Recommendations of the Czech Vaccinology Society of the J. E. Purkyně Czech Medical Association for vaccination against invasive meningococcal disease

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Meningococcal disease is a serious, human-to-human transmissible disease caused by the gram-negative diplococcus *Neisseria meningitidis,* most often by its serogroups A, B, C, W, and Y. The source of infection can be an asymptomatic carrier or a diseased person. The most serious clinical forms are meningococcal meningitis and septicaemia. These invasive meningococcal diseases (IMD) have a peracute course and may lead to death within 24-48 hours after the onset of symptoms despite early treatment. Delay in diagnosis may occur due to initial nonspecific symptoms. Fatal outcomes have been reported in 10-20 % of patients. In the Czech Republic, the average case fatality rate was 9.3 % over the last decade (range 4.7 % to 13.9 %). About 20 % of survivors have permanent sequelae such as limb amputation, deafness, or mental retardation.

Epidemiology of invasive meningococcal disease

The incidence of IMD is declining worldwide, possibly as a result of more vaccine options becoming available. However, the case fatality rates and risk for lifelong sequelae still remain rather high. In the Czech Republic, the incidence of IMD has been low over the last decade, ranging from 0.4 to 0.8 cases per 100 000 population. The most affected age groups are children 0-11 months and 1–4 years and adolescents 15-19 years. Regardless of age, the most common causative meningococcal serogroups are B (55.8 % of all cases in 2016) and C (23.3 % of all cases in 2016). Cases caused by meningococcal serogroups W (9.3 % in 2016) and Y (2.3 % in 2016) are also reported every year. Although much less commonly involved in IMD, meningococcal serogroups W and Y have the highest case fatality rates. The highest incidence of IMD and the highest case fatality rate (17.7 %) are regularly reported in children aged 0-11 months, with meningococcal serogroup B being the predominant cause. The population groups at highest risk for IMD in the Czech Republic are the individuals from the most affected age groups, those with some health conditions, those living in large collectives, selected categories of health professionals, and travellers to high incidence countries.

Meningococcal vaccine options

The European Medicines Agency (EMA) has authorised two meningococcal conjugate tetravalent vaccines containing antigens of four meningococcal serogroups, A, C, W, and Y (MenACWY vaccines) and two recombinant meningococcal vaccines containing serogroup B antigens (MenB-4C and MenB-FHbp vaccines). The MenACWY vaccine has proved protective not only against IMD caused by the respective serogroups but also against their carriage. All these vaccines are licensed for use in both children and adults. The MenACWY vaccine is indicated for use in children from the age of six weeks (Nimenrix) or two years (Menveo). The MenB-4C vaccine can be used from the age of two months (Bexsero) and the MenB-FHbp vaccine from the age of 10 years (Trumenba). The goal of vaccination against IMD is to provide protective immunity for the vaccinated individual as early as possible, and it should be as complex and as long-lasting as possible.

Recommended vaccination against invasive meningococcal disease

To achieve as high serogroup coverage as possible, it is recommended to use both the MenACWY and Men B vaccines. The two vaccines should be given at least 14 days apart, and if needed, they can also be applied simultaneously but to different sites. In the latter case, the vaccines are likely to show higher reactogenicity. In some cases, a booster dose is required to maintain long-term immunity. For the MenB-4C vaccine, a booster dose is recommended in children under two years of age, the need for such a booster dose was not established in those over two years of age. For the MenB-FHbp vaccine, the need for a booster was not defined either. For the MenACWY vaccines, a booster dose is recommended at five-year intervals in case the IMD risk persists.

Vaccination against invasive meningococcal disease is recommended for:

- Infants aged from 2 to 11 months, with the first dose given preferably during the first half year of life;
- Children between the ages of 1 and 4 years;
- Adolescents and young adults between the ages of 13 to 25 years, with the vaccine given preferably between the ages of 13 to 15 years;
- Patients regardless of age with the following high-risk health conditions:
    - Defective or absent splenic function (hyposplenism/asplenism);
    - Autologous or allogeneic transplantation of hematopoietic stem cells;
    - Primary or secondary immunodeficiency or expected immunodeficiency;
    - Terminal complement deficiency;
    - A history of meningococcal meningitis and septicaemia,
    - Before starting eculizumab therapy;
- Persons regardless of age travelling to or planning to reside in hyperendemic or epidemic areas of the world;
- Persons at occupational risk for IMD (health professionals providing care to patients with IMD and laboratory staff at risk of exposure to the causative agent);
- Persons in the focus of IMD infection.

Dosing schedules for vaccination against invasive meningococcal disease

Children **aged 2 to 5 months** are immunised with the recombinant MenB-4C vaccine as a 3+1 dose series, with three doses given at least 1 month apart and followed by a booster dose between the ages of 12 and 15 months. The conjugate MenACWY vaccine is applied at the age under 12 weeks as a 2+1 dose series and at the age under 5 months as a 2+0 dose series. The 2+1 dose series consists of two doses given at least 2 months apart, followed by a booster dose at the age of 12 months. The 2+0 dose series includes two doses given at least 2 months apart.

Children **aged 6 to 11 months** are immunised with the recombinant MenB-4C vaccine as a 2+1 dose series, with two doses given at least 2 months apart and followed by a booster dose between the ages of 13 and 24 months. The conjugate MenACWY vaccine is applied as a 2+0 dose series, with two doses given at least 2 months apart.

Children **aged 1 to 4 years** are immunised with the recombinant MenB-4C vaccine, as a 2+1 dose series at the age under 23 months or as a 2+0 dose series between the ages of 2 years and 4 years. The 2+1 dose series consists of two doses given at least 2 months apart, followed by a booster dose 12-23 months after the second dose was administered. The conjugate MenACWY vaccine is applied as a 1+0 dose series which consists of a single dose.

Adolescents and young adults **aged 13 to 25 years** are immunised with the recombinant MenB-4C vaccine or MenB-FHbp vaccine, each as a 2+0 dose series. Two doses of the MenB-4C vaccine are given at least one month apart while two doses of the MenB-FHbp vaccine are given six months apart. The MenB-FHbp vaccine as a 2+0 series should only be used in immunocompetent persons. The conjugate MenACWY vaccine is applied as a 1+0 dose series, i.e. in a single dose.

Persons **with high-risk health conditions** are immunised with the recombinant MenB-4C vaccine as a 3+1, 2+1, or 2+0 dose series depending on age or with the MenB-FHbp vaccine as a 3+0 dose series. Two of the three doses of the MenB-FHbp vaccine are given at least one month apart and are followed by the third dose at least four months after the second dose. The conjugate MenACWY vaccine is applied as a 2+0 dose series (or as a 2+1 dose series in children under 12 months of age). The 2+0 dose series includes two doses given at least 2 months apart.

Travellers, persons **at occupational risk for IMD**, or those **in the focus of IMD infection** are immunised depending on age in accordance with SPC of the respective vaccine. To provide protection as rapidly as possible, it is recommended to apply the MenB-FHbp vaccine as a 3+0 series.