Slovenian **Medical** Journal

‘Austrian syndrome’ in a healthy 16-month-old boy

“Austrianov sindrom” pri zdravem 16-mesečnem dečku

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Abstract

In this paper, we present a case report of a 16-month-old boy who was diagnosed with *Streptococcus pneumoniae* type 10A pneumonia, meningitis, and endocarditis – a triad also known as Austrian syndrome. Only three cases of the triad of pneumonia, meningitis, and endocarditis in children have been described in the literature. An initial acute presentation is described in all cases of Austrian syndrome—patients presented with either pneumonia or meningitis. In most cases, a preceding respiratory illness was defined. Infectious endocarditis caused by *Streptococcus pneumoniae* in children is rare. Today,100 serotypes of *Streptococcus pneumoniae* are known, all of which can cause invasive disease. Before introducing pneumococcal conjugate vaccines (PCV7, PCV 10, PCV 13), invasive pneumococcal disease was caused mainly by serotypes 1, 3, 6, 14, 19A, and 23F. After the introduction of PCV, epidemiology changed. A decline in invasive pneumococcal disease caused by vaccine serotypes was shown immediately after PCV 10 and PCV 13 were introduced. Still, an increase in invasive pneumococcal disease caused by non-vaccine serotypes has been shown recently. Invasive pneumococcal disease occurs due to the spread of bacteria from the nasopharynx to other body parts, including the lungs, blood, and brain. The most significant risk factor for invasive pneumococcal disease is young age.

Izvleček

V prispevku predstavljamo klinični primer 16-mesečnega dečka s pljučnico, meningitisom in endokarditisom. Iz hemokulture je bil izoliran *Streptococcus pneumoniae* tip 10A. Invazivna pnevmokokna okužba s triado pljučnica, meningitis in endokarditis je bila že opisana pri odraslih in otrocih in poimenovana po Robertu Austrianu. V literaturi so opisani le 3 primeri te triade pri otrocih. V vseh opisanih primerih Austrianovega sindroma je bil akutni začetek bolezni enak: bolniki so imeli bodisi pljučnico bodisi meningitis. V večini primerov pa so dokazali predhodno okužbo dihal. Infekcijski endokarditis, povzročen z bakterijo *Streptococcus pneumoniae*, je pri otrocih redek. Danes poznamo 100 serotipov bakterije *Streptococcus pneumoniae*. Vsi lahko povzročijo invazivno bolezen. Pred uvedbo konjugiranih pnevmokoknih cepiv (PCV) PCV7, PCV 10 in PCV 13 so invazivne pnevmokokne bolezni (IPB) povzročali predvsem serotipi 1, 3, 6, 14, 19A in 23F. Po uvedbi PCV se je epidemiologija IPB spremenila. Takoj po uvedbi PCV 10 in PCV 13 smo beležili upad invazivnih pnevmokoknih okužb, povzročenih s serotipi, zajetih pri cepivu. V zadnjem času se je povečalo število invazivnih pnevmokoknih okužb, povzročenih z necepilnimi serotipi. Invazivna pnevmokokna okužba se pojavi zaradi širjenja bakterij iz nosnega dela žrela v sterilne dele telesa, kot so pljuča, kri in osrednje živčevje. Najpomembnejši dejavnik tveganja za invazivno pnevmokokno okužbo je nižja starost.

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Key words: *Streptococcus pneumoniae*; endocarditis; meningitis; pneumonia

Ključne besede: *Streptococcus pneumoniae*; endokarditis; meningitis; pljučnica

Received / Prispelo: 5. 6. 2024 | **Accepted / Sprejeto:** 21. 1. 2025

Cite as / Citirajte kot: Weis T, Bovha Hus K, Vesel S, Mlakar G, Lah LL. ‘Austrian syndrome’ in a healthy 16-month-old boy. Zdrav Vestn. 2025;94(3–4):82–7. **DOI:** https://doi.org/10.6016/ZdravVestn.3552

1 Introduction

George Sternberg and Louis Pasteur (1,2) first recognized *Streptococcus pneumoniae* as an infectious agent in 1881. It was initially called *Diplococcus pneumoniae* because of its characteristic appearance on Gram stain and its association with pneumonia. Later, it was renamed *Streptococcus pneumoniae* because of its similarity to *Streptococci* (3). Today, there are 100 known serotypes of *Streptococcus pneumoniae*, all of which can cause invasive disease (4).

Before the introduction of pneumococcal conjugate vaccines (PCV) PCV7, PCV 10, and PCV 13, invasive pneumococcal disease (IPD) was caused mainly by serotypes 1, 3, 6, 14, 19A, and 23F (5). After the introduction of PCV, the epidemiology of IPD changed. A decline in IPD caused by vaccine serotypes was shown immediately after the introduction of PCV 10 and PCV 13, but an increase in IPD caused by non-vaccine serotypes has been shown recently (6).

Infectious endocarditis caused by *Streptococcus pneumoniae* in children is rare. A 2006 survey in Japan found that only 5.3% of cases were caused by *Streptococcus pneumoniae* (7). The triad of pneumonia, meningitis, and endocarditis caused by *Streptococcus pneumoniae* has only been reported in three children.

The first to describe this triad in patients was Heschl in 1862. He described a series of 5 patients where he found signs of pneumonia, meningitis, and endocarditis on autopsy. Osler later wrote a paper on infectious endocarditis, describing patients with endocarditis, pneumonia, and meningitis. Netter and Preble extensively researched pneumococcal endocarditis and found pneumonia and meningitis associated with pneumococcal endocarditis. Finally, Robert Austrian was the one to sum up what was known about the triad of pneumonia, meningitis, and endocarditis in 1956 (8). Since this publication, this clinical triad has been named after him.

2 Case report

We present a case of a 16-month-old boy who presented with a fever five days after the first dose of the 13-valent conjugate pneumococcal vaccine (PCV 13). He had been healthy until he started attending daycare in September 2021. He is the first child of healthy, non-consanguineous parents; he had a normal birth and has no chronic diseases. He had been vaccinated regularly.

He presented after he had a fever every day for three days until he was first seen by his paediatrician, who diagnosed an upper respiratory infection.

He was first evaluated in the emergency room on the sixth day of his fever. His clinical exam was normal, except for signs of an upper respiratory infection. Laboratory blood tests showed moderately elevated inflammatory parameters (CRP) without leukocytosis. For laboratory values, see Table 1.

Table 1: Blood laboratory values.

Laboratory marker/ day of illness (D)	D3	D6	D9	D10	D11	D14	D20	D31	D49	Reference values
CRP	68	47,8	70,1	92,2	161,8	14,9	7	<5	<5	< 5 mg/L
L	18	11,1	11,6	14,5	19,8	12,6	9,5	9	7,4	6 – 17,5 x 10^9/L
ESR	/	/	72	/	/	59	67	46	6	0 – 15 mm/h
Tr	/	341	194	185	242	563	286	562	440	150 – 410 x 10^9/L
Hb	/	107	98	98	93	95	99	92	100	102 – 134 g/L
Troponin T	/	/	/	/	6	/	3	7	18	< 58 g/L
NT-proBNP	/	/	/	/	1830	/	518,7	155,7	132	< 125 g/L
% BN/bands	/	/	7,7/0,5	6,7/0	13,9/0,4	4,7/0,2	/	/	/	1,5-8,5 10^9/L 0 – 0,4

Legend: CRP – C-reactive protein; ESR – erythrocyte sedimentation rate; L – Blood leukocyte value; Tr – thrombocytes; Hb – haemoglobin value; Trop T – troponin T value; NT-pro BNP – N-terminal proB-type natriuretic peptide; BN – blood neutrophils.

On the ninth day of illness, his general condition deteriorated. He was irritable and sleepy, and grunting was noticed. His mother reported that he seemed to be in pain. He was admitted to our hospital's children's ward. A further increase in CRP and a decrease in hemoglobin value were noted on bloodwork, see Table 1.

At admission, he was febrile, but his pulse rate, oxygen saturation, breathing rate, capillary refill, and urine output were normal. There was no nuchal rigidity. His skin color was normal, and there was no rash. The lungs were clear on auscultation, but chest X-ray (CXR) confirmed a left-sided pneumonia. There was no heart murmur. A blood culture (BC) was taken.

Due to the high suspicion of pneumococcal pneumonia and the high sensitivity of invasive isolates of *Streptococcus pneumoniae* to penicillin in children in Slovenia, we started treatment with penicillin G intravenously (200,000 units/kg/day divided into four daily doses). The next day, the growth of Gram-positive cocci in chains in the BC was reported.

After three doses of penicillin, he became afebrile, but still, his general condition worsened. He was tired, had a low appetite, and seemed sleepier than the previous day. Slight nuchal rigidity was noticed during the clinical examination.

A lumbar puncture was performed on the tenth day of illness to confirm suspicion of pneumococcal meningitis. The leukocyte value in the cerebrospinal fluid (CSF) was elevated (3040 Leucocyte x 106/L) with a predominance of neutrophils, as was the protein value - 0.50 g/L (normal value < 0.45 g/L). The CSF/blood glucose ratio was normal (>0.5). We started treatment with a third-generation cephalosporin (cefotaxime) upon pending antibiotic sensitivity results for *Streptococcus pneumoniae* isolated from the BC.

He received dexamethasone (0.6 mg/kg, divided into four daily doses) for two days. We performed a computer tomography (CT) of the skull and brain to exclude otitis media as a source of meningitis.

A few hours after the lumbar puncture and initiation of treatment with cefotaxime, the child's general condition improved.

A penicillin-susceptible *Streptococcus pneumoniae* type 10A was cultured from the BC (minimal inhibitory concentration for penicillin was 0,016 mg/L, which is full sensitivity according to EUCAST guidelines) (9). We reverted to treatment with intravenous penicillin (300,000 units/kg/day, divided into four daily doses). BC taken later were negative.

The CSF culture did not grow any microorganisms, but *Streptococcus pneumoniae* in the CSF was confirmed by polymerase-chain reaction (PCR).

On day eleven, a slight systolic murmur was heard at the apex and the left sternal border. The murmur intensified and changed in quality. An echocardiogram (ECHO) revealed a thickened posterior mitral valve leaflet with discrete vegetation and moderate mitral regurgitation. The left atrium was slightly enlarged. The size and contractibility of both ventricles were normal. The aortic valve was competent. The electrocardiogram (ECG) was appropriate for the child's age.

We continued intravenous treatment with penicillin G for four weeks. At the end of treatment, the vegetation on the mitral valve fully regressed, but mitral valve regurgitation and slight left atrium dilatation are still present two years after treatment.

A full immunology screen (specific antibody levels and complement evaluation) was normal. A formal hearing assessment showed no hearing deficits. Two years after treatment, the child is doing well, has had no further episodes of IPD, has no motor or cognitive sequelae, and no signs of cardiac failure.

3 Review of literature

PubMed and Google Scholar search revealed 58 articles with case reports of the Austrian syndrome.

Sixty-seven cases of Austrian syndrome were found in the literature. Sixty-four cases describe adult patients and only three children. 64% of patients were male. 63.9% of adult patients had previous chronic diseases or conditions. Diabetes was most common (11 patients), followed by hypertension (7 patients) and absent spleen (5 patients). One case was diagnosed simultaneously with multiple myeloma presentation. Three cases were in patients infected with the human immunodeficiency virus (HIV). A history of alcohol abuse was present in 21% of adult patients. Out of the three paediatric cases described, only one child has a previously known condition (asthma). The other two had been healthy, but factor V Leiden deficiency was uncovered during treatment in one child.

All patients had healthy native heart valves, and no patients had previously had open heart surgery. Two cases were reported in intravenous drug users (IDU).

The aortic valve was affected in 37/64 (57.8%) of adult cases, the mitral valve in 17/64 (26.5%), the tricuspid valve in 2/64 (3.1%) cases, both the mitral and aortic valves in 7 (10.9%) cases and all four valves in one case (1.5%) (10). Robert Austrian described two instances where the aortic valve had been previously affected by syphilis, but in all other cases, the valves affected were

native and healthy (8). The mitral valve was affected in ⅔ of paediatric cases.

37/64 (57,8%) adult patients underwent valve replacement surgeries (information not available for 2 cases). Surgery was not available for the first 6 cases described in 1956. Of the other 19 patients who did not have valve replacement surgery, nine died before they could undergo surgery. Ten adult patients had good outcomes only with conservative antibiotic treatment (5 mitral valves affected, four aortic; there is no information for 1 case).

The case mortality in adults was 30.6% (19/62 adult cases, outcome unknown in 2 cases).

Two of the children required heart valve replacement surgery (one with the aortic valve affected and aortic root abscess had the Ross procedure to correct the aortic root (11), and the other with large mitral valve vegetation required valve replacement surgery (12)). The second surgical case was complicated by a frontal lobe cerebral infarction upon presentation. The third case, involving a 10-month-old child, reported a good outcome after conservative treatment with a 6-week course of cefotaxime and rifampicin (13). All three cases in children had good general outcomes.

In all cases of Austrian syndrome, an initial acute presentation with one of the common syndromes of invasive pneumococcal disease is described. Patients present with either pneumonia or meningitis and, in some cases, a combination of two or even all three syndromes. A preceding respiratory illness is described in most cases. Peripheral stigmata of endocarditis were not found or described in any case. Additional septic complications like choroiditis of the eye, necrosis of skin (foot), or septic arthritis (acromioclavicular joint, sternoclavicular joint, and knee joint) were described in isolated cases.

Streptococcus pneumoniae was isolated from BC in 28/67 cases. In two cases, only the growth of Gram-positive diplococci was confirmed on Gram stain, but later, there was no growth from cultures. In some cases, *Streptococcus pneumoniae* was also confirmed from CSF culture, sputum, or heart valve samples taken post-mortem.

Whether any patients had been previously vaccinated with pneumococcal vaccines is not stated.

For patient data, see Online Supplement.

4 Discussion

Our patient was a typical young child who had entered group childcare a few months prior to an episode of IPD. He had fallen ill with an episode of mild upper respiratory infection (URI) followed by IPD. He had previously received one dose of PCV13 since PCV20 was not yet available at the time. He had been breastfed and had no known underlying conditions or previous bacterial infections.

Our patient was first evaluated and treated for pneumonia, which usually has an uncomplicated course. The isolation of *Streptococcus pneumoniae* type 10A from BC confirmed our suspicion. Despite adequate treatment and a fully susceptible *Streptococcus pneumoniae*, his clinical condition deteriorated and progressed further to involve the central nervous system and mitral heart valve, so naturally, an immunodeficiency was suspected. This suspicion was not confirmed by immunological testing or further clinical course.

IPD occurs due to the spread of bacteria from the nasopharynx to the lungs, blood, brain, bones, or other tissues (14). Pneumococci can have complex immune evasion mechanisms and virulence factors (15,16).

It is well known that nasopharyngeal carriage of *Streptococcus pneumoniae* is common in children after entering group childcare. Attendance of group childcare in the three months preceding the disease has been strongly associated with IPD (17).

Serotype 10 A has emerged as a cause of IPD since the introduction of PCVs, but it was first described in 1966 by Rao (18). According to recent epidemiological data, it was responsible for 8.4% of cases of IPD in children under 1 year of age in reporting European countries in 2018 (19). It is included in the 23-valent pneumococcal polysaccharide vaccine, and PCV20, which was introduced recently.

A serotype present in the nasopharynx can cause IPD, but this is not always the case. In some cases, newly acquired serotypes cause IPD (14,17,20,21). We do not know whether our patient had acquired *Streptococcus pneumoniae* type 10A right before his illness or had been previously colonized with this or other pneumococcal serotypes.

The connection between an acute respiratory infection and IPD could be explained by specific temperature-dependent immune evasion mechanisms that encapsulated bacteria are capable of. Eichner has investigated this in *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis*. He has shown that encapsulated bacteria grown at higher temperatures on culture (37°C) can activate RNA-mediated immune evasion mechanism, which makes the bacteria resistant to complement-mediated destruction (22).

Studies have shown that IPD could be an important marker of underlying primary immunodeficiency in areas of high vaccine coverage (23-26). In other areas, like Slovenia, where vaccine coverage is lower than

in other European countries (57.9% received the final dose of pneumococcal conjugate vaccine in 2023) (27) and the incidence of IPD is higher than the European average (6,2/100,000 inhabitants for 2018; Slovenia 12,2/100,000), IPD is not immediately associated with immune deficiency. The incidence of immunodeficiency in children with IPD in countries with high pneumococcal vaccine coverage ranges from 8 - 12% (23-26) and is more common in children with recurrent IPD(25,26).

In children with IPD, who were evaluated for immunodeficiency, antibody deficiency was found most commonly, followed by complement deficiency (factor I and C2 deficiency), asplenia, and rare defects in T-cell signalling (23).

It is unclear whether host immune deficiency or pathogen virulence factors are more pertinent in enabling IPD. An invasive multifocal pneumococcal disease such as the Austrian syndrome is an immensely complex interaction of host defenses, bacterial virulence factors and invasion mechanisms specific to the pathogen, such as *Streptococcus pneumoniae*.

5 Conclusion

We present a case report of a previously healthy 16-month-old boy who was diagnosed with *Streptococcus pneumoniae type 10A* pneumonia, meningitis, and endocarditis – a triad also known as the Austrian syndrome. *Streptococcus pneumoniae* type 10A was isolated from blood cultures. He was treated conservatively with antibiotics only. He recovered from the disease without any significant sequelae.

The progression of disease from pneumonia to meningitis and heart valve involvement could not be explained by insufficient treatment, bacterial resistance to antibiotics, or immunodeficiency.

Austrian syndrome is rare in adults as well as in children. No specific serotype of *Streptococcus pneumoniae* is associated with it.

Young age, early group childcare entry, and upper respiratory tract illness have been recognized as risk factors for IPD. A complex interaction of bacterial host evasion mechanisms and possibly primary immunodeficiency has been investigated as a risk factor for IPD.

A high level of vigilance when evaluating and treating children with IPD is necessary for hosts with underlying disease (chronic diseases, secondary immunodeficiency, anatomical abnormalities) and also in healthy children since progression of the disease is possible even in previously healthy children with IPD caused by fully susceptible *Streptococcus pneumoniae*. Children of all ages who have had an episode or multiple episodes of IPD should be investigated for underlying immunodeficiency.

Conflict of interest

None declared. No financial support was received for this work.

Inform consent of the parent

The parent of a case patient signed the informed consent form for the publication.

Online Supplement

Table 1 (Online Supplement): An overview of Austrian syndrome cases published since 1956. The file is available via this online link: https://doi.org/10.6016/ZdravVestn.3552.

References

1. Pasteur L. Études sur la bière: ses maladies, causes qui les provoquent, procédé pour la rendre inaltérable; avec une théorie nouvelle de la fermentation. Paris: Gauthier-Villars; 1893.
2. Sternberg GM. A manual of bacteriology. New York: W. Wood; 1893.
3. Winslow CE, Broadhurst J, Buchanan RE, Krumwiede C, Rogers LA, Smith GH. The Families and Genera of the Bacteria: Final Report of the Committee of the Society of American Bacteriologists on Characterization and Classification of Bacterial Types. J Bacteriol. 1920;5(3):191-229. DOI: 10.1128/jb.5.3.191-229.1920 PMID: 16558872
4. Ganaie F, Saad JS, McGee L, van Tonder AJ, Bentley SD, Lo SW, et al. A New Pneumococcal Capsule Type, 10D, is the 100th Serotype and Has a Large cps Fragment from an Oral Streptococcus. MBio. 2020;11(3). DOI: 10.1128/mBio.00937-20 PMID: 32430472
5. Hausdorff WP, Feikin DR, Klugman KP. Epidemiological differences among pneumococcal serotypes. Lancet Infect Dis. 2005;5(2):83-93. DOI: 10.1016/s1473-3099(05)01280-6 DOI: 10.1016/S1473-3099(05)70083-9 PMID: 15680778
6. Hanquet G, Krizova P, Dalby T, Ladhani SN, Nuorti JP, Danis K, et al.; SpIDnet group1. Serotype Replacement after Introduction of 10-Valent and 13-Valent Pneumococcal Conjugate Vaccines in 10 Countries, Europe. Emerg Infect Dis. 2022;28(1):137-8. DOI: 10.3201/eid2801.210734 PMID: 34932457
7. Ishiwada N, Niwa K, Tateno S, Yoshinaga M, Terai M, Nakazawa M. Pneumococcal endocarditis in children: a nationwide survey in Japan. Int J Cardiol. 2008;123(3):298-301. DOI: 10.1016/j.ijcard.2006.12.016 PMID: 17383029

8. Austrian R. The syndrome of pneumococcal endocarditis, meningitis and rupture of the aortic valve. Trans Am Clin Climatol Assoc. 1956-1957;68:40-7. PMID: 13486606
9. European committee on antimicrobial suspectibility testing. Breakpoint tables for interpretation of MICs and zone diameters. Växjö: EUCAST; 2025 [cited 2025 Jan 12]. Available from: https://www.eucast.org/organization.
10. Zheng S, Soh JX, Shafi H. Quadruple valve infective endocarditis presenting with suspected Austrian syndrome: a case report and a case series of quadruple valve infective endocarditis. Diagn Microbiol Infect Dis. 2019;94(1):60-5. DOI: 10.1016/j.diagmicrobio.2018.11.023 PMID: 30583882
11. Rammeloo L, Hruda J, Sobotka-Plojhar M, Avis W, Schoof P. Austrian syndrome in a child-aortic valve endocarditis following pneumococcal meningitis. Int J Cardiol. 2004;94(2-3):321-2. DOI: 10.1016/j.ijcard.2003.03.025 PMID: 15094001
12. Alhushki W, Rongkavilit C. Austrian syndrome associated with pandemic (H1N1) 2009 in child. Emerg Infect Dis. 2010;16(9):1493-5. DOI: 10.3201/eid1609.091779 PMID: 20735945
13. Mohapatra S, Doulah A, Brown E. Pneumococcal meningitis and endocarditis in an infant: possible improved survival with factor V Leiden mutation. Eur J Pediatr. 2017;176(10):1439-42. DOI: 10.1007/s00431-017-2973-1 PMID: 28801724
14. Ampofo K, Byington CL. Streptococcus pneumoniae. In: Long SS, Prober CG, Fischer MF., eds. Principles and Practice of Pediatric Infectious Diseases. 5th ed. Philadelphia: Elsevier; 2018 [cited 2025 Jan 12]. Available from: https://www.sciencedirect.com/book/9780323401814/principles-and-practice-of-pediatric-infectious-diseases.
15. Loughran AJ, Orihuela CJ, Tuomanen EI. Streptococcus pneumoniae: invasion and Inflammation. Microbiol Spectr. 2019;7(2). DOI: 10.1128/microbiolspec.GPP3-0004-2018 PMID: 30873934
16. van der Maten E, van den Broek B, de Jonge MI, Rensen KJW, Eleveld MJ, Zomer AL, et al. Streptococcus pneumoniae PspC Subgroup Prevalence in Invasive Disease and Differences in Contribution to Complement Evasion. Infect Immun. 2018;86(4). DOI: 10.1128/IAI.00010-18 PMID: 29378798
17. Levine OS, Farley M, Harrison LH, Lefkowitz L, McGeer A, Schwartz B. Risk factors for invasive pneumococcal disease in children: a population-based case-control study in North America. Pediatrics. 1999;103(3). DOI: 10.1542/peds.103.3.e28 PMID: 10049984
18. Rao EV, Buchanan JG, Baddiley J. The type-specific substance from Pneumococcus type 10A(34). Structure of the dephosphorylated repeating unit. Biochem J. 1966;100(3):801-10. DOI: 10.1042/bj1000801 PMID: 4381845
19. European Centre for Disease Prevention and Control. Invasive pneumococcal disease. Solna: ECDPC; 2020 [cited 2025 Jan 12]. Available from: https://www.ecdc.europa.eu/en/invasive-pneumococcal-disease.
20. Laval CB, de Andrade AL, Pimenta FC, de Andrade JG, de Oliveira RM, Silva SA, et al. Serotypes of carriage and invasive isolates of Streptococcus pneumoniae in Brazilian children in the era of pneumococcal vaccines. Clin Microbiol Infect. 2006;12(1):50-5. DOI: 10.1111/j.1469-0691.2005.01304.x PMID: 16460546
21. Sime WT, Aseffa A, Woldeamanuel Y, Brovall S, Morfeldt E, Henriques-Normark B. Serotype and molecular diversity of nasopharyngeal Streptococcus pneumoniae isolates from children before and after vaccination with the ten-valent pneumococcal conjugate vaccine (PCV10) in Ethiopia. BMC Infect Dis. 2019;19(1):409. DOI: 10.1186/s12879-019-4024-1 PMID: 31077141
22. Eichner H, Karlsson J, Spelmink L, Pathak A, Sham LT, Henriques-Normark B, et al. RNA thermosensors facilitate Streptococcus pneumoniae and Haemophilus influenzae immune evasion. PLoS Pathog. 2021;17(4). DOI: 10.1371/journal.ppat.1009513 PMID: 33914847
23. Butters C, Phuong LK, Cole T, Gwee A. Prevalence of Immunodeficiency in Children With Invasive Pneumococcal Disease in the Pneumococcal Vaccine Era: A Systematic Review. JAMA Pediatr. 2019;173(11):1084-94. DOI: 10.1001/jamapediatrics.2019.3203 PMID: 31566672
24. Phuong LK, Cheung A, Agrawal R, Butters C, Buttery J, Clark J, et al. Inborn Errors of Immunity in Children With Invasive Pneumococcal Disease: A Multicenter Prospective Study. Pediatr Infect Dis J. 2023;42(10):908-13. DOI: 10.1097/INF.0000000000004004 PMID: 37463351
25. Ingels H, Schejbel L, Lundstedt AC, Jensen L, Laursen IA, Ryder LP, et al. Immunodeficiency among children with recurrent invasive pneumococcal disease. Pediatr Infect Dis J. 2015;34(6):644-51. DOI: 10.1097/INF.0000000000000701 PMID: 25831419
26. Bijker EM, Bateman EAL, Trück J, Patel S, Kelly DF. Screening for Immunodeficiencies in Children With Invasive Pneumococcal Disease: Six-year Experience From a UK Children's Hospital. Pediatr Infect Dis J. 2022;41(7):575-8. DOI: 10.1097/INF.0000000000003554 PMID: 35421038
27. World Health Organization. Slovenia: WHO and UNICEF estimates of immunization coverage: 2023 revision. Geneva: WHO; 2024 [cited 2025 Jan 12]. Available from: https://cdn.who.int/media/docs/default-source/country-profiles/immunization/2024-country-profiles/immunization-2024-svn.pdf?sfvrsn=dffc7b96_3.