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EXAMINATION OF THE PREVALENCE OF VACCINE-PREVENTABLE PATHOGENS AND ATTITUDES TOWARDS VACCINATIONS

PhD thesis

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List of Abbreviations

App – Adhesion and penetration protein

BBB – Blood-brain barrier

BCG – Bacillus Calmette-Guérin/tuberculosis vaccine

BCSFB – Blood-cerebrospinal fluid barrier

CDC – Centers for Disease Control and Prevention

CFR – Case fatality rate

CI – Confidence interval

COVID – Coronavirus disease

CPS – Capsule polysaccharide

DC – Dendritic cell

DNA – Deoxyribonucleic acid

DRG – Dorsal root ganglia

DTPa – Diphtheria-tetanus-acellular pertussis vaccine

DTPa – Diphtheria-tetanus-acellular pertussis vaccine for revaccination purpose

ECDC – European Centre for Disease Prevention and Control

EMA – European Medicines Agency

FDA – Food and Drug Administration

fHbp – Human factor H binding protein

Hib – *Haemophilus influenzae b* vaccine

HZ – Herpes zoster

IgA – Immunoglobulin A

IL – Interleukin

IMD – Invasive meningococcal disease

IPV – Inactivated Poliovirus vaccine

LOS – Lipooligosaccharide

LPS – Lipopolysaccharide

MenA – Meningococcus serogroup A

MenACWY - Meningococcus serogroup A, C, W, and Y

MenB – Meningococcus serogroup B

MenC – Meningococcus serogroup C

MenW – Meningococcus serogroup W

MenX – Meningococcus serogroup X

MMR – Morbilli-mumps-rubella vaccine

NadA – Neisseria adhesin A

NCPHP – National Center for Public Health and Pharmacy

NHBA – Neisserial heparin binding antigen

NhhA – Neisseria hia/hsf homologue

NT – Non-typable

OR – Odds ratio

PBS - Phosphate-buffered saline

PCR – Polymerase chain reaction

PCV – Conjugated pneumococcus vaccine

PHN – Postherpetic neuralgia

RNS – Reactive nitrogen species

ROS – Reactive oxygen species

UK – United Kingdom

US – United States

VZV – Varicella-zoster virus

WHO – World Health Organization

1. Introduction

1.1. Infectious diseases

The common history of infectious diseases and mankind goes back a long way, perhaps all the way to the beginning. Written records from ancient times refer to infectious diseases, and thanks to modern technologies, their presence has been confirmed, for example, in ancient Egypt (1). Throughout history, many epidemics have shaken human communities, reducing the population to a fraction, for example plague, the Spanish flu or smallpox. These epidemics have not only led to a decline in population, but also in community and economy development. The breakthrough in understanding infectious diseases came when Anton van Leeuwenhoek developed the first microscope in the seventeenth century, with the help of which microbes began to be studied. In the fight against infections Edward Jenner's smallpox vaccine marked a milestone in the late eighteenth century, as it was the first artificial immunization in human history. From there, it was a straight path to developing vaccines and reducing infectious diseases. But we are nowhere near the end of this journey because infectious diseases were not only in store for us in the Dark Ages, and although medicine has improved tremendously with the development of humanity, infectious diseases have constantly given a lesson, partly due to changes in human habits and opportunities. Today, anyone, and anything, including pathogens, can get from one part of the world to another in just a few hours. We must therefore accept that we can hardly talk about physical, geographical barriers to infectious diseases anymore. We don't even have to look back that long, as the coronavirus disease (COVID) pandemic that broke out in 2019 is vivid in all our memories, we still bear its consequences today. Although effective and safe vaccines against the coronavirus were developed in record time using both traditional and state-of-the-art, cutting-edge new methods, this form of protection still encountered an obstacle, as vaccine hesitancy and, unfortunately, anti-vaccination also gained ground as never before. Even before the pandemic, in 2019, the World Health Organization (WHO) listed vaccine hesitancy as one of the 10 factors posing a great threat to human health (2).

The significance of infectious diseases is best described by Hans Zinsser's words in his book Rats, lice, and history: *"Infectious disease is one of the few genuine adventures left*

in the world. The dragons are all dead and the lance grows rusty in the chimney corner… But however secure and well-regulated civilized life may become, bacteria, protozoa, viruses infected fleas, lice, ticks, mosquitoes, and bedbugs will always lurk in the shadows ready to pounce when neglect, poverty, famine or war lets down the defenses… About the only sporting proposition that remains unimpaired by the relentless domestication of a once free-living human species is the war against those ferocious little fellow creatures, which lurk in dark corners and stalk us in the bodies of rats, mice and all kinds of domestic animals; which fly and crawl with the insects, and waylay us in our food and drink and even in our love" (3). This is the adventure I passionately signed myself up for.

Regarding infectious diseases, I focused on two important topics during my research. Firstly, with our research group we examined the prevalence of *Neisseria meningitidis* in Hungary, to collect information about which types of the bacterium are present in asymptomatic carriers and what might be the risk factors influencing carriage. Secondly, we wanted to understand better the attitudes towards varicella vaccination among parents and paediatric healthcare professionals before it was made mandatory in 2019 in Hungary. We also examined parental attitudes towards meningococcal vaccinations. In case of encountering a pathogen, vaccines play an important role in the protection against developing serious illnesses. Unfortunately, the increasing uncertainty concerning vaccinations in recent years is a barrier in their use. It is our responsibility to look up from the microscope and see, understand the bigger picture. As we saw during the COVID pandemic, the availability of vaccines is unavailing if people are not willing to take them.

1.2. Neisseria meningitidis

Neisseria meningitidis is an obligate human pathogen, that occurs all over the world. Encounter with the bacterium usually leads to asymptomatic carriage in the nasopharynx, which plays an important role in the spread of the pathogen (4). Disease develops only in a fraction of cases, when the bacteria enter the bloodstream, causing invasive meningococcal disease (IMD) (5). Though IMD is rare, it can be associated with very high mortality. There are an estimated 1.2 million cases of meningococcal infection per year, with ~135,000 death worldwide (6).

N. meningitidis belongs to the Neisseriaceae family as part of the Neisseria genus. On the microscopic view of the pathogen, we can see Gram-negative kidney-shaped diplococci

(Figure 1). Meningococci can be both encapsulated and without a capsule. Based on the antigen structure of the capsular polysaccharide it can be divided into 12 serogroups, the strains lacking a capsule are non-serogroupable or non-typable (NT) types. From the 12 serogroups, 6 causes most of the clinical cases, namely A, B, C, W-135, X and Y (7). Previously it was believed that the non-encapsulated strains can't cause disease, but it appears that in some strains capsule production can activate and inactivate in the bacteria (8). Moreover, there are reported cases about meningococcal disease caused by strains constitutively without capsule (9). Most of the cases the detected meningococci in carriers are not encapsulated, therefore not serogroupable.

There are several vaccines available for serogroup A, B, C, W-135 and Y, and there is one pentavalent vaccine that is also effective against serogroup X infection, but currently there is no vaccine to prevent the infection with other serogroups and with non-groupable strains. Knowing the circulating strains in the population is crucial to choose between the vaccine options, and for being prepared if a non-vaccine serogroup appears.

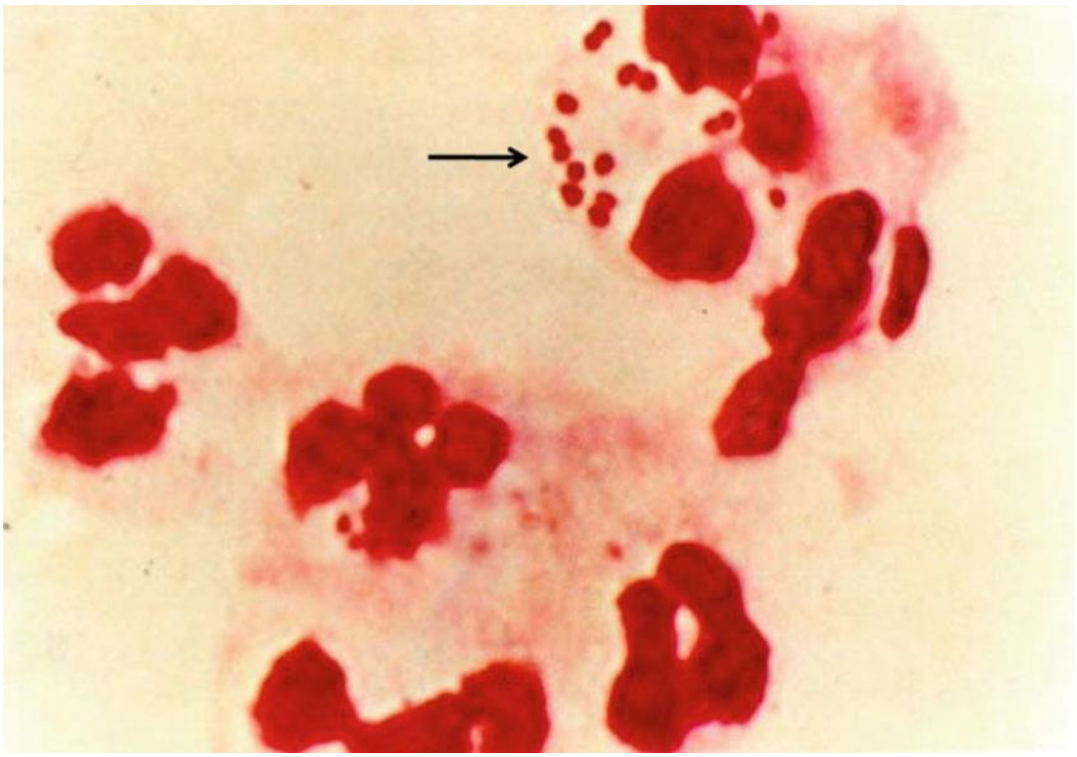

Figure 1. Gram-negative diplococci in the proximity or within leukocytes in the cerebrospinal fluid of a patient with meningitis (6). (*Reproduced with permission from Springer Nature)*

1.2.1. Epidemiology of *Neisseria meningitidis* infections

Neisseria meningitidis colonizes the mucosa of the upper respiratory tract of approximately 10% of general population worldwide without causing a disease (10). Asymptomatic carriage rate is highly variable globally, based on age and geographical location. A systematic review and meta-analysis found that in Europe carriage rate increases with age, from 4.5% in infants to peak at the age of 19 with 23.7% (11). In Africa in the so-called meningitis belt, carriage rate peaks during early adolescence (12). Those individuals carrying the bacteria without producing symptoms play an important role in the spread of the pathogen, which can occur via respiratory droplets, thus close contact with carriers or infected individuals can facilitate the spread (13). Semi-closed, crowded populations, such as university students, military recruits and pilgrims are at increased risk of infection (13). Social behavior and recent respiratory infections can also increase the risk of carriage (13).

The mechanisms leading to invasion from colonization are still not completely understood, the polysaccharide capsule can inhibit opsonization and phagocytosis, which can lead to bloodstream invasion (14). Damage to the nasopharyngeal epithelium is associated with higher incidence of meningococcal disease (15). Once entering the bloodstream, *N. meningitidis* can cause bacterial sepsis and, if crossing the brain-blood barrier, meningitis. Localized and chronic infections resulting in pneumonia, endophthalmitis, arthritis, pericarditis, or myocarditis may also occur (15, 16). All these are referred to as invasive meningococcal disease, but the most common are sepsis and meningitis. The incidence of IMD varies from 0.3 cases per 100 000 population in Europe (ECDC report from 2022) to 2-1000 cases per 100 000 population in the African meningitis belt (6, 17). In 2022 in Europe, serogroup B was the most frequent (63%), serogroup Y the second (16%) and serogroup W the third (10%) (17). Case fatality rate of the disease was 10% (17). In Africa, MenA used to be responsible for nearly all IMD cases, but as a result of the MenAfriVac program, confirmed MenA cases declined by 99%, and MenC, MenW and MenX became responsible for most of the cases (18). During epidemics, case fatality rate (CFR) ranges from 6.6 to 10.0% (18). In Hungary the National Center for Public Health and Pharmacy (NCPHP) reported 0.3 cases per 100 000 population in the latest report, from 2023, with 6% case fatality (19). In developed countries IMD is most common in infants and is the leading infectious cause of death in

early childhood, but the outcome for young adults is even worse as case fatality rate is higher (15%) in this age group (20). Even with the right treatment, CFR stands as 15%, and survivors often (10-40%) face long term sequelae of IMD, including paralysis, amputation, deafness and mental impairment (20, 21, 22).

1.2.2. Pathogenicity of *Neisseria meningitidis*

N. meningitidis enters the human body by respiratory droplets or direct contact with contaminated fluids. The pathogenesis has two important stages: the initial attachment and the resistance to host immunity (23). First the bacterium colonizes the nasopharynx via adhesion to epithelial cells. To successfully complete this task, it uses different adhesins, such as Type IV pili, NadA (Neisseria adhesin A), NhhA (Neisseria hia/hsf homologue) and App (Adhesion and penetration protein) (24). Besides mediating adhesion, Type IV pili are also involved in adhesion to endothelial cells, bacterial aggregation, twitching motility, bacterial migration, and natural transformation (24). The mechanisms meningococci use to leave the nasopharynx and invade the bloodstream are still just partially understood, supposed methods are active translocation, bacterial internalization, and trafficking within intracellular vacuoles (25). Opacity proteins Opc and Opa play an important role in internalization, but it can be enhanced by NadA and other bacterial factors, too (25). Most of the cases, if the bacterium enters the bloodstream, an immune response is generated, with the help of which bactericidal antibodies, complement, and phagocytic cells eliminate the pathogen (26). Unfortunately, *N. meningitidis* has several key factors that enhance its ability to survive within the host and evade immune responses such as IgA protease expression, LPS (lipopolysaccharide) sialylation, polysaccharide capsules and ROS/RNS detoxification (23). Among these, the polysaccharide capsule stands out as a critical virulence factor. This capsule not only protects the bacterium from phagocytosis by macrophages but also plays a crucial role in serum resistance, thus allows the pathogen to persist in the bloodstream, leading to systemic infection (23).

N. meningitidis colonizes the surface of capillary endothelial cells throughout the body including spleen, skin, liver, kidney, heart, and brain (25). The interaction between the bacterium and the endothelial cells results in loss of vessel integrity by disassembly of adherens junctions and tight junctions, causing peripheral leakage syndrome that can lead to purpura fulminans, and creating an opportunity for the bacteria to cross the blood-brain

barrier (BBB) or the blood-cerebrospinal fluid barrier (BCSFB) (5, 25). Besides this paracellular pathway, bacteria can cross the BBB or the BCSFB inside infected host macrophages ("Trojan-horse" mechanism), or transcellularly by invading the barrier cells and using signaling pathways (Figure 2) (5). The interaction with endothelial cells also increases procoagulant activity of the endothelium (25). Meningococcus, as a Gram-negative bacterium, has a pyrogenic endotoxin component in its cell wall, but instead of the usual LPS structure, it has LOS (lipooligosaccharide). The endotoxin stimulates monocytes, neutrophils, endothelial cells and promotes release of pro-inflammatory cytokines (tumor necrosis factor, IL-1, IL-8, interferon gamma) (26). The overstimulation of these can lead to septic shock.

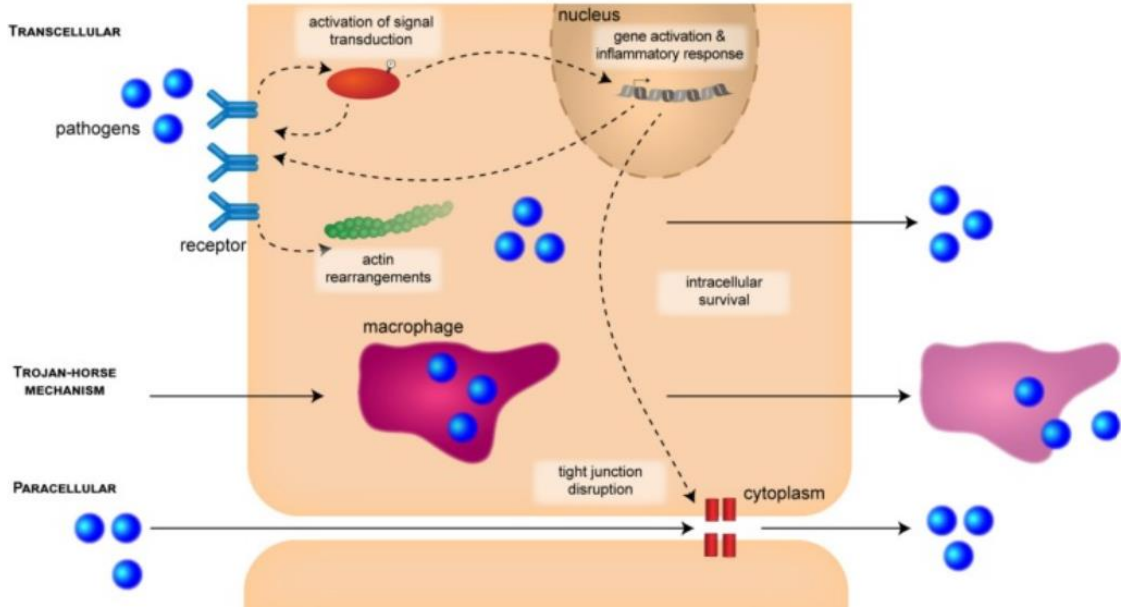

Figure 2. Possible routes for bacteria to enter the central nervous system: transcellularly, via infected macrophages, or paracellularly (5).

1.2.3. Clinical diseases caused by *Neisseria meningitidis*

Disease usually develops in the first week after colonization (it can range from 1 to 14 days) (15). Symptoms in the first 4-6 hours from onset can be mild, similar to respiratory viral infections, such as sore throat, fever, loss of appetite, nausea, vomiting, and headache, but may progress to fulminant disease, multi-organ failure and death within hours (15, 27, 28). The determination of the disease depends on the innate and acquired immune response of the host, which is affected by the bacterial load and genetic factors (15). Low level of meningococci in the bloodstream is sufficient for meningeal invasion,

while high level of bacteremia can lead to massive colonization of peripheral endothelial cells, increased vascular permeability and thrombosis, causing septic shock and purpura fulminans (29). While IMD usually progresses to either meningitis or sepsis, 12% of individuals may have symptoms of both (15). In some cases, meningococcus can cause arthritis, pericarditis, conjunctivitis or pneumonia (16).

Meningococcal sepsis develops in 20–30% of IMD cases (15). The most common symptoms are cold hands and feet, diarrhea, nausea, vomiting, fatigue, fever, rapid breathing, severe pain in the muscles, joints, chest, or abdomen, and in the later stages, a dark purple rash (30). Confusion and delirium, caused by hypotension and cerebral hypoperfusion appear later (15). Meningococcal sepsis is a typical endotoxin mediated disease, the activation of the immune response of the host can lead to increased cytokine release (29). 25% of patients develop a purpura fulminans syndrome that associates extensive cutaneous thrombosis, ischemic necrosis of skin and organs and a severe septic shock (31). Prompt recognition and treatment of meningococcal septicaemia has reduced the mortality rate from 40% to 5–20% over the last decade (15).

Meningitis is the predominant presentation of IMD, it develops in 30-60% of cases (15). The most common symptoms are fever, headache and stiff neck, additional symptoms can be altered mental status, nausea, photophobia, and vomiting (30). Infants appear to be slow or inactive, irritable, feed poorly, have a bulging anterior fontanelle, abnormal reflexes, vomit (30). These are caused by the inflammatory response triggered within the subarachnoid space, the increased intracranial pressure and oedema can lead to cerebral herniation and death (15). Even with the right antibiotic treatment, the rapidly progressing meningococcal meningitis has a case fatality rate of 4-20%, while in untreated cases it can reach up to 80% (18).

Long-term consequences of IMD affect 20% of survivors, these can be categorized as physical (mostly amputations and skin scarring), neurological (hearing loss, seizures, cognitive problems, motor deficits, visual impairment) and psychological sequelae (30, 32).

1.2.4. Vaccines against meningococcal disease

The first meningococcal vaccines, prepared from heat killed bacterial cultures, date back to the early 1900s, however, with questionable efficacy and high reactogenicity, these

efforts to make safe and effective vaccines were unsuccessful (33). The following decades meningococcal vaccine development was focusing on capsule polysaccharides (CPS). At the end of the 1960s researchers were able to develop high-molecular weight capsular polysaccharide vaccines, which showed 89.5% effectiveness against disease caused by serogroup C (34). At the time, researchers were focusing on developing a vaccine against serogroup C, because of the high incidence of MenC meningococcaemia and meningitis (34). From the 1970s, CPS vaccines were licensed targeting meningococcus serogroup A, C, W-135 and Y in monovalent forms and in different combinations as bi-, tri- and tetravalent vaccines (34). The first tetravalent meningococcal CPS vaccine was approved in 1978 (35). The immunogenicity of CPS vaccines in children under the age of 2 was unsatisfactory because of the lack of inducing T-dependent immunity (35). This problem got overcome at the end of the 1990s by the recognition of the effect of chemically conjugating the polysaccharides to carrier proteins on inducing T-dependent immunity (33). The first conjugated polysaccharide vaccine (against meningococcus C) was introduced into the rutin immunization program in the United Kingdom (UK) in 1999 and resulted 89-94% reduction in the incidence of the disease caused by MenC in each age group under 20 years by 2002 (33). The vaccine not only reduced the number of disease cases but also nasopharyngeal carriage, by 75% (35). Following the successful campaign, the Netherlands, Ireland, Spain, Australia, and Canada also decided to implement the vaccine in their national immunization program, with similar results, leading to major reduction in MenC cases worldwide (33). Multivalent conjugated polysaccharide vaccines for meningococcus A, W-135 and Y were also licensed worldwide (33). Meningococcus A, as the main source of the disease in the African meningitis belt, was the target of an enormous vaccination campaign in the 2010s aiming to reduce the incidence of the disease in Africa with a monovalent conjugated meningococcus A polysaccharide vaccine called MenAfriVac (36). The incidence of suspected meningitis cases decreased by 57% and the incidence of confirmed group A meningococcal disease with 99% in fully vaccinated populations (37). Despite the success of conjugated polysaccharide vaccines, it was a challenge for scientists to develop a vaccine against meningococcus B. When CPS vaccines were developed, vaccines against serogroup B were tested, but only a few individuals showed antibody response (34). The immunogenicity did not improve with conjugating the polysaccharides to proteins (36).

It has been revealed that the reason behind the poor immune response is that the capsule polysaccharide of meningococcus B is identical to polysialic acid found on the surface of many human cells, and this similarity may even cause autoimmune reactions (36). Therefore, researchers were focusing on other parts of the bacterium, starting with purified outer membrane vesicle, containing outer membrane protein porin A, but it only protected against specific strains, so other targets were needed (36). With the help of reverse vaccinology, potential antigens were detected: Neisserial heparin binding antigen (NHBA), human factor H binding protein (fHbp), and Neisseria adhesin A (NadA) (33, 36). The combination of these antigens with porin A led to the development of the currently used vaccines against serogroup B (Bexsero licensed since 2013 in Europe, Trumenba since 2017) (33, 34, 36).

In March 2024, history was made in Nigeria as the first pentavalent meningococcus vaccine against serogroup A, C, W, X, and Y was introduced into the national immunization program. It is a conjugated capsule polysaccharide vaccine, and is the first one against serogroup X, showing 97,2% seroconversion rate (38).

1.3. Varicella-zoster virus

Varicella-zoster virus (VZV) causes varicella (chickenpox) in children and, later in life, may reactivate in the form of herpes zoster (shingles). Varicella is one of the most common childhood diseases, usually with mild, self-limiting symptoms, but rarely it can be associated with serious complications such as bacterial superinfection, pneumonia, and encephalitis in otherwise healthy children (39, 40). The WHO estimates approximately 140 million varicella cases annually, 4.2 million severe complications leading to hospitalization, and 4200 deaths (41).

Varicella-zoster virus is a DNA virus from the *Orthoherpesviridae* family, which contains animal and human herpes viruses that have a unique replication strategy, as they can develop either a lytic or a latent infection (42). Historically based on their cytopathogenic effect and the place of latency, today based on genetic content, *Orthoherpesviridae* family members can be divided into *Alpha*-, *Beta*-, and *Gammaherpesvirinae* subfamilies with VZV, also called *Human alphaherpesvirus 3*, belonging to the *Varicellovirus* genus in the *Alphaherpesvirinae* subfamily (42). Viruses in this subfamily cause cell death during lytic infection and establish lifelong latency mostly but not exclusively in the neurons (42).

1.3.1. Epidemiology of *Varicella-zoster virus*

Varicella-zoster virus occurs worldwide. In countries without a varicella vaccination program, 90% of the population is infected before young adulthood, thus developing lifelong immunity, while approximately 5% of the adult population remains susceptible to infection with the virus (41). In the United States (US), before the start of the varicella vaccination program in 1995, an average of 4 million people got infected each year, 10500-13000 were hospitalized, and 100-150 died from varicella (43). Since then, chickenpox cases have declined overall by more than 97%, now there are fewer than 150000 cases, 1400 hospitalizations and 30 deaths each year (43). In Europe, without a vaccination program more than 5 million cases would occur annually, from which about 20000 patients would be hospitalized and 80 would die (44). In high-income countries, without vaccination, case fatality rate for varicella is approximately 3 per 100 000 cases (41). In Hungary, before the introduction of varicella vaccination into the national immunization program, the incidence of varicella was an average of 341.3 cases per 100 000 population per year (between 2015 and 2019), while the average mortality rate was 0.014 per 100 000 population (45). After the introduction of the mandatory vaccine in 2019, the number of reported cases started to decline to an average of 140.3 per 100 000 population annually (between 2020 and 2023), with 0.0075 per 100 000 population mortality rate (19). According to the European Centre for Disease Prevention and Control (ECDC), without a vaccination program 52–78% of the cases occur in children under the age of 6 and 89–95.9% of the cases under the age of 12 (46). Patients usually make full recovery from varicella, but complications can appear, the most frequent are skin and soft tissue superinfections, neurological and pulmonary complications (46). The risk of severe varicella is higher in immunocompromised individuals, still, most complications occur in otherwise healthy children (46).

Shingles, also known as zoster or herpes zoster (HZ), is a secondary disease caused by the *Varicella-zoster virus*, which usually occurs over the age of 50 years. Anyone who has had chickenpox is at risk of developing shingles. As the vaccine strain is attenuated, having shingles after vaccination has reduced risk. The lifetime risk of developing HZ in the general population is between 25% and 30%, but this increases to 50% over the age of 80 (47). The incidence of HZ in North America and in Europe is 3-5 per 1000 person-years, increasing to 8-12 per 1000 person-years at the age of 80 (48). The most common

complication of HZ is postherpetic neuralgia (PHN), defined as at least 90 days of persistent pain, which can occur in 5-30% of cases (48). Other complications can be meningoencephalitis, myelitis, vasculopathy, acute or progressive outer retinal necrosis. About 3% of patients with zoster are hospitalized, the mortality is around 0.25 per million population in the US and Europe, mostly among the elderly (49).

1.3.2. Pathogenicity of *Varicella-zoster virus*

The pathogen can be transmitted by direct contact with varicella or herpes zoster rash, or by aerosolized virions from skin lesions or respiratory fluids (50). The virus enters the body through the upper respiratory tract or the conjunctiva (41). Once in a susceptible host, the virus begins to replicate in the epithelial cells of the upper respiratory tract (51). After replicating in the epithelial cells, the virus first infects dendritic cells (DC), that can help it reach the tonsils and other local lymphoid tissues, where the virus can infect T cells (51). VZV promotes the survival of infected T cells by altering the intrinsic antiviral defenses, thus giving them time to reach different tissues (52). During the incubation period of the disease the infection progresses to viremia, thus, with the help of the infected T cells, the virus can reach the respiratory mucosa and the skin, where it infects keratinocytes causing vesiculopustular exanthema (53). The lesions disseminate across the body, including mucous membranes, such as the oral cavity (53). During the primary infection the virus spreads to the sensory ganglia either by retrograde axonal transport from the skin, or by hematogenous spread with infected T-cells (54). Both can provide access to the virus to reach the autonomic ganglia in the enteric nervous system too (55). In the neurons VZV does not replicate or indicate apoptosis, there is no lytic infection, the virus enters a dormant state called latency, that can last for years or even decades. The mechanism by which VZV reactivation is induced is unknown, but it is likely to be triggered by stress or immunosuppression (especially reduction in T-cell mediated immunity) (53). Through the reactivation process, VZV uses anterograde axonal transport from the reactivating ganglia to the innervating dermatome, where it causes a secondary infection, herpes zoster (53). The process described above is summarized in Figure 3.

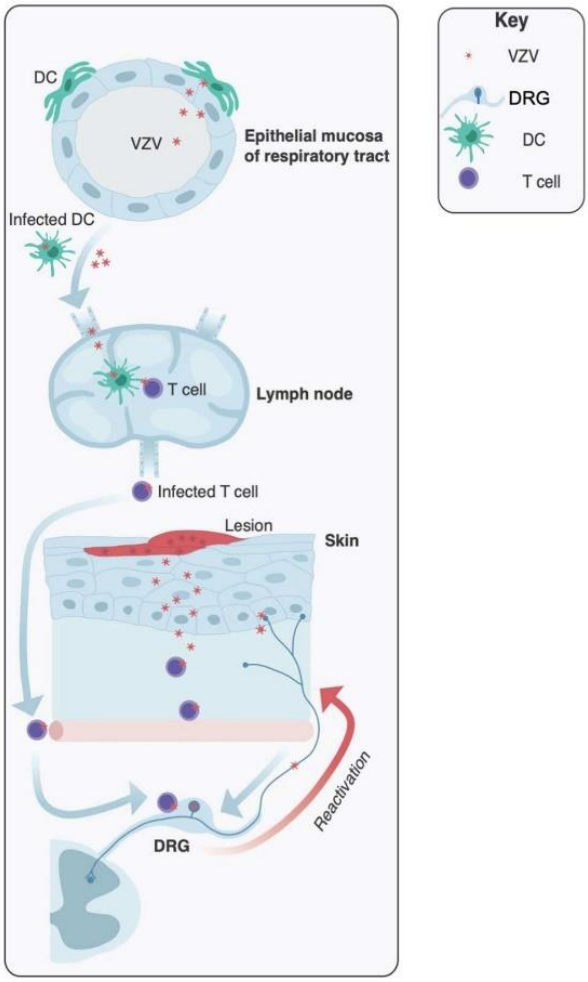

Figure 3. Key sites of infection during *Varicella-zoster virus* pathogenesis: epithelial mucosa of respiratory tract, lymph nodes, skin and dorsal root ganglia (53).
(DC = dendritic cell, DRG = dorsal root ganglia)

1.3.3. Clinical diseases caused by *Varicella-zoster virus*

The primary infection with VZV results in varicella (chickenpox). The source of the disease is an infected person. One can get infected by direct contact, with the inhalation of the aerosolized virions from skin lesions (from varicella or HZ), or via infected respiratory secretions. After the virus reaches the respiratory tract of a non-immune individual, viremia develops in 4-6 days. The infection has a 10–21-day incubation period, but the typical chickenpox rash appears after 14-16 days (56). In the prodromal phase, 1-2 days before the rash appears, fever, malaise, anorexia, and headache may occur (56). Chickenpox is characterized by a generalized, itchy rash that first appears on the trunk and face, then spreads to the entire body (57). The skin lesions first develop as

macules, papules, then vesicles, and finally pustules (Figure 4). While the first skin lesions scab, new ones appear for 5-7 days (41). When scabbing is complete, the infectiousness ceases (50). The simultaneous presence of lesions in different stages and their localization are characteristics of varicella (41). If a vaccinated person gets infected with VZV, breakthrough varicella may occur, where the rashes are mostly maculopapular with no or only a few vesicular lesions (56). While the disease is usually mild in otherwise healthy children, it can be much more severe and lead to dangerous complications in adolescents, adults, and patients with immunodeficiency (57). Newborns and pregnant women are also particularly at risk. After recovery, usually lifelong immunity develops against varicella, therefore a second appearance of chickenpox is extremely rare (57). Since the virus becomes latent in neurons after the infection, reactivation can occur later in life, causing shingles.

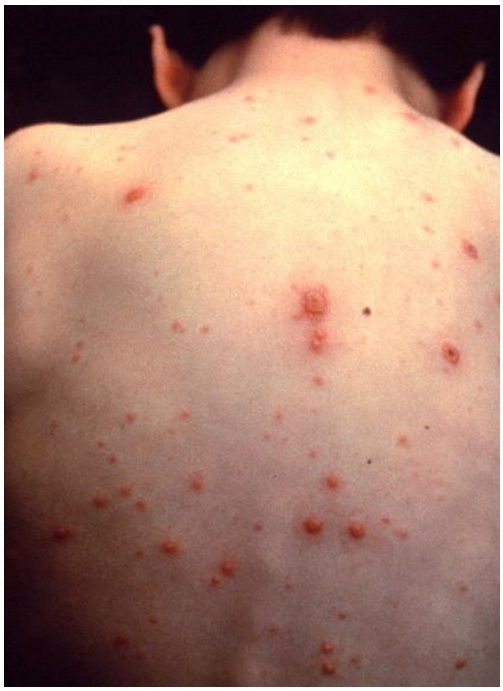

Figure 4. Typical varicella rash on the back of a child (57)

In the prodromal phase of shingles, patients experience pain and tingling at the site of the later rash in the days preceding the appearance, and in some cases headache, malaise and photophobia may also occur (58). After the prodrome a unilateral vesicular rash appears, characteristically restricted to one dermatome (Figure 5), typically accompanied by radicular pain (41). The affected dermatomes are most often on the trunk or on the face.

New vesicles form for 3–5 days, then they dry and scab over, until completely healing in 2–4 weeks (58). After the acute phase of vesicular rash, patients can experience unpleasant complications, most commonly postherpetic neuralgia, which is persistent pain in the area where the rashes were located, lasting months or even years (58). Further complications can be herpes zoster ophtalmicus (if the ophthalmic division of the trigeminal nerve is affected), or disseminated zoster, which can manifest as generalized rash or meningoencephalitis, pneumonitis, hepatitis (58).

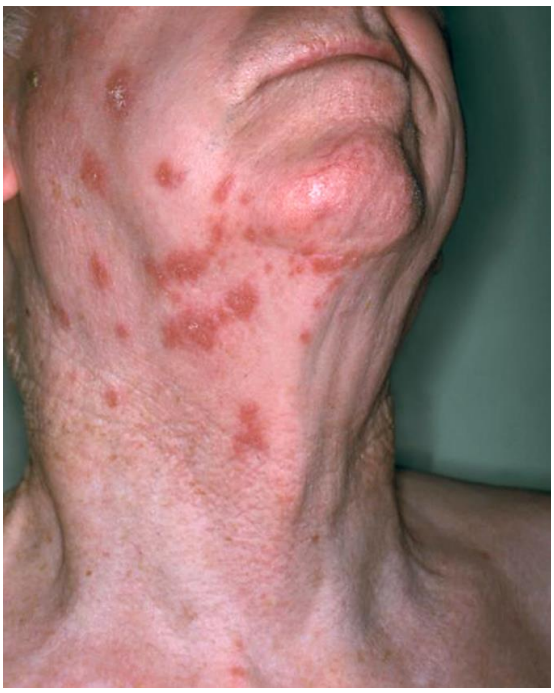

Figure 5. Vesicular rash on the neck and face of a patient with shingles (58).

1.3.4. Vaccines against varicella and herpes zoster

The development of a vaccine against varicella was motivated by the significant public health burden of the disease and the risk of severe or fatal complications in immunocompromised individuals. In 1974, the first live, attenuated VZV vaccine was developed in Japan, known as vOka (59). The first commercially available version was licensed in 1984, in Germany and Sweden (59). In the US it became available in 1995 when they introduced the vaccine into the national immunization program (59). Germany was the first country in Europe to implement routine varicella vaccination for all children between 11 and 14 months in 2004 (60). In Hungary, varicella vaccine became available in 2003 on the private market and reached about 20% vaccination coverage (61).

Awareness of the disease was raised by recommendations, professional and parental education, but still, vaccine coverage has reached a plateau (61). After considering the economic burden caused by varicella in Hungary, in 2019, the budget financed mandatory universal varicella vaccination was integrated into the National Immunization Program (62). Currently, several live, attenuated varicella vaccine formulations are available, both as monovalent (containing only varicella) and as multivalent vaccines, combined with measles, mumps, and rubella vaccine (MMR). In general, both types can be used as part of a routine, two-dose varicella vaccination schedule.

The replication of the vaccine strain is limited in human skin, but it can occur moderately in T cells and in ganglia (59). Clinical evidence also shows the attenuation: the incidence and severity of rash is significantly reduced following vaccination compared to infection with wild-type VZV, and transmission only occurs when rash is developed after vaccination (63). The disadvantage of a live, attenuated VZV vaccine strain is that it can establish latency and then reactivate, causing herpes zoster. This justifies the need to develop alternative vaccines produced by other technologies.

In 2006, the first herpes zoster vaccine, containing live, attenuated VZV from the Oka/Merck strain was licensed in the European Union and the US (64). More than ten years later, in 2017 in the US, the FDA (Food and Drug Administration) and in 2018 in Europe, the EMA (European Medicines Agency) approved a new, significantly more effective vaccine, containing VZV glycoprotein-E surface antigen, produced by recombinant technology, and an adjuvant component (AS01B) (64). This subunit vaccine does not replicate and does not have the ability to establish latency and reactivation, therefore cannot cause herpes zoster. There are alternative vaccines under development, for example mRNA vaccines, subunit vaccines with other adjuvants, vaccines based on nanoparticle technology, both to prevent herpes zoster and varicella (64).

1.4. Mandatory and non-compulsory vaccines in Hungary, vaccine hesitancy

In Hungary, vaccines to prevent several childhood diseases are involved in the national immunization program. The NCPHP provides a guideline every year to summarize the knowledge related to vaccination activities, practical tasks, general and specific indications and contraindications related to vaccinations, regulations and

recommendations. Based on this guideline, Table 1 shows the vaccination calendar in Hungary for 2025 (65).

Table 1. Vaccination calendar for 2025 in Hungary (adapted from the National Center for Public Health and Pharmacy - Guideline for vaccinations in 2025) (65)

Continuous vaccinations			
Vaccine	Age		Comment
	Mandatory	Non-compulsory	
BCG	0-4 weeks		in the maternity institution
DTPa +IPV + Hib + PCV	2 months		
DTPa +IPV + Hib	3 months		
DTPa +IPV + Hib + PCV	4 months		
PCV + Varicella	12 months		
MMR + Varicella	15 months		
DTPa + IPV + Hib	18 months		
DTPa + IPV	6 years		
Campaign vaccinations			
Vaccine	Mandatory	Non-compulsory	Comment
MMR revaccination	11 years		in September, for children in 6th class of elementary school
dTap booster vaccination	11 years		in October, for children in 6th class of elementary school
Hepatitis B	12 years		in the 2024/2025 educational year in March, for children in 7th class of elementary school - 3rd vaccination
			in the 2025/2026 educational year in September, for children in 7th

			class of elementary school - 1st vaccination
			in the 2025/2026 educational year in October, for children in 7th class of elementary school - 2nd vaccination
HPV		12 years	in the 2024/2025 educational year in April, for children in 7th class of elementary school - 2nd vaccination
			in the 2025/2026 educational year in October, for children in 7th class of elementary school - 1st vaccination
BCG = Bacillus Calmette-Guérin/tuberculosis vaccine; DTPa = diphtheria-tetanus-acellular pertussis vaccine; Hib = *Haemophilus influenzae* b vaccine; IPV = inactivated Poliovirus vaccine; PCV = conjugated pneumococcus vaccine; MMR = morbilli-mumps-rubella vaccine; DTPa = diphtheria-tetanus-acellular pertussis vaccine for revaccination purpose; HPV = human papillomavirus vaccine; Varicella = varicella vaccine			

Vaccination coverage with obligatory childhood vaccines is extremely high in Hungary, the latest data from 2023 shows that 99,5-99,9% of the obliged population got vaccinated against tuberculosis, diphtheria, tetanus, pertussis, *Haemophilus influenzae b*, Poliovirus, pneumococcus, morbilli, mumps, rubella and Hepatitis B virus (66). The uptake rate was a little lower in the case of varicella, where 99,1% got the first dose and only 98,8% got the second, but these numbers are still providing high vaccine coverage in the respective age group (66). As a result of the vaccination program, the incidence of these vaccine preventable diseases is very low in Hungary. On the other hand, exact data on the occurrence of pathogens that are not included in the vaccination calendar and can be prevented by recommended, non-compulsory vaccinations are not available, these pathogens are probably more common.

Vaccination to prevent both varicella and IMD is recommended for specific population groups in Hungary. As a work-related vaccination, meningococcal vaccine is recommended for those working in microbiological laboratories or treating infected patients. Varicella vaccination is recommended for non-immune healthcare workers treating immunocompromised patients, pregnant women or newborns and infants (65). In Hungary, as most of the IMD cases are due to MenB and MenC, vaccinations against serogroup C and B infections are recommended, for the following populations:

- infants
- children and young adults living in closed communities
- young people between the ages of 14 and 25 entering a new community
- people with increased susceptibility to disease due to their health condition, regardless of age
- young people attending secondary and higher education institutions who have a risky lifestyle in terms of invasive disease (65).

Vaccination with non-compulsory vaccines is typically low in Hungary. Before VZV vaccine was made mandatory in 2019, vaccine coverage against varicella-zoster virus was around 20% (61). In countries where VZV vaccination is not mandatory, whether children receive this vaccine depends primarily on parents' voluntary decisions and willingness to pursue vaccination (62). According to WHO data, vaccination with non-compulsory vaccines is influenced by several factors, including parents' and pediatric healthcare professionals' knowledge of the disease to be prevented, fear of possible side effects of vaccinations, confidence in the effectiveness of vaccinations, parents' education and financial situation (67). A joint study from Hungary and Poland on varicella vaccination also found that the main barriers on vaccine uptake are insufficient health-consciousness of the public, lack of information on the side of healthcare professionals, and financial constraints (61). Nothing says more about the significance of vaccine hesitancy that when the WHO published a list of “ten threats to global health in 2019” they named vaccine hesitancy as one of them (2). It is important to better understand the attitudes related to vaccinations and the reasons for rejecting vaccinations, to increase childhood vaccination and reduce the number of serious diseases that can be prevented by vaccination. To further support vaccination, we can provide data on the benefits, which usually are hard to capture and cannot be measured directly, also it is important to see population

effectiveness, that could differ from individual efficacy (61). The epidemiology of diseases we are trying to prevent is often not known, and we cannot wait for pandemics to gain evidence on vaccine effectiveness (61). Therefore, studies that assess asymptomatic carriage of a pathogen can help show the effect of vaccinations in the population.

2. Objectives

The objectives of our studies were the following:

(1) To examine the knowledge, attitudes and factors influencing the support or rejection of varicella vaccination among parents and pediatric healthcare professionals in Hungary, before the introduction of varicella vaccination into the national immunization program. Our study sought to have an answer to the question of how to increase the trust and so the vaccination rate and safety of young children in relation to VZV vaccination and other vaccinations.

(2) To assess knowledge about *Neisseria meningitidis* infection and the factors that determine refusal or support for vaccination among parents.

(3) To assess the prevalence and risk factors of asymptomatic carriage of *Neisseria meningitidis* in high school and university students in Hungary, furthermore, to identify the currently circulating serogroups in these populations.

3. Methods

3.1. Examination of the attitudes towards varicella vaccinations

3.1.1. Study population

To reach as many participants as possible, we recruited parents and pediatric healthcare providers via the internet to fill out a questionnaire about varicella vaccination (the original Hungarian questionnaires are attached at the end of the thesis). The questionnaire was available between October 2018 and February 2019, participants gave their informed consent by filling it in. 1146 parents and 194 healthcare professionals (189 pediatric health visitors and 5 pediatricians) completed the survey. The study included 1,042 parents who responded to the primary outcome question about whether they had vaccinated at least one child against varicella. The primary outcome of the survey for professionals was whether they support universal varicella vaccination or not.

The questionnaire contained questions regarding socioeconomic and demographic background of the participant, knowledge and personal experiences about varicella and its complications, attitude towards varicella vaccination and reasoning behind the decisions. Where possible, similar questions were used for professional and parent groups. The Semmelweis University Regional and Institutional Committee of Science and Research Ethics approved both the study methodology and questionnaire (SE RKEB 241/2018).

3.1.2. Data analysis

For healthcare professionals, the main outcome measured was their stance on universal varicella vaccination. They were categorized into two groups: those advocating universal vaccination for all children, and those either opposing vaccination entirely or supporting it only for specific populations. For parents, the primary outcome examined was voluntary vaccination of at least one child prior to Hungary's implementation of universal varicella vaccination. Factors analyzed as potential attitude determinants included socioeconomic background, personal experience with varicella and its complications, perceptions about disease severity, and healthcare provider recommendations. The survey also documented reasons given by professionals who did not fully endorse varicella vaccination and by parents who chose not to vaccinate all their children.

We employed logistic regression to explore the factors influencing vaccination decisions among both healthcare professionals and parents. The multivariate analysis for parental decision-making incorporated several key variables: demographic characteristics including age and gender, residential context, number of children, educational background, self-reported economic status, personal encounters with varicella and its potential complications, perceptions of the disease's severity, and recommendations from pediatric healthcare providers regarding vaccination. For healthcare professionals, we examined variables such as age, work area, number of children, perceptions of the disease's severity, and prior experience with disease complications. We calculated odds ratios with corresponding 95% confidence intervals, excluding incomplete response sets. Statistical significance was determined by a p-value threshold of less than 0.05, so the determinants were considered significantly associated with outcome if p value was less than 0.05. To compare perspectives between professionals and parents, we used a two-sided Chi-square test to analyze responses to selected questions. All statistical computations were made using MedCalc for Windows (version 19.0.4), developed by Med-Calc Software in Ostend, Belgium.

3.2. Examination of attitudes towards *Neisseria meningitidis* vaccination

3.2.1. Study population

Parents were invited to take part in an online survey assessing their knowledge of *Neisseria meningitidis* infection and their attitudes towards vaccination (the original Hungarian questionnaire is attached at the end of the thesis). The online questionnaire was available between November 2020 and July 2021, participants gave their informed consent by filling it in. Overall, 165 parents completed the survey, but only 159 of them responded to the primary outcome question about whether they had vaccinated at least one child against meningococcal infection.

Similarly to our study with varicella vaccination, the questionnaire contained questions regarding socioeconomic and demographic background, knowledge and personal experiences about *N. meningitidis* infection and its complications, attitude towards vaccination and reasons behind the decisions. We implemented an additional question to see whether the parent had completed health-related studies. The Semmelweis University

Regional and Institutional Committee of Science and Research Ethics approved both the study methodology and questionnaire (SE RKEB 215/2020).

3.2.2. Data analysis

The primary outcome examined was voluntary vaccination of at least one child against *N. meningitidis* infection. As potential determinants influencing vaccination decision included socioeconomic background, personal experience with meningococcal disease and its complications, perceptions about disease severity, and healthcare provider recommendations. The survey also documented reasons given by parents who chose not to vaccinate their children.

To examine the factors influencing vaccination decisions among parents, logistic regression analysis was applied. The involved variables were age, gender, type of settlement, number of children, educational level, self-reported financial status, personal encounters with meningococcal disease and its potential complications, view on the disease's severity, recommendations from pediatric healthcare providers regarding vaccination and health-related studies of the parent. We calculated odds ratios with 95% confidence intervals, excluding incomplete response sets. The determinants were considered significantly associated with the outcome if p-value was less than 0.05. All statistical calculations were made using MedCalc for Windows (version 23.2.0), developed by Med-Calc Software in Ostend, Belgium.

3.3. Assessing the prevalence and risk factors of asymptomatic carriage of *Neisseria meningitidis*

3.3.1. Study population

Our study examining meningococcal carriage was conducted with the participation of 610 healthy adolescents and young adults between ages 15-31 (median age 21) from November 2017 through December 2018. The participants were nearly evenly divided between Budapest public high school students (307 individuals, 50.3%) and Semmelweis University third-year students (303 individuals, 49.7%). Among high school participants, the majority were 17-18 years old (90.3%), with an overall age range of 15-20 years, and schools contributed a median of 29 students each (ranging 16-72). University participants were predominantly 21-23 years old (71.0%), with ages between 19-31 years. The gender distribution was almost equal, 50.9% of the participants were female. The research

protocol included written information for students and parents, with direct consent from participants 18 years or older and parental permission required for younger students. The Semmelweis University Regional and Institutional Committee of Science and Research Ethics approved both the study design and questionnaire (reference: SE TUKEB 4-4/2009).

3.3.2. Sample collection

We collected oropharyngeal swab samples and transported them to the laboratory in Transwab Charcoal medium (Medical Wire & Equipment, Corsham, UK) at room temperature. DNA extraction was performed using QIAamp BiOstic Bacteremia DNA Kit (Qiagen, Venlo, Netherlands), beginning with a two-hour immersion of swabs in 2ml phosphate-buffered saline (PBS). After centrifugation, the sediment was resuspended in 450µl of the initial kit solution, and after this step, we have followed the manufacturer's protocol. Final DNA concentration measurements were taken using a NanoDrop Lite spectrophotometer (Thermo Scientific), then samples were stored at -80°C until analysis.

3.3.3. Assessment of risk factors for meningococcal carriage

Participants completed an anonymous questionnaire to assess potential meningococcal carriage risk factors, including age, gender, number of siblings, smoking habits, exposure to passive smoking at home, regular attendance at crowded events, recent respiratory infections (previous two months), recent antibiotic use (previous two months), and meningococcal vaccination status.

3.3.4. Molecular identification and characterization of carriage isolates

The presence of *Neisseria meningitidis* was determined with real-time PCR (polymerase chain reaction) detection of the species-specific *sodC* gene (68). For serogroup identification (A, B, C, X, Y, W) we used serogroup-specific gene detection following WHO and CDC (Centers for Disease Control and Prevention) protocol (69). Amplifications were conducted in 25µl volumes in 96-well plates, run in triplicate using LightCycler® 96 Real-Time PCR System (Roche) and qTOWER3G thermal cycler (Analytic Jena), with high-sensitivity BioTaq polymerase (Bioline). The PCR protocol consisted of denaturation (50°C for 2min, 95°C for 10min), followed by 50 cycles of 95°C for 10sec and 60°C for 1min, then melting at 60°C for 1sec, and cooling at 40°C for 30sec. Standard reactions used 2µl template DNA, with uncertain results (equivocal cycle

threshold value) retested using 1:4 diluted DNA, to reduce any inhibitors that may be interfering with the reaction.

3.3.5. Statistical analysis

For the statistical analysis we used univariate logistic regression to calculate unadjusted odds ratios (ORs) with 95% confidence intervals for colonization risk factors, with significance defined as $p<0.05$. Comparison of variable prevalence between high school and university students two-sided Chi-squared tests were performed, with MedCalc for Windows version 22.014 (MedCalc Software, Ostend, Belgium).

4. Results

4.1. Examination of the attitudes towards varicella vaccinations

4.1.1. Study population

The survey collected responses from 1042 parents and 194 healthcare professionals (189 health visitors and 5 pediatricians). Parent respondents were predominantly females, between 30-39 years old, university educated, and with good financial status. Participants represented various residential areas across Hungary. Healthcare professional respondents were almost entirely female health visitors working throughout different regions of Hungary. Sociodemographic characteristics, as determinants, are included in Table 2 for parents and Table 4 for healthcare professionals.

4.1.2. Vaccination coverage and support

Among parent participants, 53.3% (555) had vaccinated at least one child against varicella, with 46.3% (482) having vaccinated all their children, 7.0% (73) some of their children, and 46.7% (487) none of their children. Within the healthcare professional group, 76.3% (148) endorsed universal varicella vaccination, including all five pediatricians (100%) and 75.7% of health visitors.

4.1.3. Factors influencing parental vaccination decisions

Parents with one child showed the highest vaccination rates (53.3%), which decreased significantly in families with three or more children (46.2%). Significantly higher vaccination rate was associated with parents aged 30-39 (58.0%, vs. only 48.8% for parents under 30 years of age and 44.3% over the age of 40), those holding university degrees (60% compared to 42.9% for parents who finished high school and 42.0% for parents who finished elementary school), and urban residents (65.8% in the capital city versus 38.5% in villages). Financial circumstances, respondent gender, and personal history of varicella did not significantly impact vaccination decisions, though male participants were underrepresented. Vaccination likelihood increased significantly among parents who considered varicella severe (77.7% vaccination rate) and those who had witnessed disease complications. Healthcare professional recommendation emerged as the strongest predictor of vaccination, with 77.8% of parents vaccinating after receiving such advice.

Table 2. Outcome of the survey for parents: Determinants of vaccination of at least 1 child against varicella (70).

	n	Vacci-nation rate %	OR	SE	95% CI	p
Overall	1042	53.3				
Variables						
Number of children						
1	512	53.3	1			
2	385	53.2	0.8633	0.1367	0.6604 to 1.1285	0.2822
3-5	145	46.2	0.6511	0.1897	0.4489 to 0.944	**0.0235**
Age						
<30	250	48.8	1			
30-39	600	58.0	1.4489	0.15117	1.0773 to 1.9485	**0.0141**
>40	192	44.3	0.9129	0.096332	0.7559 to 1.1027	0.344
Gender						
Male	21	52.4	1			
Female	1021	53.3	1	0.44141	0.4365 to 2.4628	0.9348
Settlement						
Capital	269	65.8	1			
Large city	152	50.7	0.5336	0.20698	0.3557 to 0.8006	**0.0024**
Town	343	56.6	0.8226	0.08424	0.6974 to 0.9703	**0.0199**
Village	278	38.5	0.6877	0.059361	0.6122 to 0.7726	**<0.0001**
Educational level						
University degree or higher	637	60.0	1			
High school	317	42.9	0.5016	0.13935	0.3817 to 0.6591	**<0.0001**
Elementary school / Middle school	88	42.0	0.6959	0.1153	0.5552 to 0.8724	**0.0015**

Financial status						
Good / very good	660	54.4	1			
Average	348	52.3	0.9193	0.13276	0.7086 to 1.1925	0.5261
Low	34	41.2	0.7661	0.17856	0.5399 to 1.0871	0.1321
Parent's personal experience						
Had no varicella	75	58.7	1			
Had varicella	933	54.8	0.9576	0.24106	0.5970 to 1.5359	0.8572
Parent's view on severity of varicella						
Mild	86	24.4	1			
Middle	723	48.8	2.953	0.2618	1.7677 to 4.9331	**<0.0001**
Severe	233	77.7	3.2823	0.14812	2.4553 to 4.3880	**<0.0001**
Parent's experience with complications of varicella						
No such experience	662	50.0	1			
Have experienced her/himself or a family member	93	55.9	1.2683	0.22285	0.8195 to 1.9630	0.2848
Have seen it on someone outside family	287	59.9	1.223	0.07168	1.0627 to 1.4074	**0.0048**
Have the child's paediatrician / health visitor recommended VZV vaccination?						
No	410	17.3	1			
Yes	585	77.8	16.7113	0.16409	12.1153 to 23.0506	**<0.0001**
Yes, but only for girls / children with impaired immunity	47	61.7	2.7735	0.16361	2.0126 to 3.8221	**<0.0001**

(n = number of participants, OR = odds ratio, SE = standard error, CI = confidence interval, p = p value)

4.1.4. Reasons for vaccine hesitancy

Of the 487 non-vaccinating parents, 365 provided explanations for their decision. The primary reasons included:

- perception that varicella was not serious enough to warrant vaccination (33.7%)
- concerns about vaccine side effects (31.0%)
- doubts about vaccine efficacy (19.7%)
- insufficient knowledge about the vaccine (15.6%)
- negative recommendations from healthcare providers (11.8%)
- financial constraints (8.8%)

Among the 228 parents who initially declined but later decided to vaccinate subsequent children, the major factors changing their minds were unexpectedly severe disease in their unvaccinated child and improved vaccine availability. Conversely, 76 parents who vaccinated their first child but declined it for later children typically cited breakthrough infection despite vaccination or adverse reactions to the vaccine as their reason. Table 3 summarizes the reasons behind parents' decision on varicella vaccination.

Table 3: Reasons of the parents who did not vaccinate their children or not all of them against varicella (70).

No varicella vaccination at all		
	n	**%**
Overall	457	46.7
Reasons for not vaccinating		
Overall	365	35.0
Found it unnecessary	123	33.7
Afraid of side effects	113	31.0
Does not believe that the vaccine is effective	72	19.7
There was no vaccine available / I did not know about the vaccine when my child was at appropriate age	68	18.6
My paediatrician/health visitor did not give me information on the vaccine	57	15.6

My paediatrician/health visitor recommended not to vaccinate	43	11.8
The vaccine is too expensive, could not afford it	32	8.8
Not vaccinated all of their children		
	n	**%**
Overall	73	7.0
If you did not vaccinate your first child, why have you/would you vaccinate your other children? *		
Overall	228	
Because of the severity of general symptoms of the disease (fever, rash, itching)	78	34.2
Change in the availability of the vaccine	72	31.6
Severe infection of the unvaccinated child	66	28.9
Improvement of the vaccine	37	16.2
Change in the general knowledge about the vaccine	16	7.0
If you vaccinated your first child, why you do not plan to / did not vaccinate your other children? **		
Overall	76	
My first child got varicella in spite of the vaccination	38	50.0
Because of the side effects of the vaccine	17	22.4
Found it unnecessary	6	7.9
The younger sibling got varicella before he/she got vaccinated	6	7.9
The first child got vaccinated because of her/his health condition	3	3.9
The younger sibling(s) did not get the vaccine because of their health condition	2	2.6
Afraid that the vaccine will not give long-time protection until reproductive age	2	2.6
* For this question parents who did not vaccinate their children at all could also answer, as they opinion might have changed since then.		

** For this question parents who vaccinated all their children could also answer, as they opinion might have changed since then.

4.1.5. Healthcare professional attitudes

Support for universal varicella vaccination was higher among healthcare professionals who were younger (under the age of 30), worked in the capital, and had no children. The perception of varicella severity strongly predicted support, with 100% of those viewing it as severe disease supporting vaccination. Direct experience with disease complications significantly increased support rates, which rose with the frequency of witnessed complications. These determinants are summarized in Table 4.

Table 4. Outcome of the survey of professionals: Determinants of support of universal varicella vaccination (70).

	n	Vacci-nation rate %	OR	SE	95% CI	p
Overall	194	76.3				
Variables						
Profession						
Paediatrician	5	100.0				
Health visitor	189	75.7				
Gender						
Male	1	100.0				
Female	193	76.2				
Age						
<30	40	80.0	1			
30-39	75	73.3	0.6875	0.47374	0.2717 to 1.7399	0.4225
>40	78	76.9	0.9129	0.23899	0.5714 to 1.4583	0.701
Number of children						
0	36	83.3	1			

1	42	67.4	0.4133	0.54674	0.1415 to 1.2070	0.0955
2	82	79.3	0.8745	0.26182	0.5235 to 1.4609	0.6037
3-5	29	72.4	0.8067	0.20348	0.5414 to 1.2020	0.2882
Work area						
Capital	24	91.7	1			
Large city	26	76.9	0.303	0.873	0.0547 to 1.6772	0.1465
Town	81	72.8	0.4938	0.38983	0.2300 to 1.0601	**0.0366**
Village	63	74.6	0.644	0.26441	0.3835 to 1.0813	0.0598
View on severity of varicella						
Mild	16	18.8	1			
Medium	154	78.6	15.8889	0.66994	4.2739 to 59.0691	**< 0.0001**
Severe	24	100.0	1.08E + 05	3197.42		**< 0.0001**
Have you seen complications of varicella?						
No	74	62.2	1			
Yes, in my patients	108	82.4	2.8744	0.35161	1.4429 to 5.7259	**0.0024**
Yes, in my own child	15	100.0	41102.13	4108.52		**0.0004**
How often do you see complicated cases of varicella?						
None	74	62.2	1			
<1 out of 10 cases	77	80.5	2.5159	0.3745	1.2076 to 5.2418	**0.012**
1-2 out of 10 cases	30	90.0	2.3406	0.32704	1.2329 to 4.4433	**0.0026**
>2 out of 10 cases	11	100.0	1170.631	3129.42		**0.002**
Do you recommend varicella vaccination for parents?						
No	26	38.5	1			

Yes, but only for girls / children with impaired immunity	20	25.0	0.5333	0.65511	0.1477 to 1.9259	0.3306
Yes, for everyone	148	89.9	3.7665	0.24325	2.3382 to 6.0674	< **0.0001**
Have you vaccinated your own child/children?						
No answer	40	85.0				
No	88	62.5	1			
Yes, but not all of them	11	72.7	1.6	0.71191	0.3964 to 6.4582	0.4979
Yes, all of them	55	92.7	2.7659	0.282	1.5914 to 4.8070	< **0.0001**

(n = number of participants, OR = odds ratio, SE = standard error, CI = confidence interval, p = p value)

Among the 46 health visitors (23.7%) who opposed universal vaccination, key objections included viewing varicella as not severe enough to justify vaccination, skepticism about vaccine effectiveness, and concerns about adverse effects (Table 5).

Table 5. Reasons of professionals not supporting universal varicella vaccination (70).

	n	**%**
Non-supporters	46/194	23.7
Gave reasons	25/46	54.3
Finds it unnecessary	11/25	44
Does not believe that the vaccine is effective	8/25	32
Afraid of side effects	7/25	28
Price of the vaccine	4/25	16
Paediatrician does not recommend it	2/25	8
Afraid that the vaccine will not give long-time protection until reproductive/older age	1/25	4
Does not have enough information on vaccine	1/25	4

4.1.6. Comparative attitudes

Significant differences emerged regarding intentional exposure to varicella: only 5.1% of parents and 1.0% of healthcare providers would deliberately expose their children to infected individuals (p=0.0063), while 60.9% of parents and 68.0% of healthcare professionals completely rejected this practice. Healthcare professionals demonstrated greater awareness of the planned 2019 introduction of mandatory varicella vaccination. Though most participants supported this policy change, parents showed significantly higher approval rates than healthcare professionals (87.2% versus 76.3%, p=0.0002). Parents identified their pediatrician as their primary vaccination information source, followed by internet resources and health visitors. These results are summarized in Table 6.

Table 6. Differences in attitudes of parents and healthcare professionals on varicella immunization (70).

	Parents		Healthcare professionals		
	n	**%**	**n**	**%**	**p value**
Overall	1042		194		
What do you think about the intentional exposure of susceptible children to varicella infected children?					
Agree with it, I would expose my child to VZV	59	5.1	2	1.0	**0.0063**
Agree with it, but I would not do it with my child	193	16.8	18	9.3	**0.0017**
I used to agree with it, but since we have vaccine available, I am not supporting it anymore	196	17.1	42	21.7	0.3573
I don’t agree with it	698	60.9	132	68.0	0.7741
What is your main source of information on varicella vaccination? - more answers					
Paediatrician	1054	95.3	n.a.		
Internet	738	66.7			

Health visitor	539	48.7			
Pharmacist	370	33.5			
Other parents	299	27.0			
Informational leaflet	192	17.4			
Did you know that varicella vaccination will be free and obligatory from the September 2019?					
Yes	438	62.8	182	93.8	**<0.0001**
No	260	37.2	12	6.2	
Do you agree with the free and obligatory varicella vaccination?					
Yes	609	87.2	148	76.3	**0.0002**
No	89	12.8	46	23.7	
If you were to decide now, would you vaccinate your child against varicella?					
Yes	721	63.2	146	75.3	0.1126
Not all of my children	21	1.8	6	3.1	0.3417
No	294	25.8	42	21.7	0.0537

4.2. Examination of attitudes towards *Neisseria meningitidis* vaccination

4.2.1. Study population

The survey collected responses from 165 parents, who were predominantly female, between 30-39 years old, university educated, with good financial status and with one child. Approximately half of the participating parents had completed health-related studies, making our study unique in this respect. Type of settlement varied from the capital city to village, representing different residential areas of Hungary. Sociodemographic characteristics, as determinants, are included in Table 7.

4.2.2. Vaccination coverage

Among the 159 participating parents, who responded for the main outcome of the study, 78.6% (125) had vaccinated at least one child against meningococcal disease. The majority of parents, 71.7% (114), had vaccinated all their children, 6.9% (11) chose to vaccinate some of their children, while 21.4% (34) decided not to vaccinate any of their children.

4.2.3. Factors influencing parental vaccination decisions

The number of children had no influence on parental decision regarding meningococcal vaccination, as parents with 1, 2, and 3 or more children showed 79.2%, 80.0% and 79.3% vaccination rates. Age did not have a significant effect on vaccination rates, but the pattern showed that younger adults are more likely to vaccinate their children, as vaccination rate moderately decreased with increasing age (87.5% under the age of 30 years, 81.9% between 30-39, and 70.0% over the age of 40). Though male participants were underrepresented in our study, we did not detect significant association between gender and vaccination rates. Significantly higher vaccination rate was associated with those holding higher education/university degrees (84.7% compared to 63.8% for parents who finished high school or lower education), and urban residents (89.7% in the capital city versus 69.2% in villages). We found that 92.9% of participants with very good financial status and 79.5% of parents with good financial status vaccinated their children, whereas only 63.6% of those with low financial status decided to vaccinate, though this reduction was not statistically significant. Interestingly, personal history of IMD did not impact vaccination decisions, moreover, those parents who did not know someone with meningococcal disease showed slightly higher vaccination rate. Vaccination rate increased significantly among parents who considered meningococcal disease severe (88.3% compared to 51.9% for those finding meningococcal disease moderate, and 36.4% for those considering it mild or do not know the severity). Healthcare professional recommendation was the strongest predictor of vaccination, as 94.7% of parents decided to vaccinate after receiving such advice. Only 37.8% of parents vaccinated their children against meningococcal disease, when they did not get healthcare professional recommendation. We also found that parents with health-related studies are significantly more likely to vaccinate their children against meningococcal disease (89.9% versus 67.9%).

Table 7. Determinants of vaccination of at least 1 child against meningococcal disease.

	n	Vaccination rate %	OR	SE	95% CI	p
Overall	159	78.6				
Variables						
Number of children						
1	72	79.2	1			
2	55	80.0	1.0526	0.4448	0.4402 to 2.5171	0.9081
3-5	29	79.3	1.0088	0.54254	0.3483 to 2.9216	0.9872
No answer	3	n.a.				
Age						
<30	24	87.5	1			
30-39	72	81.9	0.6484	0.68908	0.1680 to 2.5024	0.5165
>40	60	70.0	0.3333	0.67847	0.0882 to 1.2601	0.0791
No answer	3	n.a.				
Gender						
Female	141	79.4	1			
Male	17	70.6	0.6214	0.57162	0.2027 to 1.9053	0.4176
No answer	1	n.a.				
Settlement						
Capital	39	89.7	1			
Town	67	79.1	0.4327	0.60734	0.1316 to 1.4227	0.1466
Village	52	69.2	0.2571	0.60733	0.0782 to 0.8456	**0.0155**
No answer	1	n.a.				
Educational level						
College/Higher education degree or higher	111	84.7	1			

High school/Vocational school or lower	47	63.8	0.3191	0.40202	0.1451 to 0.7018	**0.0047**
No answer	1	n.a.				
Financial status						
Very good	14	92.9	1			
Good	132	79.5	0.2991	1.05995	0.0375 to 2.3885	0.1833
Low	11	63.6	0.1346	1.21234	0.0125 to 1.4490	0.0654
No answer	2	n.a.				
Do you know someone who had meningococcal disease?						
Yes	39	74.4	1			
No	124	79.8	1.3649	0.43206	0.5852 to 3.1834	0.4766
No answer	2	n.a.				
Parent's view on severity of meningococcal disease						
Severe	123	88.3	1			
Moderate	27	51.9	0.1422	0.47876	0.0557 to 0.3635	**0.0001**
Mild/Do not know	13	36.4	0.0755	0.68827	0.0196 to 0.2908	**0.0001**
No answer	2	n.a.				
Have the child's pediatrician/health visitor recommended vaccination against meningococcus?						
Yes	113	94.7	1			
No	47	37.8	0.034	0.52014	0.0123 to 0.0944	< **0.0001**
No answer	5	n.a.				
Have you completed health-related studies?						
Yes	79	89.9	1			
No	78	67.9	0.2389	0.44492	0.0999 to 0.5713	**0.0006**
No answer	2	n.a				

(n = number of participants, OR = odds ratio, SE = standard error, CI = confidence interval, p = p value)

4.2.4. Reasons for vaccine hesitancy

Out of the 34 parents who decided not to vaccinate their children, 31 provided explanations for their decision. The most common reason was insufficient knowledge about the vaccine (45.2%), followed by the lack of recommendation from their pediatrician (29.0%) and finding it unnecessary (16.1%). Concerns about vaccine side effects, doubts about vaccine efficacy and financial constraints were mentioned only in 9.7% of answers. Table 8 summarizes the reasons behind parents' decision on meningococcal vaccination.

Table 8. Reasons of the parents who did not vaccinate their children against meningococcal disease

No vaccination		
	n	**%**
Overall	**34**	**21.4**
Reasons for lack of vaccination		
Overall	**31**	**19.5**
Found it unnecessary	5	16.1
Afraid of side effects	3	9.7
Does not believe that the vaccine is effective	3	9.7
There was no vaccine available when my child was at appropriate age	3	9.7
I don't have enough information on the vaccine	14	45.2
My pediatrician did not recommend the vaccine	9	29.0
The vaccine is too expensive, could not afford it	3	9.7

4.3. Assessing the prevalence and risk factors of asymptomatic carriage of *Neisseria meningitidis*

4.3.1. Study population

Analysis of the study population is summarized in Table 9. Most participants were non-smokers (82.8%), lived in households without passive smoke exposure (66.2%), had not used antibiotics in the previous two months (81.3%), reported no recent upper respiratory infections (58.7%), and did not regularly attend crowded social gatherings (63.0%). While most characteristics were comparable between high school and university students,

significant differences emerged in two areas: university students reported higher rates of party attendance (37.0% compared to 22.8% for high school students, p=0.0001), while high school students showed higher meningococcal vaccination coverage (17.9% versus 10.2% for university students, p=0.0063).

Regarding vaccination history, most participants (50.7%) were uncertain about their meningococcal vaccination status. Among the 86 participants (14.4%) with confirmed vaccination, 41.9% had received monovalent vaccines targeting serogroup C (Meningitec, Menjugate, NeisVac-C), 24.4% had received tetravalent vaccines against ACWY serogroups (Mencevax, Menveo, Nimenrix), and 9.3% had been vaccinated against serogroup B (Bexsero). Six participants reported receiving multiple vaccine types, while 25 could not identify their specific vaccine. Family structure data, collected only from high school students due to their likelihood of living with family members, showed that 48.3% had at least one sibling.

Table 9. Characteristics of the population assessed for carriage of *N. meningitidis* (71).

Variable	Response	Overall number of participants (%)	High school students (%)	University students (%)	Prevalence of variables in high school students vs university students, P
Participants		610 (100)	307 (50.3)	303 (49.7)	-
Gender	**Female**	360 (59.0)	181 (59.0)	179 (59.1)	0.980
	Male	203 (33.3)	124 (40.4)	79 (26.1)	
	No answer	47 (7.7)	2 (0.6)	45 (14.9)	
Age	**15-16**	11 (1.8)	11 (3.6)	-	-
	17	138 (22.6)	138 (45.0)	-	
	18	139 (22.8)	139 (45.3)	-	
	19	18 (3.0)	17 (5.5)	1 (0.3)	
	20	17 (2.8)	1 (0.3)	16 (5.3)	
	21	125 (20.5)	-	125 (41.3)	

	22	65 (10.7)	-	65 (21.5)	
	23	25 (4.1)	-	25 (8.3)	
	24	14 (2.3)	-	14 (4.6)	
	≥25	10 (1.6)	-	10 (3.3)	
	No answer	48 (7.9)	1 (0.3)	47 (15.5)	
Recent antibiotic treatment	**Yes**	69 (11.5)	36 (11.7)	33 (10.9)	0.755
	No	496 (81.3)	271 (88.3)	226 (74.6)	
	No answer	44 (7.2)	0 (0)	44 (14.5)	
Smoking	**Yes**	60 (9.8)	36 (11.7)	24 (7.9)	0.115
	No	505 (82.8)	270 (87.9)	235 (77.6)	
	No answer	45 (7.4)	1 (0.3)	44 (14.5)	
Exposure to passive smoking at home	**Yes**	162 (26.6)	89 (29.0)	73 (24.1)	0.171
	No	404 (66.2)	218 (71.0)	186 (61.4)	
	No answer	44 (7.2)	0 (0)	44 (14.5)	
Recent upper respiratory tract infection	**Yes**	180 (29.5)	99 (32.2)	81 (26.7)	0.137
	No	358 (58.7)	208 (67.8)	177 (58.4)	
	No answer	45 (7.4)	0 (0)	45 (14.9)	
Number of siblings	**0**	38 (6.2)	38 (12.4)	-	-
	1	104 (17.0)	104 (33.9)	-	
	2	82 (13.4)	82 (26.7)	-	
	3	52 (8.5)	52 (16.9)	-	
	≥4	31 (5.1)	31 (10.1)	-	
	No answer	303 (49.7)	0 (0)	303 (100)	
	Yes	182 (29.8)	70 (22.8)	112 (37.0)	0.0001*

Attending parties and festivals regularly	**No**	384 (63.0)	237 (77.2)	147 (48.5)	
	No answer	44 (7.2)	0 (0)	44 (14.5)	
Vaccinated against meningo-coccus	**Yes**	86 (14.1)	55 (17.9)	31 (10.2)	0.006*
	No	171 (28.0)	82 (26.7)	89 (29.4)	
	Unsure	309 (50.7)	170 (55.4)	139 (45.9)	
	No answer	44 (7.2)	0 (0)	44 (14.5)	

* Significant difference

4.3.2. Meningococcal carriage findings and associated risk factors

The study identified 212 carriers of *Neisseria meningitidis* among the 610 tested students, representing 34.8% carriage rate (95% CI: 31.0-38.5%) (Table 10). Gender differences were significant, with males showing higher carriage rates than females (42.4% versus 33.1%, p=0.0279). High school students demonstrated significantly higher colonization rates than university students (48.9% versus 20.5%, $p < 0.0001$), accounting for 70.8% of all positive cases. Age emerged as a strong predictor of meningococcal carriage, with the 17-19 age group showing the highest rate at 49.8% (147/295) (Figure 6).

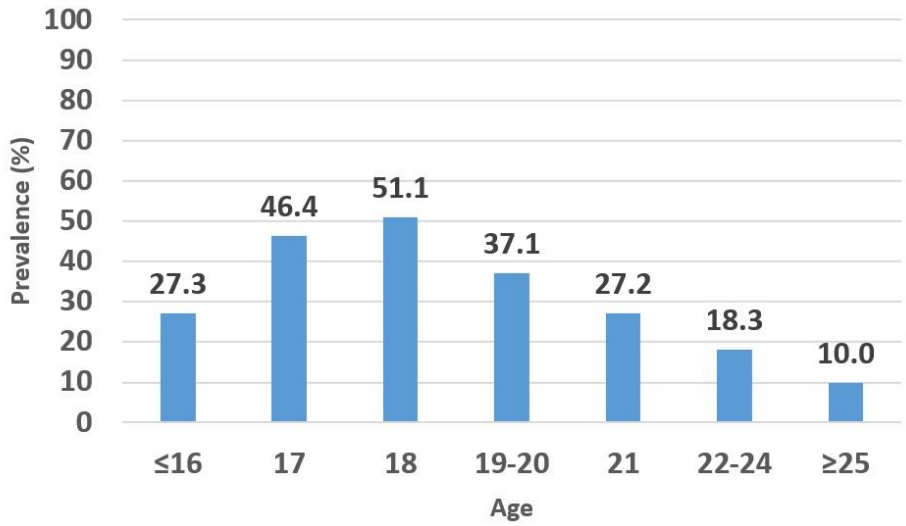

Figure 6. *N. meningitidis* carriage prevalence by age (71).

Several factors were associated with lower carriage rates, though without statistical significance: smoking (OR 0.73), household passive smoke exposure (OR 0.96), and recent antibiotic use (OR 0.72). No association was found between carriage status and recent upper respiratory infections. Regular attendance at social gatherings showed a slight, non-significant negative association with colonization (OR 0.80), though this finding was complicated by the different attendance patterns between high school and university students. Vaccination status did not significantly affect carriage rates, despite a slightly higher prevalence among vaccinated students (OR 1.45). Among high school students, number of siblings became relevant only with larger families; those with four or more siblings showed particularly high carriage rates (74.2%, OR 1.27).

Table 10. Univariate analysis of risk factors for meningococcal carriage (71).

		n	Carriage rate n (%)	OR	95% CI	p
All participants		610	212 (34.8)		31.0-38.5%	
Variables						
Type of school	**High school students**	307	150 (48.9)	1 (Ref)		
	University students	303	62 (20.5)	0.27	0.19-0.39	<0.001*
Gender	**Female**	360	119 (33.1)	1 (Ref)		
	Male	203	86 (42.4)	1.49	1.04-2.12	0.028*
Age	**15-16**	11	3 (27.3)	1.00	0.25-4.00	0.996
	17	138	64 (46.4)	2.31	1.38-3.88	0.001*
	18	139	71 (51.1)	2.79	1.67-4.68	0.001*
	19	18	12 (66.7)	5.35	1.86-15.39	0.001*
	20	17	1 (5.9)	0.17	0.02-1.31	0.031*
	21	125	34 (27.2)	1 (Ref)		
	22	65	7 (10.8)	0.32	0.13-0.78	0.006*
	23	25	6 (24.0)	0.85	0.31-2.29	0.739

	24	14	6 (42.9)	2.01	0.65-6.21	0.235
	≥25	10	1 (10.0)	0.30	0.04-2.44	0.192
Recent antibiotic treatment	**No**	496	185 (37.3)	1 (Ref)		
	Yes	69	21 (30.4)	0.72	0.42-1.24	0.229
Smoking	**No**	505	187 (37.0)	1 (Ref)		
	Yes	60	18 (30.0)	0.73	0.41-1.30	0.278
Exposure to passive smoking at home	**No**	404	148 (36.6)	1 (Ref)		
	Yes	162	58 (35.8)	0.96	0.66-1.41	0.853
Recent upper respiratory tract infection	**No**	358	140 (39.1)	1 (Ref)		
	Yes	180	66 (36.7)	1.01	0.70-1.46	0.944
Number of siblings (only for high school students)	**0**	38	20 (52.6)	1 (Ref)		
	Has sibling	269	130 (48.3)	0.84	0.43-1.66	0.619
	1	104	47 (45.2)	0.74	0.35-1.56	0.432
	2	82	38 (46.3)	0.88	0.60-1.30	0.521
	3	52	22 (42.3)	0.87	0.66-1.15	0.332
	≥4	31	23 (74.2)	1.27	0.98-1.64	0.063
Attending parties and festivals	**No**	384	164 (42.7)	1 (Ref)		
	Yes	182	60 (33.0)	0.80	0.55–1.16	0.241
Vaccinated against meningo-coccus	**No**	171	55 (32.2)	1 (Ref)		
	Yes	86	25 (40.7)	1.45	0.85–2.48	0.178
	Unsure	309	116 (37.5)	1.13	0.92–1.37	0.237

* Significant association

(n = number of participants, OR = odds ratio, CI = confidence interval, p = p value)

4.3.3. Serogroup distribution analysis

The majority, 87.3% of carriage isolates (n=185) were non-typable by real-time PCR, representing a 30.3% NT carriage rate in the overall study population. Serogroup B was identified in 9.0% (n=19) of all isolates, with significantly higher prevalence among high school students compared to university students (11.8% versus 3.2%, p=0.0282). Serogroup C accounted for 2.4% of all carriage isolates, with no significant difference between university and high school students (3.2% versus 2.0%, p=0.6007). Serogroups A, X, and W were not detected in the study population. From the vaccinated carriers 5 were colonized with vaccine-type meningococci: four students vaccinated against serogroup C carried serogroup B, and one student with menACWY vaccination carried serogroup C meningococcus. Serogroup distribution of the isolates is illustrated in Figure 7.

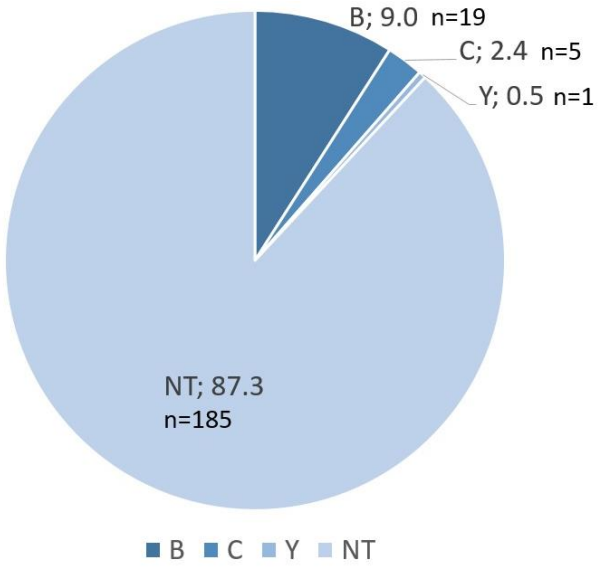

Figure 7. Serogroup distribution of the 212 *N. meningitidis* carriage isolates (%). (NT = non-typable) (71)

5. Discussion

5.1. Attitudes towards varicella vaccination

5.1.1. Key findings on vaccination rates

Our research examined attitudes towards varicella vaccination among Hungarian parents and healthcare workers (health visitors and pediatricians), investigating reasons behind vaccine acceptance or refusal. Interestingly, despite not being provided for free, we found that varicella vaccine uptake was relatively high – 53.3% of participating parents had vaccinated at least one child, with 46.3% having vaccinated all their children. Though this coverage falls below rates in countries offering free vaccination like Germany (88.9% in 2020) and the US (90.6% in 2016), it exceeds rates in other countries without government funding, such as Italy before the vaccine was made mandatory in 2017 (33,2% in 2013 and 45,6% in 2017) and Poland (2.3% in 2021) (72-75). A survey similar to ours examined parental attitudes towards varicella vaccination in the UK in 2021, where only 8.2% of participating parents claimed that they vaccinated their child against varicella (76).

5.1.2. Socioeconomic factors in vaccination decisions

Logistic regression analysis revealed that parents with university education and those living in the capital were more likely to vaccinate their children. This parallels findings from an Italian study, potentially reflecting better access to medical information among highly educated parents, and a Swedish study, highlighting that they are more likely to be aware of the availability of the vaccine (77-78). Conversely, studies from France and the Netherlands found higher-educated parents are more likely to refuse vaccination, attributed to greater autonomy in health decisions and reduced trust in authorities (79-80). Financial circumstances also influenced vaccination rates, as vaccine coverage was 41.2% in lower-income households compared to 54.4% in families reporting good or very good financial status – suggesting that the introduction of free vaccination could improve vaccine coverage. The above-mentioned Swedish study also found that with higher income vaccination rate rises, moreover, the difference in their findings was even more significant (changing from 27.8% to 57.1%) (78). On the other hand, the study from France found that household income does not influence vaccine hesitancy, indicating that on this topic sociocognitive factors are more important, than material factors (78).

5.1.3. Healthcare provider influence

The most significant positive predictor for vaccination was healthcare provider recommendation: 77.8% of parents vaccinated their children when advised by their pediatrician or health visitor, despite associated costs. Vaccine uptake was markedly lower (17.3%) when pediatricians did not recommend vaccination, making this the strongest negative predictor in our study. This result is in accordance with the UK study examining parental acceptance of varicella vaccination, as they found that most of the parents (57.9%) strongly agreed on generally following the doctor's/healthcare provider's recommendations on vaccinations (76). In contrast, a recent systematic review found that many parents reported mistrust in information provided by healthcare professionals, however they are still seen as experts and parents seek them for information about vaccination (81). Our study confirmed the latter, as nearly all parents (95.3%) identified pediatricians as their primary vaccination information source, confirming healthcare providers' crucial role in parent education and vaccination encouragement. The internet and mass media ranked as the second most important information source, potentially creating polarized vaccination viewpoints through segregated information communities.

5.1.4. Reasons for vaccine hesitancy

Among the 46.7% of parents who didn't vaccinate any children against varicella, several patterns emerged suggesting that reliable information could address vaccine hesitancy:

- 15.6% cited insufficient vaccine information
- 19.7% questioned vaccine efficacy
- 50% of parents who vaccinated one child, but not subsequent children did so because the first child had varicella despite vaccination

It's essential to provide accurate information about varicella vaccine efficacy: while not offering 100% protection, it provides 99.4% protection against severe disease after one dose and 92% protection against all forms after two doses, with mild infections possible in 8% of immunized children (82). Of non-vaccinating parents 33.7% deemed the vaccine unnecessary, unconvinced of the infection's severity. Conversely, vaccine coverage reached 77.7% among parents who considered varicella a severe disease. Parents who had witnessed complicated varicella cases were more likely to vaccinate their children. These findings are in accordance with literature, as several studies were mentioned to find

that considering varicella severe and experiencing complications are important reasons for accepting vaccination (82). The practice of intentionally exposing non-immune children to infected ones ("pox parties") as a vaccination alternative still exists, though supported by few parents and even fewer healthcare professionals. A study from the UK also found that over half of the parents disagree with this practice (76). Professionals in the UK were quite impartial when they were asked if it is better to get immunity from contracting varicella naturally, as 44% of them remained neutral on the topic (83).

5.1.5. Healthcare professional attitudes

Understanding healthcare providers' vaccination attitudes is vital given their strong influence on parental decisions. In our study, 76.3% of healthcare providers supported universal varicella vaccination, which is significantly higher than in the Netherlands, where only 28% of doctors and 17% of nurses supported universal infant varicella vaccination (80). In Sweden, 86.0% of pediatricians and general practitioners claimed that if universal varicella vaccination were recommended in the country, they would advise parents to vaccinate their children against varicella (84). In our study, support rates were significantly higher among those who recognized varicella as serious and among those who frequently encountered complications.

Primary concerns among healthcare providers not supporting universal vaccination included:

- questioning whether the severity of the infection warranted vaccination
- vaccine safety concerns
- potential side effects.

Research indicates that healthcare providers with greater knowledge are more likely to recommend vaccination, with understanding of vaccine effectiveness and safety being critical factors in their decisions. For the introduction of a new mandatory vaccination, well-informed and supportive pediatric healthcare professionals are essential for building parental trust. In the UK, before the recommendation of universal varicella vaccination by the Joint Committee of Vaccination and Immunisation in November 2023, a study found that many healthcare providers did not feel well informed enough to advise patients about the vaccine (84). They concluded that in current paediatric training or continuing professional development the topic of varicella vaccine is insufficiently covered, but only

focusing on the objective knowledge about the vaccine is not enough, as it is also crucial that healthcare professionals have the communication skills to discuss vaccines in general with families (84). A study examining communication about vaccines enhance that positive messaging and integrative communication are more effective than defensive or overly product-oriented approaches (85).

5.2. Attitudes towards meningococcal vaccination

5.2.1. Key findings on vaccination rates

Our study analyzed Hungarian parents' attitude on meningococcal vaccination, exploring factors influencing their decision to accept or decline vaccination for their children. Notably, the research revealed surprisingly high vaccination rates despite the vaccine not being freely available. Among the study participants, 78.6% had vaccinated at least one of their children against meningococcal disease, while 71.7% had vaccinated all their children. In a study from 2019 Italy, focusing on MenB vaccination, they found that only 38.7% of parents vaccinated their children against MenB (86). Another study from 2017 found that 47.3% of children were vaccinated against MenC (87). In Italy, despite the low incidence of IMD, meningococcal vaccines (both tetravalent against MenACWY and monovalent against MenB) are part of the National Vaccination Prevention Plan as recommended and publicly funded vaccines (86). However, in 2017 when the Italian government made several vaccines (including varicella vaccine) mandatory, they did not involve meningococcal vaccines, but vaccination rates still increased between 2016 and 2019 (86). In Poland, meningococcal uptake among children was 29.5% in 2018 (88). In the Netherlands, a study from 2012 revealed that 83% of parents had the intention to vaccinate their children against meningococcal B disease, which was relatively high, especially compared to 28% support rate regarding varicella vaccination in the same study (89). In the US, 17.2% of 17-year-olds are vaccinated against MenB, while 86.6% of them are vaccinated against MenACWY (90).

5.2.2. Socioeconomic factors in vaccination decisions

The results of logistic regression analysis of our data showed that number of children, age, gender, financial status and personal experience with meningococcal disease did not have statistically significant effect on vaccination rates. However, we can detect the influence of some of these factors. For example, younger adults were more likely to

vaccinate, as under the age of 30, 87.5% of parents stated that they vaccinated their child against meningococcal disease, while over the age of 40 the result was 70.0%. We found that female parents were somewhat more likely to vaccinate (79.4% versus 70.6%), although parents in our study were predominantly female (88.7% of responders), therefore male gender was underrepresented. Interestingly, an Italian study found that male gender was a positive effector on vaccinating against MenB (86). On the contrary, a study from the US found that female gender was significantly associated with MenB vaccine uptake (90). Several studies found that financial status has a significant effect on parents' willingness to vaccinate against meningococcal disease (90-91). Since these vaccines are rarely funded by the government, parents have to make their decision about vaccination by considering the risk-benefit ratio from a financial perspective too. Our study revealed that financial circumstances influenced vaccination rates, but not significantly, as vaccine coverage was 63.6% in low-income households compared to 79.5% in families reporting good financial status and 92.9% with very good financial status.

Vaccine uptake in our study was significantly associated with parents' educational level, view on severity of meningococcal disease, whether they have completed health-related studies, and with the type of settlement they live in. Parents with higher education/university degree (84.7% of them chose to vaccinate) and those living in the capital or town were more likely to vaccinate their children (89.7% vaccinated from the capital and 79.1% from towns). A study from Poland found that knowledge regarding IMD was higher among parents with higher educational level and from urban facilities (88). This parallels with a study from Turkey which identified that parents with lower education are less likely to know about meningococcal disease, its seriousness and about the vaccines available to prevent it (92). In literature regarding meningococcal and other vaccinations, one of the most important determinants on vaccine uptake is the parent's view on the severity of the disease to be prevented. Our results are in accordance with this, as 88.3% of parents who considered meningococcal disease to be severe, vaccinated their children, compared with only 36.4% of those who thought it to be mild. An Italian study found that acknowledging meningitis as a severe disease was named as main driver to vaccinate by 64.4% of parents (86). In the Netherlands one of the main drivers of intention was the perception of whether the disease is severe enough to justify vaccination

(89). In Poland a study indicated that parental awareness and knowledge related to IMD is inadequate, as only 59% of parents recognized the severity of meningococcal disease which might negatively influence their willingness to vaccinate their child against it (88). We asked the responders whether they have completed health related studies. It appeared that those with health-related education were significantly more likely to vaccinate their children against meningococcal disease (89.9% versus 67.9%), probably because of the reliable information and knowledge they gained during their studies regarding IMD and vaccines in general.

5.2.3. Healthcare provider influence

Regarding meningococcal vaccination, just like in our previous study about varicella vaccination, the most significant positive predictor for vaccination was healthcare provider recommendation: 94.7% of parents vaccinated their children when advised by their pediatrician, while only 37.8% of parents vaccinated when pediatricians did not recommend vaccination. A study from the US also found that recommendation from a healthcare professional was the most influential variable associated with vaccination/ intention to vaccinate (90). In Italy, 20.4% of parents identified suggestion of a pediatrician as a main driver for vaccination, a Spanish study found similar results (26.1%) (86, 91). In Turkey, 40% of parents who received information from their doctors stated that they wanted to vaccinate their children (92).

5.2.4. Reasons for vaccine hesitancy

Out of the 159 parents, 34 (21.4%) did not vaccinate any children against meningococcal disease, and 31 of them provided information about their reasons to do so. Almost half of these parents (45.2%) stated that they do not have enough information about the vaccine. This phenomenon is not unique as a study indicated that in the US 57% of parents were unaware of MenB vaccination (90). Polish researchers stated that inadequate parental awareness and knowledge related to IMD can be one of the reasons for poor meningococcal vaccination, highlighting that healthcare workers should provide clear and unbiased information about IMD and about vaccines to prevent it (88). We found that the second most common reason of non-vaccinators (29.0%) was that their pediatrician did not recommend the vaccine, followed by 16.1% of parents finding it unnecessary. A Turkish study had similar results on the latter, as 13.9 of parents found meningococcal vaccine unnecessary (92). The impact of healthcare provider recommendation was

discussed in the previous chapter, showing its importance on parental decision about vaccination. In our study being afraid of side effects, questioning effectiveness, and the cost of the vaccine all reached 9.7%. The cost and funding of the vaccine is an important topic when it comes to meningococcal vaccination, because MenB vaccines are relatively expensive. Several studies found that parents did not vaccinate their children against meningococcal disease because of the lack of affordability (7% of parents in a US survey, 3.4% in an Italian study, 8.4% in Turkey) (86, 90, 92). A Spanish study found that vaccine cost had the highest relative importance (26.4%) for parents when deciding about meningococcal vaccination (91). The above-mentioned Italian study highlighted that parents' intention to vaccinate was lower if parents were to be charged for the vaccination (86). Being afraid of side effect is also a recurring reason for meningococcal vaccine hesitancy, but different studies found variable weight of this, for example in Poland 56.3% while in Turkey only 8% of parents specified they fear of side effects as a reason for not to vaccinate (88, 92).

5.3. Asymptomatic meningococcal carriage and risk factors

5.3.1. Key findings on risk factors influencing meningococcal carriage

In our study we found high overall *Neisseria meningitidis* carriage rate among Hungarian adolescents and young adults (34.8%). The results revealed higher meningococcal carriage in high school students (48.9%) compared to university students (20.5%), with statistical significance. Contemporary research generally indicates lower carriage rates in these groups (93-101). For instance, Italian high school students (16-21 years old) showed only 5.3% carriage rates in a 2018 study (93). A study from Argentina, Buenos Aires, found that in adolescents between the age 10-17 years overall carriage rate was 9.4% (94). In Suizhou city in China *N. meningitidis* carriage was examined in high school students between 2013-2017, where the highest carriage rate was found in 2017 between students aged 15-19 years, as 46.7% of them were carriers (95). A carriage rate of 6.3% was demonstrated among university students (17-25 years old) in South Australia, while in Sweden carriage prevalence was 9.1% during 2018-19 (median age was 23 years) (96-97). In Lithuania, where IMD incidence is one of the highest in Europe, a study conducted between 2021-2023 found that in university students aged 18-25, meningococcal carriage is 5% (98). However, some studies have found even higher colonization prevalence than our study, but it is important to notice that the methodology impacts the results. A

Brazilian study showed dramatic differences between cultivation-based methods (12.1% carriage among university students) versus PCR detection after direct DNA extraction (69.5% positive in the same population) (102). Geographic variations also influence carriage rates. English university students consistently demonstrated high colonization rates across four studies between 2011-2017, ranging from 14.3% to 61.9% (13). In our study age emerged as an independent risk factor for meningococcal carriage, with participants aged 17-19 showing peak colonization (48.7%). This is consistent with previous experience that meningococcal carriage increases from infancy, peaks at age 19, then decreases in adulthood (11). However, a recent study in Turkey examining 0-24-years-olds found the highest carriage rate in 15 years old adolescents (24.1%) (103).

We found that gender is another important factor influencing meningococcal carriage, with males showing significantly higher carriage rates than females (42.4% versus 33.1%, odds ratio 1.49). This gender disparity is consistent with other studies with university students, identifying male gender as a risk factor (13, 97).

In our study other investigated factors, such as smoking, passive smoking, recent respiratory infections, recent antibiotic use, having siblings, party attendance, and meningococcal vaccination, did not demonstrate significant association with carriage. Surprisingly, smokers showed slightly lower carriage rates, though this association lacked statistical significance. A study from Lithuania found that smoking does not have significant influence on meningococcal carriage (98). Meanwhile, other studies found that attending pubs or parties or passive smoking are significant risk factors (94, 97).

5.3.2. The role of vaccination in asymptomatic meningococcal carriage

In our study, vaccination status did not significantly affect carriage rates. Different meningococcal vaccine types have different effects on asymptomatic carriage. There is evidence that vaccines against MenA and MenC reduced carriage and provided herd immunity, however, there is only limited and even contradictory data on the effect of the multivalent MenACWY vaccine (104-105). A study in Poland found reduced meningococcal carriage after MenACWY vaccination, while in the US serogroup Y carriage remained unchanged and serogroup W carriage increased after vaccination (106-107). MenB vaccines probably do not have effect on the prevalence of *N. meningitidis* carriage (21).

In our study four MenB carriers had received monovalent MenC vaccines, and one participant carried MenC despite MenACWY vaccination. Out of the 36 MenC vaccinated students, 18 were carriers (including the above mentioned four MenB carriers), three out of the 8 MenB-vaccinated student carried non-groupable strains, while only 2 out of the 21 ACWY-vaccinated individuals were colonized (one with MenC). Notably, none of those with combined vaccinations (B+C or B+ACWY) had meningococcal colonization. However, vaccination coverage was limited (only 86 of 610 participants confirmed vaccination, with 65 knowing their vaccine type).

Non-groupable strains dominated across both student populations, with 30.3% of participants carrying NT meningococci. This predominance of non-encapsulated *N. meningitidis* in carriers is well-documented, with these strains showing limited potential for causing invasive disease (97, 108). A study from Argentina found that in adolescents 44.7% of carriers were colonized by non-groupable meningococci (94). For university students a systematic review found that in Europe carriage rates of non-groupable strains were between 3.9-25.7%, while in the US these were between 8.0-18.9% (13). A Norwegian study indicated that 40.1% of carriage isolates were non-groupable in adolescents and young adults (99). The previously mentioned differences in the used methodology (cultivation or PCR) might explain prevalence variations (102).

Among groupable meningococci, the distribution in our study matched patterns seen in Hungarian IMD cases. Serogroup B constituted 9% of colonizing meningococci, followed by serogroup C (2.4%), and serogroup Y (0.5%). The last available data from the Hungarian National Reference Laboratory from 2021 shows that serogroups B and C caused most IMD cases between 2008-2021, with serogroup B responsible for more than 50% of the cases in this period (109). However, from 2019/2020, serogroup B declined, with serogroup C becoming dominant (54.5%) by 2020/21, when a serogroup C outbreak occurred (109). Before 2020/21, serogroup C only dominated in 2010/11 and 2011/12, during a previous MenC outbreak (109). Our sample collection derives from 2017-2018. In these years in Hungary MenB caused 56.1% of IMD cases, while MenC was responsible for 22.0% (109). Serogroups B and C have historically dominated in Europe, and while in 2018 serogroup B was still responsible for most of IMD cases (51%), the number of diseases caused by serogroup W (18%) and Y (12%) increased (110). Serogroup C started to decline, becoming only the third most common with 15% of IMD

cases (110). The latest ECDC report of IMD is from 2022, when serogroup B was still the most frequent type (63%), but serogroup Y the second (16%) and serogroup W the third (10%) (17). Serogroup C was responsible only for 6% of IMD cases (17). Serogroup Y first appeared in Hungary in 2013, maintaining a low but consistent presence (approximately 2% of IMD cases between 2013-2021) (109). Serogroup W is also increasing in Hungary (as in other European countries) responsible for 11 IMD cases between 2015-2021 (109).

6. Conclusions

6.1. Attitudes towards varicella vaccination

Our research about varicella vaccination attitudes revealed correlations between several factors that can influence vaccination decisions, such as socioeconomic background, healthcare professional recommendation, and parents' information about the disease, its complications and about vaccines. Despite the vaccine not being provided for free in Hungary at the time of our survey, we found a relatively high vaccination rate among participating parents.

The study identified several key determinants influencing vaccination decisions. Parents with university degree and those living in the capital demonstrated higher vaccination rates, showing that educational level and the type of settlement significantly influence vaccine uptake, probably due to better access to health and vaccination related information. Financial status of the family is another important factor, we found higher vaccination rates between parents with good financial status, suggesting that the cost of the vaccine can strongly influence parental decisions. Healthcare professional recommendation emerged as the strongest positive predictor of vaccination, as vaccination rate decreased significantly when parents did not get recommendation from them. This result shows that healthcare professionals play a crucial role in parental vaccination decisions.

Among vaccine-hesitant parents, besides finding the vaccine unnecessary, and being afraid of side effects, insufficient information, questioning vaccine efficacy, and not finding varicella severe were common reasons for not to vaccinate. These suggest that reliable information could lower vaccine hesitancy, and that public education is needed about this topic.

Healthcare providers generally supported universal varicella vaccination, especially those who recognized varicella as a serious disease and those who saw complications of varicella. However, concerns about vaccine necessity, efficacy, and potential side effects remained in some of them, suggesting that not only the general public, but professionals also need targeted education about the risks of natural infection, and about vaccine safety and efficacy.

6.2. Attitudes towards meningococcal vaccination

Similarly to our study about varicella vaccination attitudes, when we examined attitudes towards meningococcal vaccination, we found that vaccination rates were relatively high despite that the vaccine is not available for free, moreover, MenB vaccines have quite high price.

As key determinants leading to higher vaccination rates, we identified higher education/university degree and living in the capital, both probably providing better access to health-related information. Most significant positive determinant for vaccination was healthcare professional recommendation, confirming the same finding in our previous study. Additionally, parents with health-related educational backgrounds showed significantly higher vaccination rates, likely due to greater knowledge about IMD and vaccines in general.

Primary reasons from parents for not vaccinating their child were insufficient information, lack of pediatrician recommendation, and finding the vaccine unnecessary. Affordability, fear of side effects, and questioning vaccine efficacy were less frequent reasons. Parents' view on the severity of meningococcal disease also strongly influenced vaccination decisions. All these highlight the importance of public health education about IMD severity and about vaccines to prevent it.

Just like in the case of varicella, enhancing healthcare professional education about meningococcal vaccination and communication is essential, as their recommendations strongly influence parental decisions. Targeted public educational campaigns addressing disease severity and vaccine efficacy could result in improved parental vaccine acceptance. To further increase vaccination rates consideration should be given to financial assistance programs or to implementation of meningococcal vaccines into the national immunization program.

6.3. Asymptomatic meningococcal carriage in students

Our study is the first Hungarian meningococcal carriage report. We enrolled numerous participants of at-risk age groups across different educational levels. We found considerably high prevalence of *Neisseria meningitidis* carriage among Hungarian adolescents and young adults, compared to previous international studies. Our study indicated significant difference in carriage rate between high school students and

university students, which shows the complexity of meningococcal colonization in young adults. Age emerged as an independent risk factor, with peak colonization occurring in the 17–19-year-olds, confirming previous findings on the epidemiology of *N. meningitidis* carriage. We found that gender is also a significant determinant, with males showing higher carriage rates, which is in accordance with other international studies. Other factors frequently associated with meningococcal carriage, such as smoking, passive smoking, recent respiratory infections, recent antibiotic use, party attendance, and vaccination status did not show significant association in our study.

The predominance of non-groupable meningococci in carriers aligns with other studies describing carriage. Among groupable strains, the distribution reflected the Hungarian IMD epidemiology, with serogroup B and serogroup C dominating, followed by serogroup Y.

There are various findings in literature regarding the relationship between meningococcal vaccination and meningococcal carriage. In our study we had limited information about vaccination status, so we cannot make definitive conclusions, however, we found that vaccination does not necessarily influence carriage, as half of the MenC vaccinated students remained carriers, although MenACWY vaccines showed some protection. Combined vaccines need further investigation, as we found that there were no carriers between those who received two different types of meningococcal vaccinations.

These findings provide important information to the understanding of meningococcal carriage dynamics in Hungary, and in Europe, highlighting the importance of region-specific epidemiological monitoring. The high carriage rates found in our study support recommending broad-spectrum meningococcal vaccination for Hungarian adolescents and young adults. As this research predates COVID-19 social distancing measures, it provides valuable baseline data for future investigations.

7. Summary

During our research the main goal was gaining knowledge and information that can support the protection of children from different infectious diseases.

Our studies provide important data on parental attitudes towards varicella vaccination and meningococcal vaccination. Healthcare professionals' attitudes towards varicella vaccination also provide unique information that can be used by public health policy makers. The introduction of publicly funded vaccines would most likely increase vaccine uptake as we found both in case of varicella and meningococcus that with financial status vaccination rate reduces.

We also found in both cases that healthcare professionals have an unquestionable role in parents' vaccination decisions, so they need stable ground knowledge regarding vaccine safety, efficacy, and risk-benefit ratios. Having and providing reliable information for parents is not enough, the way of communication also has an important role when it comes to vaccination. Continuous education should also cover these topics supplemented with newest result to have up-to-date information to provide help with vaccination decisions for parents.

Another finding that needs to be highlighted is that parents do not have sufficient knowledge about the infections their offspring may face during childhood or young adulthood. Public awareness campaigns focusing on disease severity and vaccine efficacy could eliminate misinformation and mistrust.

Our carriage study is the first to provide information about the amount and type of nasopharyngeal meningococcal colonization in adolescents and young adults in Hungary and the potential risk factors associated with carriage. Since this age group is one of the risk groups for IMD, it is important to know the epidemiological status of carriage and the currently circulating serogroups. These data can help public health authorities to make vaccine related decisions, moreover, this is a good source for healthcare professionals to gain more information before vaccine recommendation for parents. As we found high carriage rate among Hungarian young adults, the recommendation of broad-spectrum meningococcal vaccination would be practical in this age group.

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9. Bibliography of publications

9.1. Publications related to the topic of the thesis

Huber A, Kovács E, Horváth A, Sahin-Tóth J, Kaptás Á, Juhász E, Kristóf K, Dobay O. **Prevalence, serogroup distribution and risk factors of *Neisseria meningitidis* carriage in high school and university students in Hungary.** Vaccine. 2024 Apr 2;42(9):2271-2277.

Huber A, Kovács E, Horváth A, Sahin-Tóth J, Juhász E, Kristóf K, Dobay O. **Survey of asymptomatic meningococcal carriage in Hungary among university and high school students.** Acta Microbiol Immunol Hung. 2023; 70: Supplement 1 pp. 22-22

Kovács E; Horváth A; Sahin-Tóth J; Kaptás Á; **Huber A**; Dobay O; Juhász E; Kristóf K. **Survey of asymptomatic meningococcal carriage in Hungary among university and high school students.** [Tünetmentes meningococcus-hordozás felmérése Magyarországon egyetemisták és középiskolások körében.] Gyermekgyógy Továbbk Szle. 2020; 25: 4 pp. 14-16. [Hungarian]

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9.2. Publications not related to the topic of the thesis

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Varicella-zoster (bárányhimlő) vírus infekciók és megelőzésük

Kedves Kitöltő!

Huber Annamária vagyok, a Semmelweis Egyetem ötödéves gyógyszerészhallgatója. Szakdolgozatomat a Varicella-zoster (bárányhimlő) vírus infekciókról és megelőzési lehetőségükről írom. Ehhez szeretném segítségét kérni az alábbi néhány perces, anonim kérdőív kitöltésével.
Köszönöm, hogy válaszaival hozzájárul kutatásom sikerességéhez.
Minden kitöltő élhet azzal a jogával, hogy nem minden kérdésre ad választ!

1. 1. Mi az Ön neme?

Soronként csak egy oválist jelöljön be.

- ◯ nő
- ◯ férfi

2. 2. Mi a születési éve?

_____

3. 3. Hány gyermeke van?

_____

4. 4. Milyen településen él?

Soronként csak egy oválist jelöljön be.

- ◯ főváros
- ◯ megyeszékhely
- ◯ város
- ◯ község
- ◯ tanya

5. 5. Mi az Ön legmagasabb iskolai végzettsége?

Soronként csak egy oválist jelöljön be.

- általános iskola 4. évfolyamánál kevesebb
- általános iskola 4-7. évfolyama
- általános iskola 8. évfolyama
- szakiskola / szakmunkásképző
- szakközépiskolai szakképesítést igazoló érettségi
- középiskolai (gimnáziumi, szakközépiskolai) általános érettségi
- főiskolai vagy egyetemi diploma
- doktori (PhD, DLA) fokozatot igazoló oklevél

6. 6. Mi az Ön családi állapota?

Soronként csak egy oválist jelöljön be.

- nőtlen/hajadon
- házas és együtt is élnek (beleértve a bejegyzett élettársi kapcsolatot is)
- házas, de külön él
- élettársi kapcsolatban él
- özvegy
- elvált (beleértve a jogilag megszüntetett élettársi kapcsolatot is)

7. 7. Milyennek ítéli meg családja anyagi helyzetét?

Soronként csak egy oválist jelöljön be.

- nagyon jó
- nincsenek anyagi gondjaink
- néha vannak anyagi gondjaink
- rendszeres anyagi gondjaink vannak
- szegények vagyunk

8. 8. Milyen információkkal rendelkezik a bárányhimlő nevű fertőző betegségről? (Ha még nincs gyermeke, azt az állítást jelölje meg, amely Önre igaz, a gyermeki részt hagyja figyelmen kívül.)

Soronként csak egy oválist jelöljön be.

- ◯ nem hallottam róla
- ◯ hallottam/olvastam róla, de sem én, sem gyermekem nem esett át rajta
- ◯ ismerem a betegséget, én magam igen, gyermekem nem esett át rajta
- ◯ ismerem a betegséget, én magam és gyermekem is átesett rajta
- ◯ ismerem a betegséget, én magam nem, gyermekem viszont átesett rajta

9. 9. Amennyiben Ön átesett a betegségen, mikor?

Soronként csak egy oválist jelöljön be.

- ◯ óvodás kora előtt
- ◯ óvodás korában
- ◯ általános iskolás korában
- ◯ középiskolás korában
- ◯ felnőttként

10. 10. Amennyiben gyermeke átesett a betegségen, mikor?

Válassza ki az összeset, amely érvényes.

- ☐ óvodás kora előtt
- ☐ óvodás korában
- ☐ általános iskolás korában
- ☐ középiskolás korában
- ☐ felnőttként

11. 11. Mi a véleménye a gyermek szándékos megbetegítéséről, az „essen át rajta minél hamarabb” hozzáállásról?

Soronként csak egy oválist jelöljön be.

- egyetértek vele, én magam is megfertőztettem/megfertőztetném gyermekemet
- egyetértek vele, de én magam nem fertőztettem/fertőztetném meg gyermekemet
- most, hogy már van védőoltás, nem értek egyet vele, de korábban én magam is megfertőztettem/megfertőztettem volna gyermekemet
- sem most, sem a védőoltás létezése előtt nem értettem egyet vele

12. 12. Milyen kategóriába sorolná a bárányhimlő nevű fertőző megbetegedést?

Soronként csak egy oválist jelöljön be.

- enyhe
- középsúlyos
- súlyos

13. 13. Tisztában van a bárányhimlő lehetséges szövődményeivel?

Soronként csak egy oválist jelöljön be.

- nem hallottam róla
- hallottam/olvastam róla, de csak felületesen
- nagyjából ismerem a témakört
- részletesen ismerem a témakört

14. 14. Találkozott már a bárányhimlő szövődményeivel?

Soronként csak egy oválist jelöljön be.

- igen, saját gyermekemen/magamon/családtagomon
- igen, máson/más gyermekén
- még nem

15. 15. Milyen szövődményes esetekkel találkozott? (Több választ is megjelölhet)

Válassza ki az összeset, amely érvényes.

- [ ] bőr bakteriális felülfertőződése
- [ ] tüdőgyulladás
- [ ] ízületi- és csontgyulladás
- [ ] kisagy gyulladása (mozgáskoordinációs zavar)
- [ ] agyvelőgyulladás
- [ ] övsömör (herpes-zoster – szekunder megbetegedés, vírus reaktiválódása)
- [ ] Egyéb: _____

16. 16. Milyen információkkal rendelkezik a bárányhimlő elleni védőoltásról?

Soronként csak egy oválist jelöljön be.

- ◯ nem hallottam róla
- ◯ hallottam/olvastam róla, de csak felületesen
- ◯ nagyjából ismerem a témakört
- ◯ részletesen ismerem a témakört

17. 17. Ajánlotta Önnek védőnője/gyermek háziorvosa a bárányhimlő elleni védőoltást?

Soronként csak egy oválist jelöljön be.

- ◯ igen, lány/fiúgyermekem esetében is
- ◯ igen, de csak lánygyermekem esetében
- ◯ igen, de csak immunrendszert érintő betegségben szenvedő/terápia alatt álló gyermekem esetében
- ◯ nem

18. 18. Beadatta gyermekének a bárányhimlő elleni védőoltást? (Csak akkor válaszoljon, ha van gyermeke.)

Soronként csak egy oválist jelöljön be.

- ◯ igen, minden gyermekemnek
- ◯ igen, de nem minden gyermekemnek
- ◯ igen, de csak lánygyermekemnek
- ◯ nem

19. 19. Ha most kéne döntenie, beadatná gyermekének a bárányhimlő elleni védőoltást?

Soronként csak egy oválist jelöljön be.

- ◯ igen, minden gyermekemnek
- ◯ igen, de nem minden gyermekemnek
- ◯ igen, de csak lánygyermekemnek
- ◯ nem

20. 20. Amennyiben egyik gyermekének sem adatta/adatná be az oltást, mi volt/mi ennek az oka? (Több válasz is megjelölhető.)

Válassza ki az összeset, amely érvényes.

- ☐ mikor gyermekeim kicsik voltak, még nem létezett a védőoltás/akkoriban nem hallottam róla
- ☐ védőnőnk/házi gyermekorvosunk nem tájékoztatott az oltásról
- ☐ védőnőnk/házi gyermekorvosunk azt javasolta ne adassam be
- ☐ nem hiszek a hatékonyságában
- ☐ feleslegesnek tartom
- ☐ tartok az esetleges mellékhatásoktól
- ☐ túl drágának találtam/nem engedhettem meg az oltás árát

21. 21. Amennyiben első gyermekének nem adatta be a védőoltást, második gyermekének miért adatta/adatná be? (Több válasz is megjelölhető.)

Válassza ki az összeset, amely érvényes.

- [ ] az oltóanyag megjelenése miatt (korábban nem volt)
- [ ] a betegség általános kellemetlenségei miatt (láz, viszketés, maradandó hegek stb.)
- [ ] be nem oltott gyermek súlyos tünetei miatt
- [ ] az oltóanyag fejlődése miatt
- [ ] társadalmi megítélés változása miatt

22. 22. Amennyiben első gyermekének beadatta, második viszont nem/nem fogja, mi ennek az oka?

Soronként csak egy oválist jelöljön be.

- ◯ gyermekem az oltás ellenére is megbetegedett
- ◯ az oltás mellékhatásai súlyosak voltak
- ◯ Egyéb: _____

23. 23. Kért/kérne gyógyszerésztől tájékoztatást a védőoltásról?

Soronként csak egy oválist jelöljön be.

- ◯ igen
- ◯ nem

24. 24. Befolyásolta/befolyásolná döntését a gyógyszertárban kapott információ?

Soronként csak egy oválist jelöljön be.

- ◯ igen
- ◯ nem
- ◯ talán

25. 25. Milyen forrásból tájékozódik, ha kérdése van az oltással vagy a betegséggel kapcsolatban? (Több válasz is megjelölhető.)

Válassza ki az összeset, amely érvényes.

- [ ] gyermekorvostól
- [ ] védőnőtől
- [ ] gyógyszerésztől
- [ ] internetről
- [ ] kiadványokból/szóróanyagokból
- [ ] ismerősöktől

26. 26. Tud róla, és örül neki, hogy 2019-től ingyenes, kötelező korosztályhoz kötött védőoltás lesz a bárányhimlő elleni védőoltás?

Soronként csak egy ovális jelöljön be.

- ◯ nem tudtam róla, nem örülök neki
- ◯ nem tudtam róla, de örülök neki
- ◯ tudtam róla, de nem örülök neki
- ◯ tudtam róla, örülök neki

27. 27. Egyéb, fontosnak tartott megjegyzés:

Varicella-zoster vírus infekciók és megelőzésük

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Köszönöm, hogy válaszaival hozzájárul kutatásom sikerességéhez.
Minden kitöltő élhet azzal a jogával, hogy nem minden kérdésre ad választ!

1. 1. Mi az Ön neme?

   Soronként csak egy oválist jelöljön be.

   - ◯ nő
   - ◯ férfi

2. 2. Mi a születési éve?

   _____

3. 3. Hány gyermeke van?

   _____

4. 4. Védőnőként, vagy gyermek háziorvosként tölti ki ezt a kérdőívet?

   Soronként csak egy oválist jelöljön be.

   - ◯ védőnőként
   - ◯ gyermek háziorvosként

5. 5. Milyen településen dolgozik?

Soronként csak egy oválist jelöljön be.

- főváros
- megyeszékhely
- város
- község
- tanya

6. 6. Tanulmányain és munkáján kívül milyen saját tapasztalatokkal rendelkezik a bárányhimlő nevű fertőző betegségről?

Soronként csak egy oválist jelöljön be.

- átestem rajta – gyermekeim/családtagjaim viszont nem
- átestem rajta – gyermekeim/családtagjaim szintén
- nem estem át rajta – gyermekeim/családtagjaim sem
- nem estem át rajta – gyermekeim/családtagjaim viszont igen

7. 7. Amennyiben Ön átesett a betegségen, mikor?

Soronként csak egy oválist jelöljön be.

- óvodás kora előtt
- óvodás korában
- általános iskolás korában
- középiskolás korában
- felnőttként

8. 8. Amennyiben gyermeke/családtagja átesett a betegségen, mikor?

Soronként csak egy oválist jelöljön be.

- ◯ óvodás kora előtt
- ◯ óvodás korában
- ◯ általános iskolás korában
- ◯ középiskolás korában
- ◯ felnőttként

9. 9. Mi a véleménye a gyermek szándékos megbetegítéséről, az „essen át rajta minél hamarabb” hozzáállásról?

Soronként csak egy oválist jelöljön be.

- ◯ egyetértek vele, én magam is megfertőztettem/megfertőztetném gyermekemet
- ◯ egyetértek vele, de én magam nem fertőztettem/fertőztetném meg gyermekemet
- ◯ most, hogy már van védőoltás, nem értek egyet vele, de korábban én magam is megfertőztettem/megfertőztettem volna gyermekemet
- ◯ sem most, sem a védőoltás elérhetősége előtt nem értettem egyet vele

10. 10. Milyen kategóriába sorolná a bárányhimlő nevű fertőző megbetegedést?

Soronként csak egy oválist jelöljön be.

- ◯ enyhe
- ◯ középsúlyos
- ◯ súlyos

11. 11. Tisztában van a bárányhimlő lehetséges szövődményeivel?

Soronként csak egy oválist jelöljön be.

- nem hallottam róla
- hallottam/olvastam róla, de csak felületesen
- nagyjából ismerem a témakört
- részletesen ismerem a témakört

12. 12. Találkozott már a bárányhimlő szövődményeivel?

Soronként csak egy oválist jelöljön be.

- igen, saját gyermekemen/magamon/családtagomon
- igen, betegemen/más gyermekén
- még nem

13. 13. Amennyiben már találkozott szövődményes esetekkel, milyen gyakran fordult ez elő?

Soronként csak egy oválist jelöljön be.

- 10 betegből kevesebb, mint 1 esetében
- 10 betegből 1-2 esetében
- 10 betegből 3-4 esetében
- 10 betegből 5, vagy több esetében

14. 14. Milyen szövődményes esetekkel találkozott? (Több választ is megjelölhet.)

Válassza ki az összeset, amely érvényes.

- [ ] bőr bakteriális felülfertőződése
- [ ] tüdőgyulladás
- [ ] ízületi- és csontgyulladás
- [ ] kisagy gyulladása (mozgáskoordinációs zavar)
- [ ] agyvelőgyulladás
- [ ] övsömör (herpes-zoster – szekunder megbetegedés, vírus reaktiválódása)
- [ ] Egyéb: _____

15. 15. Milyen információkkal rendelkezik a bárányhimlő elleni védőoltásról?

Soronként csak egy oválist jelöljön be.

- ◯ nem hallottam róla
- ◯ hallottam/olvastam róla, de csak felületesen
- ◯ nagyjából ismerem a témakört
- ◯ részletesen ismerem a témakört

16. 16. Szokta ajánlani a bárányhimlő elleni védőoltást a szülőknek?

Soronként csak egy oválist jelöljön be.

- ◯ igen, mindig
- ◯ igen, de csak immunrendszert érintő betegség/terápia esetén
- ◯ igen, de csak leánygyermekeknek
- ◯ nem

17. 18. Beadatta gyermekének a bárányhimlő elleni védőoltást? (Csak akkor válaszoljon, ha van gyermeke.)

Soronként csak egy oválist jelöljön be.

- ◯ igen, minden gyermekemnek
- ◯ igen, de nem minden gyermekemnek
- ◯ igen, de csak lánygyermekemnek
- ◯ nem

18. 19. Ha most kéne döntenie, beadatná gyermekének a bárányhimlő elleni védőoltást?

Soronként csak egy oválist jelöljön be.

- ◯ igen, minden gyermekemnek
- ◯ igen, de nem minden gyermekemnek
- ◯ igen, de csak lánygyermekemnek
- ◯ nem

19. 20. Amennyiben egyik gyermekének sem adatta/adatná be az oltást, mi volt/mi ennek az oka? (Több válasz is megjelölhető.)

Válassza ki az összeset, amely érvényes.

- ☐ mikor gyermekeim kicsik voltak, még nem létezett a védőoltás/akkoriban nem hallottam róla
- ☐ akkoriban védőnőnk/házi gyermekorvosunk nem tájékoztatott az oltásról
- ☐ akkoriban védőnőnk/házi gyermekorvosunk azt javasolta ne adassam be
- ☐ nem hiszek a hatékonyságában
- ☐ feleslegesnek tartom
- ☐ tartok az esetleges mellékhatásoktól
- ☐ túl drágának találtam/nem engedhettem meg az oltás árát

20. 21. Amennyiben első gyermekének nem adatta be a védőoltást, második gyermekének miért adatta/adatná be? (Több választ is megjelölhet.)

Válassza ki az összeset, amely érvényes.

- [ ] az oltóanyag megjelenése miatt (korábban nem volt)
- [ ] be nem oltott gyermek súlyos tünetei miatt
- [ ] az oltóanyag fejlődése miatt
- [ ] társadalmi megítélés változása miatt

21. 22. Amennyiben első gyermekének beadatta, második viszont nem/nem fogja, mi ennek az oka?

Soronként csak egy ovális jelöljön be.

- ◯ gyermekem az oltás ellenére is megbetegedett
- ◯ az oltás mellékhatásai súlyosak voltak
- ◯ Egyéb: _____

22. 23. Konzultált bármilyen okból gyógyszerésszel az oltással kapcsolatban?

Soronként csak egy ovális jelöljön be.

- ◯ igen
- ◯ Nem

23. 24. Ha igen, miről?

_____

_____

_____

_____

_____

24. 25. Tud róla, és örül neki, hogy 2019-től ingyenes, kötelező korosztályhoz kötött védőoltás lesz a bárányhimlő elleni védőoltás?

Soronként csak egy oválist jelöljön be.

- nem tudtam róla, nem örülök neki
- nem tudtam róla, de örülök neki
- tudtam róla, de nem örülök neki
- tudtam róla, örülök neki

25. 26. Szakmailag indokoltnak tartja a bárányhimlő elleni kötelező korosztályos védőoltás bevezetését?

Soronként csak egy oválist jelöljön be.

- igen
- nem

26. 27. Egyéb, fontosnak tartott megjegyzés:

Meningococcus fertőzések és megelőzésük – kérdőív szülőknek

Kedves Kitöltő!
Az alábbi kérdőív a Neisseria meningitidis (meningococcus) által okozott járványos agyhártyagyulladásról és a fertőzés megelőzéséről szól.
Kérjük, segítse kitöltésével kutatásunk sikerességét!
A kérdőív önkéntes és anonim, a kitöltők nem beazonosíthatók, személyes adatot nem gyűjtünk. A felmérésben való részvétel nem kötelező, jogában áll bármelyik kérdést válasz
nélkül hagyni, illetve a kitöltést félbehagyni.
Kitöltésével belegyezését adja, hogy megadott válaszait anonim módon kezelve a kutatásunkhoz felhasználjuk.
A felmérés a Semmelweis Egyetem Orvosi Mikrobiológiai Intézetében zajlik. A felmérést végzi: dr. Huber Annamária PhD hallgató. Elérhetősége:
huber.annamaria@phd.semmelweis.hu

1. Hány éves?

_____

2. Mi az Ön neme?

Soronként csak egy oválist jelöljön be.

- ◯ nő
- ◯ férfi

3. Mi az Ön lakóhelye?

Soronként csak egy oválist jelöljön be.

- ◯ főváros
- ◯ város
- ◯ község/falu

4. Mi az ön legmagasabb iskolai végzettsége?

Soronként csak egy oválist jelöljön be.

- általános iskola
- szakiskola/szakközépiskola
- gimnázium
- főiskola/egyetem
- doktori fokozat
- Egyéb: _____

5. Egészségügyi tanulmányokat végzett?

Soronként csak egy oválist jelöljön be.

- igen
- nem

6. Milyen az Ön anyagi helyzete?

Soronként csak egy oválist jelöljön be.

- kifejezetten jó
- jó
- nem jó
- kifejezetten rossz

7. Hány gyermeke van?

Soronként csak egy oválist jelöljön be.

- 1
- 2
- 3
- több, mint 3

8. Mennyi idős a gyermeke? (Több gyermek esetén több választ is megjelölhet.)

Válassza ki az összeset, amely érvényes.

- [ ] 0-2 éves
- [ ] 3-5 éves
- [ ] 6-10 éves
- [ ] 11-15 éves
- [ ] 16-20 éves
- [ ] 21-25 éves
- [ ] több, mint 25 éves

9. Hallott már a meningococcus okozta megbetegedésről?

Soronként csak egy oválist jelöljön be.

- ◯ igen
- ◯ nem

10. Milyen forrásból szerezte információit? (Több választ is megjelölhet.)

Válassza ki az összeset, amely érvényes.

- [ ] nincs információm a betegségről
- [ ] internet
- [ ] TV/rádió/újság
- [ ] család/barátok
- [ ] háziorvos/védőnő
- [ ] tanulmányok
- [ ] Egyéb: _____

11. Milyen típusú kórokozó a meningococcus?

Soronként csak egy oválist jelöljön be.

- ◯ vírus
- ◯ baktérium
- ◯ gomba
- ◯ nem tudom
- ◯ Egyéb: _____

12. Mik a meningococcus okozta betegség jellemző tünetei? (Több választ is megjelölhet.)

Válassza ki az összeset, amely érvényes.

- ☐ láz
- ☐ köhögés
- ☐ tarkómerevség
- ☐ hasmenés
- ☐ fejfájás
- ☐ tüsszögés
- ☐ bevérzések a bőrön
- ☐ orrfolyás
- ☐ nem tudom

13. Hogyan terjed a betegség?

Soronként csak egy oválist jelöljön be.

- ◯ tárgyak közvetítésével
- ◯ fertőzött állatoktól
- ◯ élelmiszerrel vagy ivóvízzel
- ◯ szexuális úton
- ◯ cseppfertőzéssel
- ◯ kullancscsípéssel
- ◯ nem tudom

14. Melyek a meningococcus fertőzés szempontjából legveszélyeztetettebb korcsoportok? (Több választ is megjelölhet.)

Válassza ki az összeset, amely érvényes.

- [ ] 0-5 évesek
- [ ] 5-15 évesek
- [ ] 15-25 évesek
- [ ] 25-35 évesek
- [ ] 35-50 évesek
- [ ] 50 év felettiek
- [ ] nem tudom

15. Lehetséges, hogy valaki tünetmentesen hordozza a betegséget okozó mikróbát?

Soronként csak egy ovális jelöljön be.

- ◯ igen
- ◯ nem
- ◯ nem tudom

16. Megfelelő kezelés mellett mekkora a halálozási aránya a meningococcus betegségnek?

Soronként csak egy ovális jelöljön be.

- ◯ megfelelő kezelés mellett sosem jár halállal
- ◯ 1000 betegből 1 haláleset
- ◯ 100 betegből 1 haláleset
- ◯ 10 betegből 1 haláleset
- ◯ 5 betegből 1 haláleset
- ◯ nem tudom

17. Van mód a betegség megelőzésére?

Soronként csak egy oválist jelöljön be.

- nincs
- igen, megfelelő higiéné
- igen, védőoltás
- Igen, megfelelő élelmiszerbiztonság
- nem tudom

18. A meningococcus mely típusai a leggyakoribbak?

Soronként csak egy oválist jelöljön be.

- 1-es és 2-es típus
- A, B, C, Y, W típusok
- D, M, N, O, Z típusok
- nem tudom

19. Lehetséges, hogy a gyógyulást követően krónikus idegrendszeri szövődmény marad vissza?

Soronként csak egy oválist jelöljön be.

- nem, gyógyulást követően semmilyen szövődmény nem alakulhat ki
- igen, 1000 betegből 1-nél alakul ki krónikus szövődmény
- igen, 100 betegből 1-nél alakul ki krónikus szövődmény
- igen, 10 betegből 1-nél alakul ki krónikus szövődmény
- nem tudom

20. Ismer valakit, aki meningococcus betegségen esett át?

Soronként csak egy oválist jelöljön be.

- igen
- nem

21. Beoltatta gyermekét meningococcus betegség ellen?

Soronként csak egy oválist jelöljön be.

- ◯ igen, minden gyermekemet
- ◯ Igen, de nem mindegyik gyermekem kapta meg az oltást
- ◯ nem

22. Amennyiben beoltatta gyermekét, melyik oltással? (Több választ is megjelölhet.)

Válassza ki az összeset, amely érvényes.

- ☐ Nimenrix (A, C, W, Y)
- ☐ Menveo (A, C, W, Y)
- ☐ Bexsero (B)
- ☐ Trumenba (B)
- ☐ NeisVac-C (C)
- ☐ Menjugate (C)
- ☐ nem tudom
- ☐ Egyéb: _____

23. Ismétlő oltást is adatott be gyermekének?

Soronként csak egy oválist jelöljön be.

- ◯ igen
- ◯ nem

24. Amennyiben nem oltatta be valamely gyermekét, mi ennek az oka? (Több választ is megjelölhet.)

Válassza ki az összeset, amely érvényes.

- [ ] nem találom szükségesnek
- [ ] nem rendelkezem elegendő információval az oltásról
- [ ] aggódom a mellékhatások miatt
- [ ] az oltás ára miatt
- [ ] vallási/kulturális okok miatt
- [ ] az oltás nem volt elérhető
- [ ] kételkedem az oltás hatékonyságában
- [ ] a háziorvosom nem javasolta
- [ ] Egyéb: _____

25. Ajánlotta Önnek háziorvosa/védőnője az oltás beadatását?

Soronként csak egy oválist jelöljön be.

- ◯ igen
- ◯ nem

26. Ön szerint mennyire súlyos a meningococcus okozta megbetegedés?

Soronként csak egy oválist jelöljön be.

- ◯ nagyon súlyos
- ◯ közepesen súlyos
- ◯ enyhe
- ◯ tünetmentes
- ◯ nem tudom

27. Ön szerint mennyire fontos a meningococcus elleni védőoltás?

Soronként csak egy oválist jelöljön be.

- nagyon fontos
- közepesen fontos
- nem fontos
- nem tudom

28. Ön szerint az oltások általánosságban biztonságosak?

Soronként csak egy oválist jelöljön be.

- teljesen biztonságosak
- többnyire igen
- többnyire nem
- egyáltalán nem
- nem tudom

29. Ön szerint általában fontos a védőoltások beadatása?

Soronként csak egy oválist jelöljön be.

- mindenképpen fontos
- többnyire igen
- többnyire nem
- egyáltalán nem
- nem tudom

30. Kapott gyermeke bármilyen nem kötelező védőoltást?

Soronként csak egy oválist jelöljön be.

- igen
- nem
- nem tudom

31. Amennyiben nem oltatta be valamely gyermekét meningococcus ellen, mi miatt döntene úgy, hogy kéri az oltást? (Több választ is megjelölhet.)

Válassza ki az összeset, amely érvényes.

- [ ] ha több információm lenne az oltásról
- [ ] ha több információm lenne a betegségről
- [ ] ha a gyermekorvos ajánlaná az oltást
- [ ] ha olcsóbb lenne az oltás
- [ ] ha benne lenne a kötelező oltási rendben
- [ ] semmiképpen nem adatnám be
- [ ] Egyéb: _____

Köszönjük, hogy kitöltötte kérdőívünket!