










# Guidelines of the Polish Society of Gynecologists and Obstetricians, the Polish Society for Vaccinology, and the Polish Society for Family Medicine on vaccinating women with reproductive plans and pregnant or breastfeeding women

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The following Guidelines present the most up-to-date treatment and management recommendations, which may be modified and altered after detailed analysis of a specific clinical situation, which in turn might lead to future modifications and updates.

Pregnant women constitute a unique group of patients, who require an individualized approach to vaccination, with special emphasis on maternal and fetal safety. Based on individual immune response, vaccination will result in the development of varying levels of immunity, which offers protection to the mother and the fetus/neonate. Depending on the preparation, administration of a vaccine to a pregnant woman results in the synthesis of various types of specific antibodies, followed by their transport across the placenta to the fetus. As a result, maternal an-

tibodies protect the neonates during the first few weeks of their life [1, 2].

Mandatory vaccination in Poland is free of charge (until the patient is 19 years old), whereas all additional vaccines for adults of all ages, including pregnant women, are voluntary. Still, these vaccines are recommended, especially if there is risk of serious health consequences after being infected with, for example, COVID-19, influenza, pertussis. Some of the vaccines are refunded but the cost of others will need to be fully covered by the patient.

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In order to provide the mother and the child with the highest possible level of protection, immunization should be initiated in a timely manner, preferably already at the stage of preconception. When planning for pregnancy, it is useful to analyze the immunization records of the woman, as well as collect a detailed history of pediatric infectious diseases. It helps the physician to establish the immunological status of the patient and allows to prepare an individualized plan for the recommended immunizations. Therefore, it is prudent to design the immunization schedule already during the preconception period and adjust it to both, maternal health status and the characteristics of the given vaccine, taking into account time elapsed before full immunity is achieved [3]. Immunity following childhood vaccinations is often insufficient so the importance of a booster dose, especially in cases of some vaccines (e.g., tetanus, pertussis) needs to be emphasized. Such management would offer a unique opportunity to optimize maternal and neonatal health [4–6].

Standard protocol needs to be followed in case of both, the eligibility process and the vaccination procedure in the group of pregnant women. As far as immunization during pregnancy is concerned, breastfeeding is not a contraindication. Taking into account maternal and fetal safety, and possible consequences resulting from various infections, it is necessary to classify the preparations into priority vaccines as well as secondary importance vaccines, which should be administered only in special circumstances and if there is high risk for infection.

It is vital to differentiate between vaccines which **may** be used in pregnant women and those which are contraindicated in pregnancy.

Vaccines which contain inactivated pathogens or their fragments **may be administered to pregnant women**, and these include:

- recombinant;
- subunit;
- polysaccharide;
- conjugate;
- toxoid;
- mRNA and non-replicating viral vaccines.

Vaccines which contain live weakened (attenuated) pathogens **cannot be administered to pregnant women** and these include:

- measles, mumps, rubella (combination) vaccine;
- varicella vaccine;
- tuberculosis vaccine;
- nasal spray flu vaccine.

### RECOMMENDED VACCINES

These vaccines are recommended due to high probability of severe adverse effects resulting from an infection.

#### Inactivated, quadrivalent influenza vaccine (split virion or subunit)

**Administered only seasonally, directly before or during the peak incidence season (September–March) — 1 dose.**

- Believed to be effective as it significantly lowers the risk for contracting the flu, providing temporary protection for both, the mother and the neonate.
- Safe for both, the mother and the child.
- Should be recommended and administered to pregnant women with no permanent or temporary contraindications to vaccination.
- May be administered in any trimester of pregnancy.

#### Combination vaccine against diphtheria, tetanus, and pertussis (dTaP) with reduced amount of diphtheria toxoid, tetanus toxoid, and acellular pertussis antigens

The dTaP vaccine is administered in pregnancy for passive protection against pertussis during the early neonatal period. **Administered between 27 and 36 weeks of gestation, 1 dose (0.5 mL).**

- Believed to be effective because it offers temporary protection both, to the mother and the child. As compared to pre-pregnancy or postpartum immunization, this offers significantly higher protection against contracting pertussis to neonates and infants.
- Safe for both, the mother and the child.
- Considered to be safe for both, the mother and the child - the vaccine differs from the tetanus (T) shot as it contains a two-fold reduced amount of tetanus toxoid (at least 20 IU) and is recommended exclusively as a booster dose to adults, children > 4 years, and pregnant women.
- Should be recommended and administered to pregnant women with no permanent or temporary contraindications to immunization,
- Due to the fact that high antibody titer is **only temporary**, repeat vaccination is recommended in each subsequent pregnancy.

The dTaP vaccine, with reduced amount of diphtheria toxoid, acellular pertussis component and tetanus toxoid, is believed to be safe for pregnant women. Administration between 27 and 36 weeks of gestation ensures that a sufficiently high concentration of antibodies will be transferred to the fetus through the placenta and will provide protection to the neonate in the first week of life [7]. In Poland, immunization of pregnant women with a pertussis vaccine has been recommended by the National Immunization Program (NIP) since 2016.

#### COVID-19 (SARS-CoV-2) vaccine — mRNA-based vaccines only

The dosing regimen in accordance with the current recommendation protocols (**30.09.2022**). **Primary 2-dose schedule and booster doses are recommended.**

- Believed to be effective because it offers temporary protection against severe course of the disease to the mother and the child.
- Safe for both, the mother and the child.
- Should be recommended and administered to pregnant women with no permanent or temporary contraindications to immunization.
- May be received at any stage of pregnancy, however a full vaccination course (2 doses) should be completed before the beginning of the third trimester, as the risk for severe course of COVID-19 in pregnant women increases significantly after the second trimester.

In light of the fact that the SARS-CoV2 virus is relatively recent, and because new mutations continue to emerge, which may be associated with changes in their characteristics and the immunization protocol, the above recommendations may be modified as a result of the Polish and the international updates in the trends and the management protocols. Based on the data about immunization of pregnant women during the phase of the epidemic with the dominant Delta virus, published until the end of 2021, the effectiveness of COVID-19 vaccines among pregnant women was found to be similar to that of non-pregnant patients, as far as hospitalization and mortality rates are concerned.

### OPTIONAL VACCINES

These vaccines are recommended before travelling or due to the current epidemiological situation in a given area, and due to individual risk factors (e.g., chronic diseases):

- hepatitis B;
- hepatitis A;
- pneumococcal disease.

It is advised to start with the 13-valent conjugate vaccine, followed by 23-valent polysaccharide vaccine, no sooner than after 8 weeks. However, if the 23-valent polysaccharide vaccine is first, the 13-valent vaccine should be administered after 12 months. At present, there are no data about the safety of using 20-valent conjugate vaccine during pregnancy.

Immunization against meningococcal disease with the use of the following vaccines:

- monovalent meningococcal serogroup B vaccine;
- monovalent meningococcal serogroup C vaccine;
- conjugate meningococcal serogroups A, C, W, Y vaccine;
- polysaccharide meningococcal serogroups A, C, W, Y vaccine.

It is possible to co-administer the vaccine against serogroup B and against serogroups A, C, W, Y, *i.e.*, using two different anatomical sites, but the risk of adverse event following immunization (AEFI) increases (including fever), so it is advisable to consider the benefits but also the risks associated with such management.

Immunization against acute poliomyelitis using the following vaccines:

- inactivated poliovirus vaccine (IPV);
- combination dTaP-IPV vaccine against diphtheria, tetanus, pertussis and poliomyelitis (routine management if used in travel medicine).

### REQUIRED VACCINES

These vaccines need to be immediately administered in urgent situations and when the risk of complications and mortality is very high (post-exposure vaccination):

- tetanus T;  
the basic course consists of three doses of the T vaccine (different from the dTaP vaccine, which is recommended for pregnant women). Tetanus toxoid — min. 40 IU, adsorbed to aluminum hydroxide hydrated to max. 0.7 mg Al 3+
- rabies.

### CONTRAINDICATED VACCINES

These vaccines are contraindicated either because they contain live attenuated pathogens or due to the information found in the product characteristics:

- measles, mumps, rubella (combination vaccine);
- varicella;
- tuberculosis vaccine;
- typhoid fever (contains live attenuated (weakened) S.Typhi strain (Ty21a); oral administration);
- nasal influenza vaccine (live attenuated nasal spray vaccine);
- HPV vaccine.

### INTRODUCTION

Despite the fact that immunization during pregnancy is an important component of infectious disease prophylaxis, it needs to be emphasized that in many countries, including Poland, public interest as well as awareness of the importance of vaccines continue to be low. The percentage of women in other countries who are vaccinated during pregnancy, although different, remains high, whereas in Poland it is unknown but and presumably very low.

As far as immunization during pregnancy is concerned, the main obstacles seem to be as follows:

- insufficient or non-existent education, resulting in concern about vaccine effectiveness and safety (this is true not only about pregnant women but patients in general, as well as medical personnel);
- underestimation of disease seriousness and contesting the need for creating prophylaxis programs to prevent the spread of infectious diseases;
- limited access to vaccines, both temporary and permanent;

- low social and economic status of some societies, and the consequent low-quality or sometimes even non-existent basic health care.

Studies in Poland have identified the following obstacles associated with immunization during pregnancy:

- insufficient/no knowledge about immunization in pregnancy among physicians;
- insufficient/no knowledge about vaccinating pregnant women among patients;
- concern about the possibility of adverse event following immunization (AEFI), expressed by both, medical personnel and patients.

As far as patient refusal is concerned, the most common reasons for vaccination refusal among pregnant women are as follows [3]:

- concern for the safety of the child;
- unfavorable opinions about vaccines expressed by friends, family and others;
- negative comments or false information posted on various websites (including specialized and social media websites), which cause or consolidate false conviction about insignificant prophylaxis or even harm associated with immunization during pregnancy;
- negative opinion about vaccines expressed by a physician or other individuals affiliated with healthcare professionals.

Importantly, guidelines for vaccinating pregnant women, which have been a part of the National Immunization Program (NIP) in Poland for a number of years, and which are included in the section of recommended vaccines, apply to flu and pertussis vaccines.

Similar guidelines have been issued in other European countries, the United States, Australia, and New Zealand. Various medical and academic associations, including the Polish Society of Gynecologists and Obstetricians (PTGiP-PSGO), the Advisory Committee on Immunization Practice (ACIPs), the American College of Obstetricians and Gynecologists (ACOG), the American Academy of Pediatrics (AAP), and the World Health Organization, (WHO) have confirmed the safety of using COVID vaccines in pregnancy and their effectiveness in preventing severe course of disease, hospitalization, and death.

Detailed presentation of immunizations for pregnant women, classified as follows:

- recommended;
- optional;
- required;
- contraindicated.

## RECOMMENDED IMMUNIZATIONS

These vaccines are recommended due to the high incidence of severe disease-related consequences.

Immunization during pregnancy, which is recommended by numerous medical associations and societies (including PTGiP, WHO, ACIP, ACOG), is currently limited to the following:

- seasonal flu shots (only inactivated vaccines);
- combination dTaP vaccine against diphtheria, tetanus, and pertussis, with reduced amount of diphtheria toxoid, tetanus toxoid, and acellular pertussis component;
- COVID-19 vaccine (mRNA vaccine only).

## Quadrivalent (split virion or subunit) inactivated influenza vaccine

Influenza incidence among pregnant women is similar to that of the general population, but infection during pregnancy is associated with severe and complicated course, especially in the third trimester. At that time, the following complications are particularly common: severe pneumonia, severe respiratory insufficiency, cardiological complications, neurological disorders, and, as a result, higher risk of maternal and fetal mortality [8, 9].

In case of contracting the flu, the risk of fetal infection is relatively low. However, some studies have demonstrated a link between the infection and the risk for miscarriage, preterm labor, intrauterine fetal demise, neonatal death, low neonatal birth weight, and higher risk for cesarean section. Fever in the mother may cause tachyarrhythmia and subsequent hypoxia in the fetus [10, 11].

Influenza among neonates is a rare occurrence, but neonates and infants are at high risk for severe and complicated course of the disease (severe pneumonia, otitis media, myocarditis, acute respiratory failure). Approximately 10% of children >12 months of age who contracted influenza require admission to the intensive care unit, which is indicative of a possible severe course of disease in that age group [12]. According to the inactivated vaccine registration, flu vaccinations may be considered for children >6 months, so vaccinating pregnant women is essential as it lowers the risk for contracting the disease not only by the mother but also the infant [13].

Immunization of pregnant women against influenza has been validated by the PTGiP, together with the National Flu Immunization Program (OPZG), as well as international expert organizations, *e.g.*, ACIP, ACOG. WHO also recommends that all pregnant women without absolute contraindications, temporary or permanent, should be immunized, irrespective of the pregnancy trimester [14–16].

Immunization needs to be performed before the flu season starts. The peak incidence for the northern hemisphere, which includes Poland, is observed between January and the end of March. Immunization is also possible when high circulation of the flu virus in the general population is reported. Quadrivalent (split virion or subunit) inactivated

vaccine is used to immunize pregnant women against influenza [17, 18].

According to the Polish National Immunization Program (2022), flu vaccine is only recommended, which means that the cost needs to be covered by the patient. However, since September 2021, inactivated flu vaccine has been included in the "Pregnancy+" program, meaning it is free of charge for pregnant women. In Poland, two types of flu vaccines are currently available for pregnant women: split virion (contains all parts of the virus) and subunit (contains fragments of viral surface glycoproteins). Immunogenicity and safety of both vaccines are comparable, also in case of pregnant patients. The vaccines may be administered by the intramuscular or subcutaneous route [19].

**Live Attenuated Influenza Vaccine (LAIV) registered in Europe for nasal administration to children and adolescents, between the ages of 2 and 18, is contraindicated in pregnancy [16].** Breastfeeding is not a contraindication to influenza vaccine.

Immunization of pregnant women against the flu using inactivated (split virion or subunit, non-adjuvanted) vaccines is safe both, for the mother and the infant [20–23]. The immunological effectiveness of the flu vaccine among pregnant women is comparable to that of the general population (similar antibody levels). Immunization prevents the disease and the possible complications both, in the mother and the neonate [24, 25].

### **Combination dTaP vaccine against diphtheria, tetanus and pertussis (with reduced antigen content)**

Pertussis (whooping cough) is a disease caused by Gram-negative *Bordetella pertussis* bacillus. The disease is mainly transmitted via the droplet route, less often through direct contact. It needs to be emphasized that pertussis is highly contagious (1 individual may infect 12–14 people in their surroundings). According to 2018 ECDC (European Center for Disease Prevention and Control) report, the highest notification rates were reported by Germany, the Netherlands, Norway, Austria, and Poland [26]. Unfortunately, underestimation of pertussis incidence rates constitutes the greatest obstacle in identifying the actual scale of the problem.

The results of the Polish Pertussis Study (OBEK) conducted by the National Institute of Public Health — National Institute of Hygiene (NIZP-PZH) demonstrated that pertussis incidence is massively underestimated (12–320-fold, depending on the age group) [27].

Despite the fact that the incidence of pertussis decreased significantly, as compared to the time before mandatory immunization was introduced, the disease may still cause severe infection and death, especially among children,

also in the developed countries, which includes Poland [4, 5]. Between 2000 and 7000 cases of pertussis are reported each year in Poland. However, the disease is largely underreported, which is the consequence of a low number of diagnostic tests or a misapprehension that pertussis is typically a childhood disease [6, 7]. The fact that immunity wanes after a few years is an important aspect of the current epidemiologic situation in the country. Since pertussis immunity obtained during childhood is not permanent, booster doses are necessary.

Immunization against pertussis among adults in Poland is only recommended, so the cost of the vaccine needs to be covered by the patient. According to the Polish National Immunization Program, pertussis vaccines are recommended to the following groups of people:

- adults (every 10 years);
- medical personnel (especially caring for neonates and infants);
- pregnant women (between 27 and 36 weeks of gestation);
- individuals who expect to be in close contact with a child up to 12 months of age (cocooning strategy).

Satisfactory or mild but temporary pertussis immunity is achieved after vaccination or after contracting the disease. Post-vaccine immunity lasts for 5 to 10 years, depending on the vaccine (acellular or whole-cell). Currently, adults are the main reservoir for pertussis and, as a potential source of infection, constitute a serious threat to the youngest children, who present with the most severe disease course. Even among populations with high immunization coverage rates, the *Bordetella pertussis* bacillus continues to pose a threat, with epidemic peaks every two to five years, much like before mandatory immunization had been introduced. Pertussis is dangerous almost exclusively to non-vaccinated individuals and deadly for neonates born to mothers without significantly high antibody titer [28]. Therefore, maternal immunization in pregnancy constitutes an important element of pertussis prophylaxis among the youngest children, who may contract the disease but are too young to receive the vaccine.

The course of disease in adults is typically arduous (persistent cough, lasting up to three months, mainly at night), but complications (*e.g.*, secondary pneumonia, urinary incontinence, rib fracture) — although possible — are less common than in younger children. Pertussis in unvaccinated infants is associated with high mortality rates (80% of deaths are reported for that age group).

Complications of pertussis include pneumonia, apnea, pulmonary hypertension, seizures, and cerebral defects (pertussis encephalopathy), with frequent need for mechanical ventilation.

**In light of the above-mentioned reasons, pertussis immunization during pregnancy is a much-needed**



**method of protecting the infants, already in the first days and weeks of their life.** Immunization of the infants may start as early as at 6 weeks of neonatal life. Vaccination is often delayed, sometimes due to trivial reasons, and administration of one or even two doses does not offer complete protection against pertussis. **It needs to be emphasized that despite administering 3 doses of pertussis vaccine in the first six months of neonatal life, it is not until the second half of the first year of life that sufficient antibody titer is achieved. Therefore, it is essential to protect each child with maternal antibodies and, as a secondary measure, to use the cocooning strategy – i.e., immunizing all people in close contact with the neonate (parents, grandparents, older siblings, and caretakers) to minimize the risk of pathogen transmission.**

The Polish Society of Gynecologists and Obstetricians, similarly to ACIP and other organizations, recommends for the pertussis vaccination to be administered between 27 and 36 weeks of gestation, as the transplacental transfer of maternal antibodies to the fetus is the most effective at that time. Earlier administration of the dTaP vaccine, despite less effective antibody transfer, is not associated with maternal or fetal risk. In the UK, in 2016, the dTaP vaccine was recommended to pregnant women at 20 weeks of gestation (although the vaccine could be administered as early as 16 weeks of gestation). The subsequent analysis revealed that, after extending the time window for vaccinating pregnant women against pertussis, the number of premature babies hospitalized due to pertussis in the first 60 days of neonatal life decreased by half. These results demonstrated possible benefits of pertussis vaccination performed earlier in pregnancy [29].

Delayed immunization (after 36 weeks of gestation) presents no danger to the mother or the child. However, it may prove to be ineffective in terms of protecting the neonate and the infant. If the delivery takes place a mere few days after immunization, the times elapsed was insufficient to produce and transfer the antibodies to the fetus. In such situations, immunization will be beneficial for the mother (protection against the disease) and may be treated as an element of the cocooning strategy. Importantly, cocooning strategy, implemented to minimize the risk of contracting pertussis by the child, is not as effective as immunization of the pregnant women, and it should be treated as a complementary strategy, not as a replacement.

According to the Polish National Immunization Program (2022), pertussis vaccine is mandatory for children and adolescents, realized in neonates > 6 weeks of age (3 doses: at 2, 4 and 6 months of life). An additional dose, which is the part of the primary series, is administered during the second year of life (between 16-18 months of life), and booster doses are received at the ages of 6 and 14 years. As men-

tioned above, pertussis vaccine received during childhood or adolescence does not offer lifelong immunity. Therefore, due to short-term immunity, from 5 to 10 years, depending on the vaccine (acellular or whole-cell), booster doses for adults are required. In case of adults, including pregnant women, pertussis immunization is performed using vaccines which contain tetanus toxoid and reduced (as compared to the vaccine administered to children) amount of diphtheria toxoid and pertussis antigens with acellular component (dTaP). **Adults, including pregnant women, should not receive the pertussis vaccines which are administered to children (DTPa or DTPw).**

Immunization with the dTaP (diphtheria, tetanus, pertussis) vaccine is not contraindicated while breastfeeding.

Safety and immunogenicity of the acellular pertussis vaccines (Pa) in infants and children have been the focus of numerous studies, which unequivocally demonstrated that the vaccines were well-tolerated and were less often associated with adverse events as compared to whole-cell pertussis vaccines (Pw) [4]. Although pregnant women were excluded from the studies conducted before the dTaP was licensed for use, there were never any concerns about its safety, as it is an inactivated vaccine [30]. Moreover, numerous reports confirmed the safety of using vaccines which contain tetanus toxoids and diphtheria toxoids in pregnant women, which was the main reason initiatives to eradicate infant pertussis were launched all over the world. Vaccine manufacturers have designed registries (immunization information systems) to collect information about women who received the dTaP vaccine in pregnancy [30]. Based on their data, no evidence for higher number of adverse events, such as miscarriage or abnormal neonatal development, was found, which was later confirmed by various studies [31–38].

### **COVID-19 vaccines (SARS-CoV-2 viral infection — immunization only with mRNA vaccines)**

The SARS-CoV-2 virus is the causative factor for COVID-19. The droplet route is the main mode of transmissions, while transmission via contaminated surfaces is rare. Cases of intrauterine transmission have been reported, which indicates that transient viremia may be associated with the risk of intrauterine transmission of the virus, and that the presence of the infection-specific receptors in the placenta is probably minimal. The course of COVID-19 infection in pregnant women is relatively mild, with fever, hacking cough, fatigue, muscle pain, headache and throat ache, loss of taste and smell, conjunctivitis. However, the characteristic symptoms will most probably undergo changes over time due to constant mutations of the virus.

Neither pregnancy nor delivery increase the risk for SARS-CoV-2 infection, but they do increase the risk for severe and complicated course of the disease, particularly in the

third trimester, especially among women over the age of 35, with comorbidities (pregestational diabetes, gestational diabetes hypertension, preeclampsia, cholestasis, and obesity) [39, 40]. As compared to non-pregnant women, pregnant women during the course of COVID-19 are at an elevated risk for the following conditions:

- pneumonia;
- hospitalization at an intensive care unit (approximately 3-fold higher);
- mechanical ventilation and ECMO (almost 2.5-fold more frequent);
- death (> 1.5 higher).

In the first trimester of pregnancy, no significantly elevated risk for miscarriage or congenital abnormalities has been found, but a higher risk (approximately 17%) for premature birth, in most cases iatrogenic, has been confirmed [41, 42].

Data collected by June 2021 revealed that the risk of transmission via breastfeeding by a SARS-CoV-2 positive mother is low. If the child gets infected, it will most likely be the result of a direct contact, via droplet transmission. In neonates and infants, the course of COVID-19 is typically mild or asymptomatic. At present, neither isolation nor breastfeeding cessation are advised, but strict sanitary regime is recommended.

Of note, the SARS-CoV-2 virus continues to mutate and, depending on the variant, the ease and speed of disease spread, characteristic symptoms and possible adverse effects also change. Therefore, continuous monitoring of the disease-related information among pregnant women and neonates is required to create a reliable data source.

The first vaccines against COVID-19, introduced in the United States, used the mRNA technology. In December 2020, those preparations were approved by the Food and Drug Administration (FDA) for use during pregnancy in emergent cases. Currently, the Polish Society of Gynecologists and Obstetricians, the Polish Society for Vaccinology, the Polish Society for Family Medicine, and numerous other societies all over the world recommend immunizing all pregnant women against COVID-19 at any stage of pregnancy. Ideally, the full course should be completed before the start of the third trimester, when the risk for severe course infection is significantly elevated. COVID-19 vaccine may be co-administered with an influenza vaccine. Until now (January 2023), there have been no reports about a possible detrimental effect of COVID-19 mRNA vaccines on fetal development. Also, there is no evidence for higher risk associated with immunizing pregnant women against COVID-19 as compared to their non-pregnant age peers [43–46].

**Gynecologists, obstetricians, general physicians, and vaccinologists should inform, educate, and encourage**

**patients with reproductive plans, as well as pregnant or breastfeeding women, to be immunized against COVID-19. The mRNA vaccines are recommended to pregnant women as the literature offers more evidence of their safety.**

### OPTIONAL IMMUNIZATIONS

These vaccines may be administered before travelling, or due to the epidemiologic situation in a given area, or due to medical risk factors (*e.g.*, chronic diseases).

Apart from the three abovementioned vaccines routinely used in pregnant women, certain vaccines may be administered in special circumstances, such as deteriorating epidemiologic situation (epidemic), the need to travel to the territory which is endemic to a particular disease (immunization in travel medicine), post-exposure management, or individual risk factors (chronic diseases).

#### Hepatitis A

Hepatitis A infection is caused by the HAV (*hepatitis A*) virus. The modes of transmission include the fecal-oral route, sexual activity, and especially contact with waste, production of food, and traveling to countries with low social and economic status. Acute hepatitis A in pregnancy is associated with elevated risk for liver failure, which in pregnant women may lead to preterm labor and complications related to prematurity. There is no evidence of vertical transmission between a mother and a child. Inactivated hepatitis A vaccine is characterized by high immunogenicity and safety.

In Poland, **immunization against hepatitis A** in children and adults is recommended but non-mandatory, which means the cost is covered by the patient. A 2-dose schedule (at 0 and 6 months) is realized in adults, including pregnant women. Inactivated vaccine may be administered to pregnant women after considering the risk of a possible HAV infection [47, 48]. Immunization should be recommended to women planning for pregnancy who are seronegative or who have no medical records of immunization.

#### Hepatitis B

Hepatitis B is caused the HBV (*hepatitis B*) virus. The disease is transmitted through blood and sexual activity. If the infection develops in pregnancy, chronic hepatitis, cirrhosis, and primary liver cancer are observed more often. Vertical transmission is possible at any stage of pregnancy (risk for fetal infection: 5–8%).

The highest risk for maternal-fetal/neonatal transmission is observed in the third trimester of pregnancy and during labor, also during a cesarean section, and immediately after birth. The risk factors include high-level HBV DNA viremia and positive HBsAg/HBeAg antigen test (infection risk: 85–90%). Among children, long-term carrier state is

associated with developing cirrhosis and primary liver cancer during adulthood.

**In Poland, hepatitis B vaccination is mandatory for children and medical personnel and recommended to the rest of the adults. In case of adults, including pregnant women, hepatitis B immunization is realized using a 3-dose schedule (at 0, 1 and 6 months). Hepatitis B vaccine is a recombinant preparation. Immunization should be recommended to women planning for pregnancy who are seronegative or who have no medical records of immunization.**

No relationship between hepatitis B vaccine and elevated risk for pregnancy failure has ever been demonstrated [49, 50]. The vaccine may be recommended to all pregnant women with high risk for developing hepatitis B [51]. Hepatitis B vaccine may be administered to a pregnant woman in order to complete the immunization course which was initiated before pregnancy (there is no need to delay the next dose until after delivery).

Post-exposure prophylaxis for a non-infected and not immunized earlier person consists of hepatitis B immune globulin and 3 doses of the vaccine (at 0, 1 and 6 months). A previously immunized person with levels of anti-HBs below < 10 mIU/mL (and no history of  $\geq$  10 mIU/mL titer), should receive hepatitis B immune globulin and the vaccine. An immunized person with levels of anti-HBs above > 10 mIU/mL (currently or at any time in the past) — does not require prophylaxis. Post-exposure hepatitis B immunization maybe performed during pregnancy, puerperium, breastfeeding, and the preconception period.

### Immunization against pneumococcal disease

The Gram-positive *Streptococcus pneumoniae* bacterium, with droplet route of transmission, causes infections which may present as invasive pneumococcal disease (meningitis, septicemia, bacteremic pneumonia) and non-invasive pneumococcal disease (pneumonia without bacteremia, rhinosinusitis, otitis media). In Poland, immunization against pneumococcal disease is mandatory in children born after December 31, 2016, and is recommended in the rest of the population.

Immunization is advised to patients who are at high risk for invasive pneumococcal disease, *i.e.*, with the following conditions: chronic respiratory diseases (asthma), chronic diseases of the cardiovascular system, chronic renal and hepatic diseases, oncological diseases, metabolic conditions (diabetes), immunosuppression, asplenia.

Two types of vaccines against pneumococcal disease may be administered to adults, including pregnant women:

- 13-valent conjugate vaccine;
- 23-valent polysaccharide vaccine.

Adults receive one dose of the vaccine against pneumococcal disease. It is advised to start with the 13-valent

conjugate vaccine, followed by the 23-valent polysaccharide vaccine, with an 8-week interval between them. However, if the 23-valent polysaccharide vaccine was administered first, the 13-valent vaccine should be administered after 12 months. A 20-valent pneumococcal conjugate vaccine has been available in Poland since June 2022, and may be administered to adults over 18 years of age. However, according to the product characteristics records, the vaccine was not tested in pregnant women, and animal tests demonstrated no teratogenic potential. Possible immunization should be preceded by thorough analysis of risks and benefits.

### Immunization against meningococcal disease

The Gram-negative *Neisseria meningitidis* bacterium, transmitted through the droplet route, causes meningitis and/or septicemia. Typically, the infections are characterized by a rapid course, with non-specific symptoms during the preliminary stages of the diseases, which makes the diagnosis challenging and delays antibiotic therapy, resulting in worsened prognosis.

Currently, in Poland as well as many other European countries, most cases (67%) of invasive meningococcal disease (IMD) are caused by serogroup B, followed by serogroup C (19%). Recent years have witnessed higher rates of infection caused by serogroup W (19% in 2020 and 12% in 2021). Invasive meningococcal disease is mostly found in infants and children up to 5 years, but the second peak is observed in adolescents and young adults (between 15 and 25 years of age), who often are asymptomatic carriers of a meningococcus in the nasopharyngeal cavity, or due to other risk factors (closed communities, sharing food and drink, smoking, sexual activity).

**Immunization against meningococcal disease** in Poland is recommended, which means the cost is covered by the patient. The risk groups for invasive meningococcal disease include individuals with anatomic or partial asplenia, congenital or acquired complement deficiency (C3, C5-C9), properdin, factor H and factor D, patients who receive eculizumab (Soliris) used to treat paroxysmal nocturnal hemoglobinuria, with atypical hemolytic-uremic syndrome, HIV positive individuals, personnel of microbiology laboratories who routinely have contact with *Neisseria meningitidis* isolates, and groups at high risk in case of an epidemic focus (the choice of the vaccine depends on the meningococcal serotype, which is responsible for the given focus).

Immunization of adults, including pregnant women, against meningococcal disease maybe performed with the use of the following vaccines:

- monovalent vaccine against meningococcal serogroup B;
- monovalent vaccine against meningococcal serogroup C;
- conjugate vaccine against meningococcal serogroups A, C, W, Y;



- polysaccharide vaccine against meningococcal serogroups A, C, W, Y.

The current epidemiologic situation in Poland is the reason why indications for monovalent vaccines have been significantly limited in favor of the 4-valent vaccine, which prevents infection caused by serogroups A, C, W, Y. Adults receive one dose of the 4-valent conjugate A, C, W, Y vaccine and two doses of vaccine against serogroup B (with a 1–6-month interval, depending on the manufacturer's recommendations).

It is possible to co-administer the vaccine against serogroup B and against serogroups A, C, W, Y, *i.e.*, using two different anatomical sites, but the risk of adverse event following immunization (AEFI) increases (including fever), so it is advisable to consider the benefits as well as possible risks associated with such management.

### Immunization against poliomyelitis

Adults, including pregnant women, who travel to polio-endemic countries are advised to receive a polio vaccine every 10 years. The following vaccines are recommended:

- Inactivated polio vaccine (IPV);
- Live attenuated poliomyelitis vaccine is contraindicated to oral administration (apart from that, the vaccine has been unavailable in Poland since 2016).

Adults, including pregnant women, may receive a combination the dTaP-IPV vaccine against diphtheria, tetanus, pertussis, and polio (poliomyelitis) within travel medicine, or when the dTaP vaccine is not available.

### Typhoid immunization

*Salmonella typhi* is a Gram-negative bacterium which is the etiological agent of typhoid fever. The disease is spread via contaminated food and direct contact. In Poland, typhoid fever is a rare occurrence, but typhoid vaccine is recommended to people traveling to typhoid-endemic regions (South and East Asia, Africa, Central and South America).

Two types of typhoid vaccines are currently available:

- killed (inactivated) — contains whole *S. Typhi* strain bacillus, killed with formaldehyde and temperature or the purified polysaccharide capsule (Vi) (injection); the vaccine can be administered to pregnant women;
- live attenuated (weakened) — contains *S. Typhi* strain (Ty21) (oral administration); the vaccine cannot be administered to pregnant women.

### Yellow fever immunization

Yellow fever is a viral disease which is transmitted by infected mosquitoes. The disease is not found in Poland, but numerous cases have been reported for the tropical regions (Africa, Central and South America). Immunization is recommended to people who travel to yellow fever-endemic regions.

The vaccine contains live attenuated fragments of the virus and is very effective, offering a lifelong immunity. Until recently, yellow fever vaccine has been contraindicated in pregnancy. At present, in justified cases (the need to travel to yellow fever-endemic regions), the vaccine may be administered to a pregnant woman after discussing the benefit-to-risk ratio with the patient, although caution is advised.

### Cholera immunization

Inactivated oral cholera vaccine contains killed whole *V. cholerae bacillus* and a purified cholera toxin subunit. The vaccine may be received by people who plan to travel to cholera-endemic regions. The vaccine may be considered for pregnant and breastfeeding women after detailed analysis of the benefit-to-risk ratio [52]. The available observational studies, which investigated immunization of pregnant women against cholera, found no significant relationship between oral cholera vaccine and unfavorable pregnancy outcomes, but they also did not completely exclude the possibility of such outcomes [53].

### REQUIRED IMMUNIZATIONS

These vaccines may be recommended in special circumstances, when urgent administration is required, and in case of high risk for disease-related complications or mortality (post-exposure vaccination).

That group includes vaccines which are absolutely indicated during pregnancy due to some external circumstances, which require emergent immunization (post-exposure immunization).

### Rabies vaccine

In light of the fact that the mortality rate in case of rabies is practically 100%, it is necessary to administer a post-exposition vaccine. Post-exposition prophylaxis is used in people who had contact with a sick or suspected of rabies animal. The course of action depends on the type of exposition and condition of the animal. Eligibility for immunization should be determined by a specialist at an infectious diseases clinic.

### Tetanus vaccine

The type of the prophylactic measure depends on the immune status of the exposed person and the risk for infection (circumstances and type of wound). The T tetanus or Td vaccine is routinely administered if a tetanus vaccine is indicated.

Depending on availability, if a recipient wishes to take a recommended, non-mandatory, vaccine, the following preparations may be administered to pregnant women:

- combination dTaP vaccine against diphtheria, tetanus, and pertussis, with reduced antigen content;
- combination dTaP-IPV vaccine against diphtheria, tetanus, pertussis, and poliomyelitis (**if the dTaP vaccine is**

**not available or the patient will travel to polio-endemic countries).**

In cases when active-passive immunization against tetanus is indicated, human tetanus immunoglobulin is administered, also to pregnant women, apart from the vaccine. If the medical records are not available and patient immunization history remains unknown, it is safer to administer a vaccine than fail to immunize.

**CONTRAINDICATED VACCINES**

These vaccines are contraindicated due to the fact that they contain live, although weakened (attenuated), pathogens or because of the information found in the product characteristics. Live attenuated vaccines which contain a fragment of wakened viruses and bacteria are contraindicated in pregnancy, and these include:

- measles, mumps, rubella (MMR);
- varicella (VZV);
- tuberculosis (BCG vaccine);
- human papilloma virus (HPV);
- typhoid fever (oral route);
- live attenuated influenza (LAIV) nasal spray.

Importantly, if the abovementioned vaccines are accidentally administered during pregnancy — in cases when the mother is unaware of her condition - it is not an indication to terminate the pregnancy. However, in such cases it is advised to counsel the patient about the potential vaccine-related risk for the fetus [51, 52].

Theoretically, there is a risk of congenital defects after administration of live attenuated vaccines, but observational studies found no evidence for elevated risk of congenital defects, fetal infection, and complicated course of pregnancy in such cases. There have been no reports of abnormal fetal development after immunizing the mothers, who were unaware of the pregnancy, with live attenuated vaccines.

Vaccines which contain live attenuated pathogens should be administered to women planning for pregnancy or during the puerperium. Breastfeeding is not a contraindication to immunization.

Immunization during the preconception period should be especially recommended to young women who have frequent contact with children (teachers, kindergarten teachers, nurses and physicians at hospitals and clinics), as they are at a particularly high risk for contracting varicella and rubella.

Due to severe consequences of contracting rubella or varicella during pregnancy, these vaccines have been discussed in great detail in this study.

**Measles, mumps, and rubella immunizations**

Rubella and measles constitute a particular threat to all pregnant women. Rubella is caused by the RNA (*Rubeola*,

*Morbili virus*) virus, with droplet route of transmission. However, the diseases may also be transmitted through contact with eye, and nasopharyngeal secretions, and through the placenta (congenital rubella). Human beings are the only reservoirs of the virus. The disease is highly contagious, with post-exposure risk ranging from 90 to 95%. The affected pregnant women present with flu-like symptoms and erythematous rash. In severe course, the disease affects the respiratory, gastrointestinal, and nervous (encephalomyelitis) systems.

In the course of rubella, the following events may develop:

- miscarriage;
- preterm labor;
- fetal demise.

Infection in the first trimester results in rubella embryopathy/congenital rubella syndrome, with the characteristic Gregg's triad (cataract, deafness, heart deformation).

In the course of congenital rubella, the following may develop:

- microcephaly;
- intellectual disability;
- intrauterine growth retardation;
- hearing impairment;
- speech impairment.

The mortality rate for rubella embryopathy has been estimated at 15% [54].

Measles is caused by the RNA virus from the *Paramyxoviridae* family, with airborne and droplet route of transmission. In most (98%) cases, the patients typically present with high fever and characteristic red, maculopapular skin eruptions. Immunocompromised and/or malnourished individuals, **pregnant women**, and children are at particularly high risk for measles-related complications and death.

**Measles, mumps, and rubella (MMR) vaccine** — at present, monovalent vaccines (against measles, against mumps, against rubella) are not available, and only a combination MMR vaccine may be administered. The MMR vaccine should be recommended to women planning for pregnancy, min. 4 weeks before conception. History of any of the three (measles, mumps, or rubella) diseases is not a contraindication to MMR vaccine.

According to the Polish National Immunization Program guidelines, the MMR vaccine is mandatory in children and recommended in adults. In case of adults, immunization is performed using a 2-dose schedule (at 0 and 1 months). If only one dose had been received earlier, the second dose needs to be administered as soon as possible. Each administered dose is counted as a valid dose, and there is no need to start the whole immunization course again.

The MMR vaccine should be recommended to women planning for pregnancy, who are seronegative and have no medical records of immunization [55].

The MMR vaccine may be safely administered to people who are in close contact with the pregnant woman (e.g., children, in accordance with the National Immunization Program guidelines). Women who are not immune to rubella should receive the vaccine after delivery, as fast as possible. Immunization with the MMR vaccine should not be delayed because of earlier administration of the anti-Rh(D) immunoglobulin or other blood preparations with antibody containing products (ACPs), administered in the third trimester or postpartum. If a woman who received the MMR vaccine had been given ACPs earlier, serologic testing after three months since immunization is required to verify her immune status.

### Varicella vaccine

Varicella is caused by the Varicella-Zoster Virus (VZV), transmitted person to person by airborne respiratory droplets. The disease is highly contagious, with post-exposure risk of infection ranging from 80 to 90%. The period of contagiousness starts two days before the rash appears and lasts until all lesions are dry and crusted (approximately 6 days).

Primary infection during pregnancy, particularly in the third trimester, is associated with a severe course of the disease, with high risk for complications such as encephalitis, pneumonia, hepatitis, and maternal death. If the infection develops until 28 weeks of gestation, it may cause the fetal varicella syndrome (FVS), with developmental disorders, low birth weight, neurological symptoms (microcephaly, hydrocephalus, encephalitis, motor and cognitive developmental disorders), bulbus oculi defects (microphthalmia, cataract, optic nerve atrophy resulting in blindness, retinitis), scar-like skin lesions, and limb hypoplasia. FVS is associated with a 25% mortality rate in the first month of neonatal life. The risk for developing FVS increases with each subsequent trimester (1<sup>st</sup> trimester — 0.7%, 2<sup>nd</sup> trimester — 2%). The highest risk for FVS is associated with maternal infection during the third trimester (5 days before delivery to 2 days postpartum). The infection may be very dangerous for the neonate due to the risk of developing multiorgan viral infection, with severe course, sepsis, and death [56, 57].

According to the Polish National Immunization Program, immunization against varicella is a recommended vaccine, which means the cost is covered by the patient. Immunization is performed using a 2-dose schedule (at 0 and 6 weeks). If only one dose had been received earlier, the second dose needs to be administered as soon as possible. Each administered dose is counted as a valid dose, and there is no need to start the whole immunization course again.

Immunization should be recommended to women who are planning for pregnancy. The whole course should be completed at least four weeks before conception. The vaccine should be recommended to women with no history of

or no medical records of earlier immunization or varicella infection. Routine serologic testing for immunity, either post-infection or post-immunization, is not recommended.

### Tuberculosis vaccine (BCG)

Tuberculosis (TB) is caused by bacteria from the *Mycobacterium tuberculosis complex* group and the disease is transmitted in airborne particles. In Poland, tuberculosis vaccine is mandatory and is administered as early as the first days of neonatal life, before the child is discharged home from the hospital. The BCG vaccine contains live attenuated bacteria and, as a preventive measure, it immunizes the host predominantly against the most severe type of tuberculosis, namely tuberculous meningitis. The vaccine is contraindicated in immunocompromised children, HIV positive individuals, patients with history of tuberculosis, children born to mothers with tuberculosis, and in pregnant women.

### HPV vaccine

Human papilloma virus (HPV) vaccine is not recommended during pregnancy, although the literature offers no reports about health threats associated with HPV immunization (recombinant vaccine) of pregnant women. Since there are no urgent indications for HPV immunization, it is not necessary to administer the vaccine to pregnant women. Immunization may be postponed until after puerperium and breastfeeding. Information found in product characteristics also indicates that these vaccines are contraindicated in pregnancy.

## ABSOLUTE CONTRAINDICATIONS TO IMMUNIZATION DURING PREGNANCY

Live attenuated and HPV vaccines are contraindicated during pregnancy. Regardless, as there are exceptions to every rule, live attenuated vaccines maybe administered during pregnancy if the benefits significantly outweigh the risks, e.g., an anthrax vaccine in case of a bioterrorist attack or yellow fever vaccine if travel to an endemic region is absolutely necessary and the risk for contracting the disease is very high.

Permanent contraindications to immunization during pregnancy include:

- history of severe allergic response to previous dose;
- allergic reaction (anaphylaxis level) to any of the vaccine components.

Temporary contraindications to immunization include:

- exacerbation of a chronic disease;
- presentation with symptoms of an acute infection.

Moreover, administration of anti-Rh-D immunoglobulin is not a contraindication to immunization with inactivated and attenuated vaccines.

## CONCLUSIONS

Immunization during pregnancy is an effective method of preventing the development of infectious diseases in the mother and the fetus/neonate, but so far that tool has not been used to its potential. It is vital to provide women, planning for pregnancy or pregnant, with reliable, evidence-based medicine (EBM) information about the benefits of immunization. In the course of obstetric care, it is necessary to emphasize the safety of the recommended vaccines, both for the mother and the child, and present the rationale behind immunization during pregnancy.

Since studies about adverse events following immunization confirmed the safety of using the vaccines in question during pregnancy, all women planning for pregnancy, pregnant, and breastfeeding should be routinely informed about the benefits of immunization against influenza, pertussis, and COVID-19. Vaccines which contain live attenuated virus or bacteria should be used in women planning for pregnancy or those who already delivered. Vaccines against hepatitis A and B, pneumococcal and meningococcal disease as well as poliovirus may be administered to pregnant women at high risk or in special circumstances (unfavorable epidemiological situation).

As the benefits of immunizing reproductive-age women, planning for pregnancy or pregnant, are unquestionable, further efforts to educate the general public about immunization are necessary.

**Obstetricians, gynecologists, general physicians, and vaccinologists should inform, educate, and encourage women with reproductive plans, as well as pregnant and/or breastfeeding women, to receive the vaccines which are recommended for the preconception and pregnancy period.**

## Article information and declarations

### Conflict of interest

All authors declare no conflict of interest.

## REFERENCES

- Castillo E, Patey A, MacDonald N. Vaccination in pregnancy: Challenges and evidence-based solutions. *Best Pract Res Clin Obstet Gynaecol.* 2021; 76: 83–95, doi: [10.1016/j.bpobgyn.2021.03.008](https://doi.org/10.1016/j.bpobgyn.2021.03.008), indexed in Pubmed: [34090801](https://pubmed.ncbi.nlm.nih.gov/34090801/).
- Sebghati M, Khalil A. Uptake of vaccination in pregnancy. *Best Pract Res Clin Obstet Gynaecol.* 2021; 76: 53–65, doi: [10.1016/j.bpobgyn.2021.03.007](https://doi.org/10.1016/j.bpobgyn.2021.03.007), indexed in Pubmed: [33965331](https://pubmed.ncbi.nlm.nih.gov/33965331/).
- Jagielska A, Jasik, Nitsch-Osuch A. Lekarze rodzinni w Polsce wobec szczepienia kobiet w ciąży - podstawy i praktyka. <https://www.mp.pl/szczepienia/szczepienia/szczepionki/grupyryzyka/ciaza/190836>, lekarze-rodzinni-w-polsce-wobec-szczepienia-kobiet-w-ciazy.
- Singh T, Otero CE, Li K, et al. Vaccines for Perinatal and Congenital Infections-How Close Are We? *Front Pediatr.* 2020; 8: 569, doi: [10.3389/fped.2020.00569](https://doi.org/10.3389/fped.2020.00569), indexed in Pubmed: [33384972](https://pubmed.ncbi.nlm.nih.gov/33384972/).
- Etti M, Calvert A, Galiza E, et al. Maternal vaccination: a review of current evidence and recommendations. *Am J Obstet Gynecol.* 2022; 226(4): 459–474, doi: [10.1016/j.ajog.2021.10.041](https://doi.org/10.1016/j.ajog.2021.10.041), indexed in Pubmed: [34774821](https://pubmed.ncbi.nlm.nih.gov/34774821/).
- Badell ML. Hepatitis B: Time to Evaluate Universal Screening and Vaccination in Pregnancy? *Obstet Gynecol.* 2022; 139(3): 355–356, doi: [10.1097/AOG.0000000000004694](https://doi.org/10.1097/AOG.0000000000004694), indexed in Pubmed: [35119420](https://pubmed.ncbi.nlm.nih.gov/35119420/).
- Sandmann F, Jit M, Andrews N, et al. Evaluating the impact of a continued maternal pertussis immunisation programme in England: A modelling study and cost-effectiveness analysis. *Vaccine.* 2021; 39(32): 4500–4509, doi: [10.1016/j.vaccine.2021.06.042](https://doi.org/10.1016/j.vaccine.2021.06.042), indexed in Pubmed: [34183204](https://pubmed.ncbi.nlm.nih.gov/34183204/).
- Abdullahi H, Elnahas A, Konje JC. Seasonal influenza during pregnancy. *Eur J Obstet Gynecol Reprod Biol.* 2021; 258: 235–239, doi: [10.1016/j.ejogrb.2021.01.005](https://doi.org/10.1016/j.ejogrb.2021.01.005), indexed in Pubmed: [33476926](https://pubmed.ncbi.nlm.nih.gov/33476926/).
- Nypaver C, Dehlinger C, Carter C. Influenza and Influenza Vaccine: A Review. *J Midwifery Womens Health.* 2021; 66(1): 45–53, doi: [10.1111/jmwh.13203](https://doi.org/10.1111/jmwh.13203), indexed in Pubmed: [33522695](https://pubmed.ncbi.nlm.nih.gov/33522695/).
- Gunnes N, Gjessing HK, Bakken IJ, et al. Seasonal and pandemic influenza during pregnancy and risk of fetal death: A Norwegian registry-based cohort study. *Eur J Epidemiol.* 2020; 35(4): 371–379, doi: [10.1007/s10654-020-00600-z](https://doi.org/10.1007/s10654-020-00600-z), indexed in Pubmed: [31950373](https://pubmed.ncbi.nlm.nih.gov/31950373/).
- Adeyanju GC, Engel E, Koch L, et al. Determinants of influenza vaccine hesitancy among pregnant women in Europe: a systematic review. *Eur J Med Res.* 2021; 26(1): 116, doi: [10.1186/s40001-021-00584-w](https://doi.org/10.1186/s40001-021-00584-w), indexed in Pubmed: [34583779](https://pubmed.ncbi.nlm.nih.gov/34583779/).
- Jash S, Sharma S. Pathogenic Infections during Pregnancy and the Consequences for Fetal Brain Development. *Pathogens.* 2022; 11(2), doi: [10.3390/pathogens11020193](https://doi.org/10.3390/pathogens11020193), indexed in Pubmed: [35215136](https://pubmed.ncbi.nlm.nih.gov/35215136/).
- Raut S, Apte A, Srinivasan M, et al. Determinants of maternal influenza vaccination in the context of low- and middle-income countries: A systematic review. *PLoS One.* 2022; 17(1): e0262871, doi: [10.1371/journal.pone.0262871](https://doi.org/10.1371/journal.pone.0262871), indexed in Pubmed: [35081138](https://pubmed.ncbi.nlm.nih.gov/35081138/).
- Baïssas T, Boisnard F, Cuesta Esteve I, et al. Vaccination in pregnancy against pertussis and seasonal influenza: key learnings and components from high-performing vaccine programmes in three countries: the United Kingdom, the United States and Spain. *BMC Public Health.* 2021; 21(1): 2182, doi: [10.1186/s12889-021-12198-2](https://doi.org/10.1186/s12889-021-12198-2), indexed in Pubmed: [34844567](https://pubmed.ncbi.nlm.nih.gov/34844567/).
- Antczak A, Kuchar E, Nitsch-Osuch A, et al. Stanowisko Ekspertów Ogólnopolskiego Programu Zwalczenia Grypy oraz Polskiego Towarzystwa Ginekologów i Położników dotyczące szczepienia przeciw grypie kobiet w ciąży. *Ginekologia i Perinatologia Praktyczna.* 2020; 5(3): 112–118.
- Alhendyani F, Jolly K, Jones LL. Views and experiences of maternal healthcare providers regarding influenza vaccine during pregnancy globally: A systematic review and qualitative evidence synthesis. *PLoS One.* 2022; 17(2): e0263234, doi: [10.1371/journal.pone.0263234](https://doi.org/10.1371/journal.pone.0263234), indexed in Pubmed: [35143531](https://pubmed.ncbi.nlm.nih.gov/35143531/).
- Morales KF, Menning L, Lambach P. The faces of influenza vaccine recommendation: A Literature review of the determinants and barriers to health providers' recommendation of influenza vaccine in pregnancy. *Vaccine.* 2020; 38(31): 4805–4815, doi: [10.1016/j.vaccine.2020.04.033](https://doi.org/10.1016/j.vaccine.2020.04.033), indexed in Pubmed: [32499068](https://pubmed.ncbi.nlm.nih.gov/32499068/).
- Offeddu V, Tam CC, Yong TT, et al. Coverage and determinants of influenza vaccine among pregnant women: a cross-sectional study. *BMC Public Health.* 2019; 19(1): 890, doi: [10.1186/s12889-019-7172-8](https://doi.org/10.1186/s12889-019-7172-8), indexed in Pubmed: [31277611](https://pubmed.ncbi.nlm.nih.gov/31277611/).
- Nitsch-Osuch A, Woźniak Kosek A, Brydak LB. [Vaccination against influenza in pregnant women - safety and effectiveness]. *Ginekol Pol.* 2013; 84(1): 56–61, doi: [10.17772/gp/1541](https://doi.org/10.17772/gp/1541), indexed in Pubmed: [23488311](https://pubmed.ncbi.nlm.nih.gov/23488311/).
- Macías Saint-Gerons D, Solà Arnau I, De Mucio B, et al. Adverse events associated with the use of recommended vaccines during pregnancy: An overview of systematic reviews. *Vaccine.* 2021; 39 Suppl 2: B12–B26, doi: [10.1016/j.vaccine.2020.07.048](https://doi.org/10.1016/j.vaccine.2020.07.048), indexed in Pubmed: [32972737](https://pubmed.ncbi.nlm.nih.gov/32972737/).
- Regan AK, Munoz FM. Efficacy and safety of influenza vaccination during pregnancy: realizing the potential of maternal influenza immunization. *Expert Rev Vaccines.* 2021; 20(6): 649–660, doi: [10.1080/14760584.2021.1915138](https://doi.org/10.1080/14760584.2021.1915138), indexed in Pubmed: [33832397](https://pubmed.ncbi.nlm.nih.gov/33832397/).
- Lu QC, Zhang TY, Bundhun PK, et al. One “misunderstood” health issue: demonstrating and communicating the safety of influenza a vaccination in pregnancy: a systematic review and meta-analysis. *BMC Public Health.* 2021; 21(1): 703, doi: [10.1186/s12889-021-10740-w](https://doi.org/10.1186/s12889-021-10740-w), indexed in Pubmed: [33836695](https://pubmed.ncbi.nlm.nih.gov/33836695/).
- Moro P, Baumblatt J, Lewis P, et al. Surveillance of Adverse Events After Seasonal Influenza Vaccination in Pregnant Women and Their Infants in the Vaccine Adverse Event Reporting System, July 2010–May 2016. *Drug Saf.* 2017; 40(2): 145–152, doi: [10.1007/s40264-016-0482-1](https://doi.org/10.1007/s40264-016-0482-1), indexed in Pubmed: [27988883](https://pubmed.ncbi.nlm.nih.gov/27988883/).

24. Zaman K, Roy E, Arifeen SE, et al. Effectiveness of maternal influenza immunization in mothers and infants. *N Engl J Med.* 2008; 359(15): 1555–1564, doi: [10.1056/NEJMoa0708630](https://doi.org/10.1056/NEJMoa0708630), indexed in Pubmed: 18799552.
25. Benowitz I, Esposito DB, Gracey KD, et al. Influenza vaccine given to pregnant women reduces hospitalization due to influenza in their infants. *Clin Infect Dis.* 2010; 51(12): 1355–1361, doi: [10.1086/657309](https://doi.org/10.1086/657309), indexed in Pubmed: 21058908.
26. <https://www.ecdc.europa.eu/en/pertussis>.
27. Stefanoff P, Paradowska-Stankiewicz IA, Lipke M, et al. Incidence of pertussis in patients of general practitioners in Poland. *Epidemiol Infect.* 2014; 142(4): 714–723, doi: [10.1017/S0950268813001684](https://doi.org/10.1017/S0950268813001684), indexed in Pubmed: 23870166.
28. Berbers G, van Gageldonk P, Kasstelee Jv, et al. Serosurveillance Study Team. Circulation of pertussis and poor protection against diphtheria among middle-aged adults in 18 European countries. *Nat Commun.* 2021; 12(1): 2871, doi: [10.1038/s41467-021-23114-y](https://doi.org/10.1038/s41467-021-23114-y), indexed in Pubmed: 34001895.
29. Tessier E, Campbell H, Ribeiro S, et al. Impact of Extending the Timing of Maternal Pertussis Vaccination on Hospitalized Infant Pertussis in England, 2014–2018. *Clin Infect Dis.* 2021; 73(9): e2502–e2508, doi: [10.1093/cid/ciaa836](https://doi.org/10.1093/cid/ciaa836), indexed in Pubmed: 32569365.
30. Khodr ZG, Bukowski AT, Gumbs GR, et al. Tetanus, diphtheria, and acellular pertussis vaccination during pregnancy and reduced risk of infant acute respiratory infections. *Vaccine.* 2017; 35(42): 5603–5610, doi: [10.1016/j.vaccine.2017.08.041](https://doi.org/10.1016/j.vaccine.2017.08.041), indexed in Pubmed: 28916245.
31. Shakib JH, Korgenski K, Sheng X, et al. Tetanus, diphtheria, acellular pertussis vaccine during pregnancy: pregnancy and infant health outcomes. *J Pediatr.* 2013; 163(5): 1422–6.e1, doi: [10.1016/j.jpeds.2013.06.021](https://doi.org/10.1016/j.jpeds.2013.06.021), indexed in Pubmed: 23896191.
32. Vygen-Bonnet S, Hellenbrand W, Garbe E, et al. Safety and effectiveness of acellular pertussis vaccination during pregnancy: a systematic review. *BMC Infect Dis.* 2020; 20(1): 136, doi: [10.1186/s12879-020-4824-3](https://doi.org/10.1186/s12879-020-4824-3), indexed in Pubmed: 32054444.
33. Becerra-Culqui TA, Getahun D, Chiu V, et al. Prenatal Tetanus, Diphtheria, Acellular Pertussis Vaccination and Autism Spectrum Disorder. *Pediatrics.* 2018; 142(3), doi: [10.1542/peds.2018-0120](https://doi.org/10.1542/peds.2018-0120), indexed in Pubmed: 30104424.
34. Becerra-Culqui TA, Getahun D, Chiu V, et al. The Association of Prenatal Tetanus, Diphtheria, and Acellular Pertussis (Tdap) Vaccination With Attention-Deficit/Hyperactivity Disorder. *Am J Epidemiol.* 2020; 189(10): 1163–1172, doi: [10.1093/aje/kwaa074](https://doi.org/10.1093/aje/kwaa074), indexed in Pubmed: 32378703.
35. DeSilva M, Vazquez-Benitez G, Nordin JD, et al. Maternal Tdap vaccination and risk of infant morbidity. *Vaccine.* 2017; 35(29): 3655–3660, doi: [10.1016/j.vaccine.2017.05.041](https://doi.org/10.1016/j.vaccine.2017.05.041), indexed in Pubmed: 28552511.
36. Griffin JB, Yu L, Watson D, et al. Pertussis Immunisation in Pregnancy Safety (PIPS) Study: A retrospective cohort study of safety outcomes in pregnant women vaccinated with Tdap vaccine. *Vaccine.* 2018; 36(34): 5173–5179, doi: [10.1016/j.vaccine.2018.07.011](https://doi.org/10.1016/j.vaccine.2018.07.011), indexed in Pubmed: 30031662.
37. Kharbanda EO, Vazquez-Benitez G, Lipkind HS, et al. Evaluation of the association of maternal pertussis vaccination with obstetric events and birth outcomes. *JAMA.* 2014; 312(18): 1897–1904, doi: [10.1001/jama.2014.14825](https://doi.org/10.1001/jama.2014.14825), indexed in Pubmed: 25387187.
38. Layton JB, Butler AM, Li D, et al. Prenatal Tdap immunization and risk of maternal and newborn adverse events. *Vaccine.* 2017; 35(33): 4072–4078, doi: [10.1016/j.vaccine.2017.06.071](https://doi.org/10.1016/j.vaccine.2017.06.071), indexed in Pubmed: 28669620.
39. Kalafat E, Heath P, Prasad S, et al. COVID-19 vaccination in pregnancy. *Am J Obstet Gynecol.* 2022; 227(2): 136–147, doi: [10.1016/j.ajog.2022.05.020](https://doi.org/10.1016/j.ajog.2022.05.020).
40. Vitiello A, Ferrara F, Zovi A, et al. Pregnancy and COVID-19, focus on vaccine and pharmacological treatment. *J Reprod Immunol.* 2022; 151: 103630, doi: [10.1016/j.jri.2022.103630](https://doi.org/10.1016/j.jri.2022.103630), indexed in Pubmed: 35483212.
41. Prasad S, Kalafat E, Blakey H, et al. Systematic review and meta-analysis of the effectiveness and perinatal outcomes of COVID-19 vaccination in pregnancy. *Nat Commun.* 2022; 13(1): 2414, doi: [10.1038/s41467-022-30052-w](https://doi.org/10.1038/s41467-022-30052-w), indexed in Pubmed: 35538060.
42. Male V. SARS-CoV-2 infection and COVID-19 vaccination in pregnancy. *Nat Rev Immunol.* 2022; 22(5): 277–282, doi: [10.1038/s41577-022-00703-6](https://doi.org/10.1038/s41577-022-00703-6), indexed in Pubmed: 35304596.
43. Pietrasanta C, Ronchi A, Crippa BL, et al. Coronavirus Disease 2019 Vaccination During Pregnancy and Breastfeeding: A Review of Evidence and Current Recommendations in Europe, North America, and Australasia. *Front Pediatr.* 2022; 10: 883953, doi: [10.3389/fped.2022.883953](https://doi.org/10.3389/fped.2022.883953), indexed in Pubmed: 35573944.
44. Shimabukuro TT, Kim SY, Myers TR, et al. CDC v-safe COVID-19 Pregnancy Registry Team. Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. *N Engl J Med.* 2021; 384(24): 2273–2282, doi: [10.1056/NEJMoa2104983](https://doi.org/10.1056/NEJMoa2104983), indexed in Pubmed: 33882218.
45. Falsaperla R, Leone G, Familiari M, et al. COVID-19 vaccination in pregnant and lactating women: a systematic review. *Expert Rev Vaccines.* 2021; 20(12): 1619–1628, doi: [10.1080/14760584.2021.1986390](https://doi.org/10.1080/14760584.2021.1986390), indexed in Pubmed: 34592123.
46. Fu W, Sivajohan B, McClymont E, et al. Systematic review of the safety, immunogenicity, and effectiveness of COVID-19 vaccines in pregnant and lactating individuals and their infants. *Int J Gynaecol Obstet.* 2022; 156(3): 406–417, doi: [10.1002/ijgo.14008](https://doi.org/10.1002/ijgo.14008), indexed in Pubmed: 34735722.
47. Moro PL, Museru OI, Niu M, et al. Reports to the Vaccine Adverse Event Reporting System after hepatitis A and hepatitis AB vaccines in pregnant women. *Am J Obstet Gynecol.* 2014; 210(6): 561.e1–561.e6, doi: [10.1016/j.ajog.2013.12.036](https://doi.org/10.1016/j.ajog.2013.12.036), indexed in Pubmed: 24378675.
48. D'Acromont V, Tremblay S, Genton B. Impact of vaccines given during pregnancy on the offspring of women consulting a travel clinic: a longitudinal study. *J Travel Med.* 2008; 15(2): 77–81, doi: [10.1111/j.1708-8305.2007.00175.x](https://doi.org/10.1111/j.1708-8305.2007.00175.x), indexed in Pubmed: 18346239.
49. Prabhu M, Susich MK, Packer CH, et al. Universal Hepatitis B Antibody Screening and Vaccination in Pregnancy: A Cost-Effectiveness Analysis. *Obstet Gynecol.* 2022; 139(3): 357–367, doi: [10.1097/AOG.0000000000004652](https://doi.org/10.1097/AOG.0000000000004652), indexed in Pubmed: 35115449.
50. Sangkomkarn US, Lumbiganon P, Laopaiboon M, et al. Hepatitis B vaccination during pregnancy for preventing infant infection. *Cochrane Database Syst Rev.* 2011; 2014(3): CD007879, doi: [10.1002/14651858.CD007879.pub2](https://doi.org/10.1002/14651858.CD007879.pub2), indexed in Pubmed: 21412913.
51. Centers for Disease Control and Prevention. Pregnancy guidelines and recommendations by vaccine. 2016. <https://www.cdc.gov/vaccines/pregnancy/hcp-toolkit/guidelines>.
52. Arora M, Lakshmi R. Vaccines - safety in pregnancy. *Best Pract Res Clin Obstet Gynaecol.* 2021; 76: 23–40, doi: [10.1016/j.bpobgyn.2021.02.002](https://doi.org/10.1016/j.bpobgyn.2021.02.002), indexed in Pubmed: 33773923.
53. Zhang Y, Zhang H, Wang B, et al. Pregnancy outcomes after a mass vaccination campaign with an oral cholera vaccine: a systematic review and meta-analysis. *BJOG.* 2020; 127(9): 1066–1073, doi: [10.1111/1471-0528.16260](https://doi.org/10.1111/1471-0528.16260), indexed in Pubmed: 32289871.
54. Terracciano E, Amadori F, Pettinicchio V, et al. Strategies for elimination of rubella in pregnancy and of congenital rubella syndrome in high and upper-middle income countries. *J Prev Med Hyg.* 2020; 61(1): E98–E9E108, doi: [10.15167/2421-4248/jpmh2020.61.1.1310](https://doi.org/10.15167/2421-4248/jpmh2020.61.1.1310), indexed in Pubmed: 32490275.
55. Mangtani P, Evans SJW, Lange B, et al. Safety profile of rubella vaccine administered to pregnant women: A systematic review of pregnancy related adverse events following immunisation, including congenital rubella syndrome and congenital rubella infection in the foetus or infant. *Vaccine.* 2020; 38(5): 963–978, doi: [10.1016/j.vaccine.2019.11.070](https://doi.org/10.1016/j.vaccine.2019.11.070), indexed in Pubmed: 31839467.
56. Nanthakumar MP, Sood A, Ahmed M, et al. Varicella Zoster in pregnancy. *Eur J Obstet Gynecol Reprod Biol.* 2021; 258: 283–287, doi: [10.1016/j.ejogrb.2021.01.009](https://doi.org/10.1016/j.ejogrb.2021.01.009), indexed in Pubmed: 33494028.
57. Gnann JW. Varicella-zoster virus: Prevention through vaccination. *Clin Obstet Gynecol.* 2012; 55(2): 560–570, doi: [10.1097/GRF.0b013e3182510b67](https://doi.org/10.1097/GRF.0b013e3182510b67), indexed in Pubmed: 22510639.