible strain of SARS-CoV-2 to date. XBB.1.5 is the dominant strain in the United States of America, spreading worldwide, including in Europe and Asia. XBB.1.5 has properties to evade the immune system and reinfect individuals who have had COVID-19 before due to its strong binding to angiotensin-converting enzyme 2, and antibody evasion. Treatment and postexposure prophylaxis using monoclonal antibodies are ineffective against the Kraken variant, which is especially problematic for immunocompromised individuals and those with contraindications for vaccination, for example due to severe anaphylaxis or anaphylactic shock after prior administration of the vaccine, who require additional preventive measures. However, antiviral drugs including remdesivir, molnupiravir, nirmatrelvir, and ensitrelvir are still effective in treating COVID-19 caused by the XBB.5 variant. Currently, vaccine efficacy against XBB.1.5 variant is yet unknown. However, according to early studies, XBB and its sublineages have a greater ability for immune evasion than other variants, and the protection against infection via vaccination is reduced.

Keywords: COVID-19, SARS-CoV-2, XBB.1.5 – Kraken, B.1.1.529 – Omicron

Streszczenie

W wyniku zmian genetycznych i mutacji powstają nowe warianty wirusa SARS-CoV-2, które wykazują właściwości odmienne od jego pierwotnych szczepów, co stanowi wyzwanie dla zdrowia publicznego. XBB.1.5, znany również jako kraken, to subwariant omikronu – jak dotąd najbardziej zakaźny i najłatwiej przenoszący się szczep SARS-CoV-2. XBB.1.5 jest szczepem dominującym w USA, rozprzestrzeniającym się na całym świecie, w tym w Europie i Azji. XBB.1.5 cechuje się zdolnościami unikania układu odpornościowego i reinfekowania osób, które wcześniej chorowały na chorobę koronawirusową 2019 (COVID-19), ze względu na silne wiązanie z enzymem konwertującym angiotensynę 2 i zdolność unikania przeciwciał. Leczenie i profilaktyka poekspozycyjna za pomocą przeciwciał monoklonalnych są wobec krakena nieskuteczne, co jest szczególnie problematyczne w przypadku osób z obniżoną odpornością oraz osób z przeciwwskazaniami do szczepienia, np. z powodu ciężkiej anafilaksji lub wstrząsu anafilaktycznego po wcześniejszym podaniu szczepionki – u tych pacjentów należy stosować dodatkowe środki, aby zapobiec ich zachorowaniu na COVID-19. Jednak leki przeciwwirusowe – remdesiwir, molnupirawir, nirmatrelwir i ensitrelwir – nadal wykazują się skutecznością w leczeniu COVID-19 spowodowanego przez wariant wirusa XBB.5. Skuteczność szczepionki przeciwko subwariantowi XBB.1.5 nie jest jeszcze znana, jednak według wczesnych badań XBB i jego podrodzaje mają większą zdolność do unikania odpowiedzi immunologicznej niż inne warianty, a ochrona przed infekcją poprzez szczepienie jest zmniejszona.

Słowa kluczowe: SARS-CoV-2, COVID-19, XBB.1.5 – kraken, B.1.1.529 – omikron

INTRODUCTION

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a RNA virus. Similarly to other RNA viruses, it undergoes genetic evolution, and as a result of genetic changes and mutations, new variants of the virus emerge, with different characteristics, features, and properties in comparison to the original strains of the virus[1–4].

The SARS-CoV-2 pandemic started as an epidemic in Wuhan, China. The original strain was known as Wuhan-Hu-1, and its genetic sequence was 80% the same as the sequence of the virus called SARS-CoV that was responsible for severe acute respiratory syndrome (SARS) in the South East of Asia in the years 2002 and 2003. Wuhan-Hu-1 started to spread worldwide, and soon, the emergence of new variants was observed, especially in developing countries, where it was challenging to implement public health measures. Many of the mutations were associated with changes in the *S* gene responsible for encoding the spike protein of the virus. Specific new variants were referred to by scientists as "variants of concern" because they had new features, which made them more dangerous; for instance, they had more abilities to infect human cells and to evade the response of the immune system[1,3,5].

The first virus variant described as a variant of concern was Alpha (B.1.1.7 lineage, also called GRY or "English variant"). It was reported for the first time in the United Kingdom in November 2020. Alpha was found to be 29% more transmissible than the original Wuhan strain of the virus (Wuhan-Hu-1). However, clinical studies showed that vaccination against COVID-19, especially the entire cycle, is also effective against the Alpha variant[1,3].

The second variant of concern was Beta (also known as B.1.351 lineage), which had nine mutations in the spike protein. Some were responsible for increased binding affinity for the angiotensin-converting enzyme 2 (ACE2) receptors. The third variant of concern was Gamma (also known as P.1 lineage), which had ten mutations in the spike protein. Both Beta and Gamma variants were associated with an increased risk of transmission and decreased neutralisation by therapeutic monoclonal antibodies[1,3].

The fourth variant of concern was Delta, also known as B.1.617.2 or Indian variant, based on the fact that it was detected for the first time in India in December 2020. Delta quickly surpassed the Alpha variant as the world's dominant strain. Delta was 97% more transmissible than the original Wuhan-Hu-1 strain. It had ten mutations in the spike protein and, as a result, had an increased ability to evade the immune system's response. Delta was also a remarkable threat to the protection provided via vaccination and therapeutic monoclonal antibodies[1–3].

The Omicron variant (B.1.1.529) was first discovered in November 2021[1,3,4,6]. It quickly replaced the older strains of the virus, including the Delta variant, as the main factor driving the pandemic, with each new variant responsible for a new pandemic wave. The emergence of this variant caused the transmission of the virus across the world and posed a threat that the variant might overcome even the protection provided by an entire course of primary vaccinations and most neutralising monoclonal antibodies used so far in managing COVID-19[1,3].

Since then, Omicron has evolved continually and become a dominant variant worldwide[7–10]. Omicron has the propensity to induce new mutations. As a result, there is a sudden appearance of many stronger subvariants that can better evade the immune system with the potential to drive new pandemic waves[4,8,10,11]. For now, the Omicron variant has five main lineages, including BA.1, BA.2, BA.3, BA.4 and BA.5, and many other sublineages, such as BA.1.1, BA.2.12.1, BA.2.11, BA.2.75, and BA.4.6[11,12]. Each is characterised by distinctive and unique combinations, mutations, and genetic changes that influence virulence, infectivity, and antibody evasion, such as resistance to antibodies[8]. There is also evidence that new emerging subvariants of Omicron are able to reinfect individuals who have previously been infected with earlier Omicron subvariants[13].

Emerging new variants of SARS-CoV-2 pose a challenge for public health systems, so monitoring the new lineages and their new properties is very important for making decisions regarding vaccination policy, the use of antiviral drugs, and the capacity of healthcare[14].

XBB and BQ.1 lineages are dominant Omicron variants worldwide[12,15]. XBB lineage is a recombinant of two highly diversified BA.2 lineages (more precisely, BA.2.10.1 and BA.2.75 sublineages), and BQ.1 lineages are derived from BA.5. Both XBB and BQ.1 lineages are characterised by amino acid substitutions in the spike protein, also known as S protein. They are dominant in the West (BQ.1) and East (XBB) parts of the world[8,12–18]. S protein is the primary target of vaccines against COVID-19 and therapeutic monoclonal antibodies. Therefore, the mutation of S protein in XBB and BQ.1 lineages is the cause of their higher immune-evasion capabilities in comparison to earlier variants[12,14–18].

XBB was detected for the first time in the United States of America (US) in August 2022, and it is associated with a higher risk of reinfection than other Omicron subvariants. Also, according to the available studies, XBB can evade neutralising antibodies in individuals who have received BNT162b2 (also known as Pfizer) and CoronaVac (also known as Sinovac COVID-19 vaccine; produced by a Chinese company) vaccines[14] (Tab. 1).

OMICRON XBB.1.5

Omicron XBB.1.5 was first identified in the US in October 2022. XBB.1.5 variant evolved from the XBB sublineage, which is a recombinant of 2 BA.2 sublineages. The variant contains an accessory spike receptor-binding domain (RBD) change, S486P, which was absent in the original XBB variant[12,14,15,17].

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SARS-CoV-2 variant	Key information
Alpha variant (B.1.1.7 lineage, also called "English variant")	First variant of concern 29% more transmissible than Wuhan-Hu-1 Vaccination is effective against the variant
Beta (also known as B.1.351 lineage)	Second variant of concern Nine mutations in the spike protein Increased binding affinity for the ACE2 receptors
Gamma (also known as P.1 lineage)	Third variant of concern Ten mutations in the spike protein Increased risk of transmission and decreased neutralisation by therapeutic monoclonal antibodies
Delta (also known as B.1.617.2 or Indian variant)	Fourth variant of concern 97% more transmissible than the Wuhan-Hu-1 strain Ten mutations in the spike protein Increased ability to evade the immune system's response

Tab. 1. SARS-CoV-2 variants of concern[1–4,6]

Omicron XBB.1.5 is also commonly referred to as Kraken, i.e. with the name of a sea monster originating from legends and Norse mythology, resembling an octopus, and feared among sailors[12,18]. English writer Alfred Tennyson wrote a poem about that mythical creature, which was published in 1830. Citing the article by Parums, the poem symbolises fear and doubt about the advances of science in the 19th century[12].

XBB.1.5 is more contagious than XBB because in addition to evading the immune system due to its mutation, it has more ability to infect cells[12,13]. Also, it can attach to the upper respiratory tract cells, so it does not have to travel down to the lungs to cause an infection[13]. XBB.1.5 is characterised by F486P mutation in spike protein[12]. The mutation is associated with greater contagiousness due to increased binding affinity to the ACE2 receptor, which serves as a receptor that allows the virus to enter cells and, as a result, infect them[12,15,17]. Therefore, Kraken's extreme affinity to the human ACE2 receptor increases the rate of transmission of SARS-CoV-2[12,15,17]. Another reason why Kraken is characterised by enhanced transmissibility and infectivity is that it has an antibody evasion ability[12–15]. However, XBB and XBB.1.5 have very similar properties of immune evasion. Therefore, a higher affinity for human ACE2 of XBB.1.5 is a primary factor contributing to its high transmissibility and rapid expansion in the US[17]. According to the World Health Organization (WHO), Omicron XBB.1.5 is the most infectious and transmissible strain of SARS-CoV-2 to date[12,13,15]. XBB.1.5 currently accounts for over 40% of new COVID-19 cases in the US[13]. It also spread across Europe and Asia, and was identified in over 38 countries, including the United Kingdom, Denmark, and India[8,12,15,19]. According to studies, one person infected with Kraken can pass it and infect approximately another 1.6 individuals[13]. The US Centers for Disease Control and Prevention (CDC) described XBB.1.5 as a "variant of concern". BQ.1.1 was a dominant lineage in the US in December 2022. The relative adequate reproduction number of Kraken is higher than parental XBB.1 and higher than BQ.1.1, suggesting that XBB.1.5 will spread rapidly around the world[12,15,16].

VACCINE EFFICACY AGAINST XBB.1.5

There are a number of vaccines against COVID-19. However, vaccine efficacy (VE) may differ depending on the variant of SARS-CoV-2, and some strains of the virus are associated with reduced VE. Vaccination aims to reduce morbidity and mortality resulting from severe illness. For public health, ongoing monitoring of VE is vital because new variants of SARS-CoV-2, with unique properties, continuously appear[14,16]. Currently, VE against the XBB.1.5 variant is unknown. WHO and CDC still lack data about improving transmissibility and evading the immune responses from vaccination or, in the case of COVID-19 convalescents, prior infection, for XBB.1.5[12–14,16]. However, some studies on this topic and the previous XBB.1 variants exist. According to the early studies, XBB and its sublineages have a greater ability for immune evasion than other variants. This means the protection against infection achieved with vaccination, antibodies created during past infection, or treatment based on monoclonal antibodies is reduced. For example, in one study described by Miller et al., with the participation of 35 individuals, it was shown that neutralising antibody levels against newer Omicron subvarieties were 12 to 26 times lower than those of the original SARS-CoV-2 strain in individuals who received a monovalent booster vaccine[12,13,20]. In another study, it was found that XBB subvariants were resistant to current monoclonal antibody treatment and had an increased ability to evade neutralising antibodies, even in individuals who have received a bivalent mRNA booster dose of vaccination[12,13]. In their article, Cao et al. described studies using deep mutational scanning (DMS) about the growth trends of the BA.2.75 and BA.5 subvariants of the Omicron[21]. Their study shows that concurrent mutations of their receptor-binding domains are the leading cause of immune response evasion from infections with precedent SARS-CoV-2 variants. Also, according to their study results, booster doses of vaccination against COVID-19 caused by Omicron BA.4/BA.5 may be ineffective in preventing infection from convergent variants of the Omicron. However, according to another study, with the use of spike (S)-gene target presence as a proxy for BA.2 sublineages, conducted by Link-Gelles et al., a booster dose of bivalent mRNA vaccination ensures extra protection against symptomatic infection caused by XBB or XBB.1.5 variants for a minimum of 3 months after the administration of the vaccine for the individuals who before received 2, 3 or 4 doses of monovalent vaccination[16].

EFFICACY OF MONOCLONAL ANTIBODIES AND ANTIVIRAL DRUGS IN THE TREATMENT OF COVID-19 CAUSED BY XBB.1.5

Monoclonal antibody treatment and using monoclonal antibodies as postexposure prophylaxis is ineffective against

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the new Omicron subvariants. Yue et al. showed that monoclonal antibodies, such as Evusheld (a formula containing long-acting monoclonal antibodies tixagevimab and cilgavimab) and bebtelovimab (a recombinant neutralising human IgG1λ monoclonal antibody to the spike protein of SARS-CoV-2), were not effective in the neutralisation of XBB.1 and its closely related XBB.1.5 variant[20,22]. Evusheld is a drug approved for postexposure prophylaxis of COVID-19 for individuals aged 12 or older and with body mass equal to or higher than 40 kg who cannot receive a vaccination due to moderate or severe immunocompromised state or a history of severe adverse effects, such as anaphylaxis or anaphylactic shock, after the use of the vaccine. Also, Uraki et al. showed that monoclonal antibodies imdevimab–casirivimab, tixagevimab–cilgavimab, sotrovimab, and bebtelovimab did not neutralise XBB.1.5, even at the highest 50% focus reduction neutralisation titre (FRNT50) of the monoclonal antibodies[17].

In their studies, Uraki et al. also tested the efficacy of antiviral drugs that are approved by the Food and Drug Administration (FDA) in the treatment of COVID-19, such as remdesivir (an RNA-dependent RNA polymerase (RDRP) inhibitor), molnupiravir (an RDRP inhibitor) and nirmatrelvir (a main protease inhibitor)[17]. They also reviewed the efficacy of ensitrelvir (a primary protease inhibitor), which is currently in phase 3 of clinical trials in the US. Their study showed that susceptibilities of XBB.1.5 to antivirals drugs were similar to those of preexisting strains, and that remdesivir, molnupiravir, nirmatrelvir, and ensitrelvir are still effective in the treatment of COVID-19, both *in vitro* and *in vivo*. They also found that the XBB.1.5 variant could successfully evade humoral immunity induced by mRNA vaccines or natural prior infection. However, booster bivalent vaccines might enhance the humoral responses to XBB.1.5.

POSSIBILITIES TO PROTECT IMMUNOCOMPROMISED INDIVIDUALS AGAINST XBB.1.5

In immunocompromised patients, the elderly, and individuals who have not been vaccinated due to, for instance, contraindications, the XBB.1.5 subvariant may cause severe illness. As mentioned before, using monoclonal antibodies, such as tixagevimab and cilgavimab, in postexposure prophylaxis against SARS-CoV-2 infection is ineffective against the Kraken variant[17]. Therefore, it is vital for individuals who are moderately to severely immunocompromised to use additional preventive measures, such as wearing face masks or respirator masks that decrease the transmissibility of the virus by the respiratory route to others from a person that is infected, physical distancing (maintaining a 1.8 m distance from other individuals), ventilation by opening doors and windows (concentration of viral particles is higher in enclosed spaces compared to open areas), spending time outdoors (viral particles are easier to spread between individuals indoors than outdoors), frequent handwashing with soap and water or using of hand sanitiser that contains more than 60% of alcohol, and testing for SARS-CoV-2 after developing symptoms of infection[23].

POST SCRIPTUM

The article was written in March 2023, and since then, a few more variants have emerged due to genetic changes and mutations of SARS-CoV-2. Examples include strains XBB.1.16 (nicknamed Arcturus), EG.5.1 (nicknamed Eris), BA.2.86 (nicknamed Pirola), and FL.1.5.1 (nicknamed Fornax).

XBB.1.16, also known as Arcturus, is an Omicron variant closely related to XBB.1.5, the Kraken variant. Citing the article written by Looi, the name Arcturus means "Guardian of the Bear" in the Greek language[24]. It was first discovered in India in January 2023, and since then, it has been reported to be present in 33 countries or more[24]. Arcturus is known to spread faster than XBB.1.5. Infection with the variant presents with symptoms involving the upper respiratory tract. In addition, a new, previously unseen sign appeared: severe conjunctivitis with epiphora and ocular pruritus[25]. The occurrence of conjunctivitis is more common among children. According to the WHO, infections caused by the Arcturus variant are not reported to be more severe than infections with previously circulating virus variants[24].

EG.5, also known as Eris, is derived from XBB.1.9.2, which has the same spike amino acid profile as XBB.1.5, the Kraken variant. According to Parums, its name is derived from the Greek goddess of strife and discord from mythology[26]. It was reported for the first time by the WHO in February 2023, and in August 2023, Eris and its sublineages (EG.5.1, EG.5.1.1, and EG.5.2) were marked as a variant of interest (VOI). It is derived from the XBB Omicron strain of SARS-CoV-2 and is characterised by F456L amino acid mutation in the spike protein, which increases its transmission. One of its sublineages, EG.5.1, is characterised by an additional spike mutation, Q52H. Symptoms of infection with the Eris variant are similar to those of other Omicron variants[26].

The first infection with BA.2.86 variant, also known as Pirola, was reported in Denmark in July 2023. It has 36 more mutations in the spike protein than XBB.1.5, the Kraken variant[27]. According to the WHO, Pirola is marked as a variant under monitoring[27]. According to the CDC, infections caused by the Pirola variant are not more severe than infections with previously circulating virus variants; however, the number of reported cases is currently limited[28].

FL.1.5.1 is also nicknamed Fornax, and it is currently the second most common cause of COVID-19 in the US (Eris is responsible for approximately 20% of cases, Fornax – 13%, Arcturus – 10%)[26].

CONCLUSION

The SARS-CoV-2 pandemic started in 2019 as an epidemic in Wuhan, China. It is still a big challenge to public health systems, as new variants of SARS-CoV-2 are continuously

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emerging. Each new variant contains genetic changes associated with higher transmissibility, properties to evade the immune system, and reinfect individuals who have had COVID-19 before. Omicron XBB.1.5, also known as the Kraken, is characterised by enhanced transmissibility, infectivity, and immune resistance due to its strong ACE2 binding and antibody evasion. In a very short period, the variant spread worldwide, mainly across the US, Europe, and Asia, and became the dominant variant in many countries. It is also a challenge and concern because treatment and postexposure prophylaxis using monoclonal antibodies are ineffective against Kraken. It is mainly a problem for immunocompromised individuals and those with contraindications for vaccination, for example, due to severe anaphylaxis or anaphylactic shock after prior vaccine administration. Also, vaccine efficacy against XBB.1.5 is currently unknown. However, according to some early studies, XBB and its sublineages have a greater ability for immune evasion than other variants, and the protection against infection with vaccination is reduced. Furthermore, as a result of genetic modifications and mutations in the SARS-CoV-2 virus, other new variants emerged in 2023, characterised by increased infectivity rates. The new variants encompass XBB.1.16 (Arcturus; with a faster spread rate than Kraken), EG.5.1 (Eris; a variant of concern) along with its sublineages, BA.2.86 (Pirola; designated as a variant under monitoring) and FL.1.5.1 (Fornax). Based on the information accessible at the time of writing this article, infections associated with the Arcturus, Eris, and Pirola variants are generally not deemed more severe than infections caused by the previously prevalent virus strains. However, in the instance of Arcturus variant-induced infections, a novel and previously unobserved symptom has been reported: severe conjunctivitis.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author contributions

Collection, recording and/or compilation of data: DMJP, JAK. Writing of manuscript: DMJP, AWC, JAK. Critical review of manuscript: AWC. Final approval of manuscript: DMJP, AWC.

References

1. Aleem A, Akbar Samad AB, Vaqar S: Emerging variants of SARS-CoV-2 and novel therapeutics against coronavirus (COVID-19). 2023 May 8. In: StatPearls [Internet]. StatPearls Publishing, Treasure Island, FL 2023 Jan–.
2. Bai Y, Jiang D, Lon JR et al.: Comprehensive evolution and molecular characteristics of a large number of SARS-CoV-2 genomes reveal its epidemic trends. Int J Infect Dis 2020; 100: 164–173.
3. Pavan M, Bassani D, Sturlese M et al.: From the Wuhan-Hu-1 strain to the XD and XE variants: is targeting the SARS-CoV-2 spike protein still a pharmaceutically relevant option against COVID-19? J Enzyme Inhib Med Chem 2022; 37: 1704–1714.
4. Wang Y, Long Y, Wang F et al.: Characterization of SARS-CoV-2 recombinants and emerging Omicron sublineages. Int J Med Sci 2023; 20: 151–162.
5. Castells M, Lopez-Tort F, Colina R et al.: Evidence of increasing diversification of emerging Severe Acute Respiratory Syndrome Coronavirus 2 strains. J Med Virol 2020; 92: 2165–2172.
6. Callaway E: Beyond Omicron: what's next for COVID's viral evolution. Nature 2021; 600: 204–207.
7. Xia X: Domains and functions of spike protein in SARS-CoV-2 in the context of vaccine design. Viruses 2021; 13: 109.
8. Ghosh S, Shree A: Possible threat of the Omicron subvariants XBB.1.5 and BF.7 to the Indian subcontinent: a correspondence. New Microbes New Infect 2023; 52: 101089.
9. Karim SSA, Karim QA: Omicron SARS-CoV-2 variant: a new chapter in the COVID-19 pandemic. Lancet 2021; 398: 2126–2128. Erratum in: Lancet 2022; 399: 142.
10. Kandeel M, Mohamed MEM, Abd El-Lateef HM et al.: Omicron variant genome evolution and phylogenetics. J Med Virol 2022; 94: 1627–1632.
11. Paz M, Aldunate F, Arce R et al.: An evolutionary insight into Severe Acute Respiratory Syndrome Coronavirus 2 Omicron variant of concern. Virus Res 2022; 314: 198753.
12. Parums DV: Editorial: The XBB.1.5 ('Kraken') subvariant of Omicron SARS-CoV-2 and its rapid global spread. Med Sci Monit 2023; 29: e939580.
13. Vogel L: What to know about Omicron XBB.1.5. CMAJ 2023; 195: E127–E128.
14. Velavan TP, Ntoumi F, Kremsner PG et al.: Emergence and geographic dominance of Omicron subvariants XBB/XBB.1.5 and BF.7 – the public health challenges. Int J Infect Dis 2023; 128: 307–309.
15. Uriu K, Ito J, Zahradnik J et al.; Genotype to Phenotype Japan (G2P-Japan) Consortium: Enhanced transmissibility, infectivity, and immune resistance of the SARS-CoV-2 omicron XBB.1.5 variant. Lancet Infect Dis 2023; 23: 280–281.
16. Link-Gelles R, Ciesla AA, Roper LE et al.: Early estimates of bivalent mRNA booster dose vaccine effectiveness in preventing symptomatic SARS-CoV-2 infection attributable to Omicron BA.5- and XBB/XBB.1.5-related sublineages among immunocompetent adults – increasing community access to testing program, United States, December 2022–January 2023. MMWR Morb Mortal Wkly Rep 2023; 72: 119–124.
17. Uraki R, Ito M, Kiso M et al.: Antiviral and bivalent vaccine efficacy against an omicron XBB.1.5 isolate. Lancet Infect Dis 2023; 23: 402–403.
18. Popovic ME: XBB.1.5 Kraken cracked: Gibbs energies of binding and biosynthesis of the XBB.1.5 variant of SARS-CoV-2. Microbiol Res 2023; 270: 127337.
19. Kelleni MT: Evolution of SARS CoV-2 Omicron subvariants BF.7 and XBB.1.5: time to follow Africa and abort all COVID restrictions. J Infect 2023; 86: 405.
20. Miller J, Hachmann NP, Collier AY et al.: Substantial neutralization escape by SARS-CoV-2 Omicron variants BQ.1.1 and XBB.1. N Engl J Med 2023; 388: 662–664.
21. Cao Y, Jian F, Wang J et al.: Imprinted SARS-CoV-2 humoral immunity induces convergent Omicron RBD evolution. Nature 2023; 614: 521–529.

 DOI: 10.15557/PiMR.2023.0031

22. Yue C, Song W, Wang L et al.: ACE2 binding and antibody evasion in enhanced transmissibility of XBB.1.5. Lancet Infect Dis 2023; 23: 278–280.

23. Patel P, Twentyman E, Koumans E et al.: Information for persons who are immunocompromised regarding prevention and treatment of SARS-CoV-2 infection in the context of currently circulating Omicron sublineages – United States, January 2023. MMWR Morb Mortal Wkly Rep 2023; 72: 128–131.

24. Looi MK: What do we know about the Arcturus XBB.1.16 subvariant? BMJ 2023; 381: 1074.

25. Mohapatra RK, Mishra S, Dhama K et al.: Potential threat and possible global spread of the novel SARS-CoV-2 Omicron subvariants including XBB.1.16 during the Indian Premier League 2023: strict implementation of traveller guidelines suggested. New Microbes New Infect 2023; 53: 101149.

26. Parums DV: Editorial: A rapid global increase in COVID-19 is due to the emergence of the EG.5 (Eris) subvariant of Omicron SARS-CoV-2. Med Sci Monit 2023; 29: e942244.

27. Looi MK: Covid-19: scientists sound alarm over new BA.2.86 "Pirola" variant. BMJ 2023; 382: 1964.

28. Harris E: CDC assesses risk from BA.2.86, highly mutated COVID-19 variant. JAMA 2023; 330: 1029.

DOI: 10.15557/PiMR.2023.0031 PEDIATR MED RODZ Vol. 19 No. 3, p. 169–174