

## VACCINATION IN PREGNANCY – CHALLENGES AND NOVELTIES

### VAKINACIJA U TRUDNOĆI – NOVINE I IZAZOVI

Bojana Ivić<sup>1</sup>, Ivana Filipović<sup>2</sup>, Slađana Mihajlović<sup>2,3</sup>

<sup>1</sup>Gynecology and Obstetrics Clinic Narodni Front, Belgrade, Serbia

<sup>2</sup>Clinical Hospital Center "Dr Dragiša Mišović", Hospital for Gynecology and Obstetrics, Belgrade, Serbia

<sup>3</sup>University of Belgrade, Faculty of Medicine, Belgrade, Serbia

ORCID iD: Bojana Ivić <https://orcid.org/0009-0006-2346-5152>  
Ivana Filipović <https://orcid.org/0000-0003-1042-6411>  
Slađana Mihajlović <https://orcid.org/0000-0002-9013-0401>

**Summary** Vaccines are the most effective way to prevent infectious diseases. Immunization is a key component of primary healthcare. Maternal immunization before and/or during the pregnancy proves to significantly reduce maternal and infant morbidity and mortality associated with the diseases caused by pathogens that are relevant to the perinatal period and early life, and for which there are currently no other effective alternative preventive measures. Women can be vaccinated before or during the pregnancy to protect themselves and pass immunity directly to their babies. The mother's immune system in pregnancy plays a key role in the development of child's immunity. Therefore it is important to explore this area that presents a challenge for decision-making regarding how, when, and why vaccinate women in a reproductive period.

**Keywords:** vaccination, pregnancy, newborn

**Sažetak** Vakcine su najefikasniji način za sprečavanje zaraznih bolesti. Imunizacija je ključna komponenta primarne zdravstvene zaštite. Majčina imunizacija pre i/ili tokom trudnoće značajno smanjuje morbiditet i mortalitet majki i odojčadi povezan sa bolestima uzrokovanim patogenima koji su relevantni za perinatalni period i rani život, a za koje trenutno ne postoje druge efikasne alternativne preventivne mere. Žene se mogu vakcinisati pre ili tokom trudnoće kako bi se zaštitile i direktno prenele imunitet na svoje bebe. Majčin imuni sistem u trudnoći igra ključnu ulogu u razvoju imuniteta deteta. Stoga je važno istražiti ovu oblast koja predstavlja izazov za donošenje odluka o tome kako, kada i zašto vakcinisati žene u reproduktivnom periodu.

**Ključne reči:** vakcinacija, trudnoća, novorođenče

Vaccines are the most effective way to prevent infectious diseases. Immunization is a key component of primary healthcare. Vaccines are crucial to prevent and control infectious-disease outbreaks and are able to save up to 2-3 million lives every year. Many infectious diseases, previously prevalent, are increasingly rare thanks to vaccination, and some of these communicable diseases, such as smallpox and polio, have been almost eradicated (1,2). Currently vaccines are available to prevent more than 20 life-threatening diseases. The key value of the vaccines is the protection of not only vaccinated but unvaccinated subjects as well. Global vaccination provides a "herd immunity" to those vulnerable groups that are not able to get vaccinated. "Herd immunity" occurs when a high percentage of the population is protected against a virus or bacteria through the vaccination, making it difficult for a disease to spread and is yet another example of the unique public health benefits of vaccination. Vaccination protects lives at every stage of life from newborns to elderly (3,4).

### SPECIAL CONSIDERATION OF VACCINATION DURING PREGNANCY

Maternal immunization before and/or during the pregnancy proves to significantly reduce maternal and infant morbidity and mortality associated with the diseases caused by pathogens that are relevant to the perinatal period and early life, and for which there are currently no other effective alternative preventive measures (5).

Due to physiological changes in maternal immunity, pregnant women should be considered as a particularly vulnerable group, susceptible to a great variety of viral and bacterial pathogens. Infections in pregnancy are potentially dangerous for both the mother and the fetus, and some infections have been linked with adverse perinatal outcomes and congenital malformations such as in the case of measles, mumps, and rubella. Vaccination against pertussis and influenza during pregnancy is of great importance, as maternal protective antibodies provide early short-term protection for their children who are particularly at risk to those infections. On the other side newborns are particularly vulnerable to infectious diseases themselves (6).

The neonatal immune milieu is deferent to those seen in older children and adults. The main characteristics is predominance of Th2-immune response upon Th1 immunity. These adaptations prevent alloimmune reactions between mother and fetus, enable microbial colonisation and avoid excess pro-inflammatory responses. Contrary those specificity of neonatal immune response make them more vulnerable to different viral and bacterial infection (7). Neonatal and infants immune system is also characterized by the presence of IgG antibodies. They are transferred from mothers to their newborns from 13 weeks of pregnancy and increase until the end of the third trimester. IgA antibodies are available from the breastfeeding (8). On the other side, pregnant women are considered a special population group due to a change in the status of the immune system caused by pregnancy. The mother's immune system in pregnancy plays a key role in the development of

child's immunity. Therefore it is important to explore this area that presents a challenge for decision-making regarding how, when, and why vaccinate women in a reproductive period.

### The Best Timing for Vaccination

Women can be vaccinated before or during the pregnancy to protect themselves and pass immunity directly to their babies (8,9). Newborns cannot be vaccinated against whooping cough in the first two months of life while they are at the highest risk of *Bordetella pertussis* infections. Flu vaccination during pregnancy can reduce the chances of newborns to develop influenza, as they are in the first six months of life too young to be vaccinated against flu.

The best timing for vaccination is the preconception period particularly to prevent serious diseases during pregnancy such as hepatitis A, hepatitis B, human papillomaviruses (HPV), influenza, measles, mumps and rubella (MMR), meningococcal disease, invasive pneumococcal disease, tetanus, diphtheria, and pertussis. For pregnant women who plan to travel, Japanese encephalitis, typhoid and yellow fever vaccines should be also considered (9,10). Timely and appropriate vaccine administration during pregnancy provides protection for the mother, for the fetus, and in some cases for the newborn as well. However, the administration of several vaccines simultaneously is contraindicated during pregnancy if the risks of vaccination outweigh any possible benefits, but immunization with certain vaccines may be acceptable under specific clinical situations. Several factors should be considered before deciding to vaccinate pregnant women and the cost-benefit balance should be evaluated individually according to potential risks and benefits. Pregnant women should be always vaccinated when infections impose a risk to mother and/or fetus, and when the vaccine is unlikely to cause any serious side effects to both of them. Pregnant women can be vaccinated safely with inactivated virus or bacterial vaccines or toxoids. The risk to a developing fetus damage related to vaccination of the mother during pregnancy is theoretical. Viral or bacterial live attenuated vaccines are generally contraindicated during the pregnancy, unless the risk of infections is greater than the risk of the vaccination. If the case of a high risk of infections, it is highly recommended to vaccinate women during the preterm period. Vaccination against MMR (measles, mumps, and rubella)\*\* before pregnancy will provide protection to both mother and newborns, but it is also important when taking into consideration that rubella can cause severe congenital malformation with lifelong consequences (11).

### Immune Response to Vaccines during the Pregnancy

Several factors could influence the efficiency of IgG transcytosis, including gestation, IgG sub-class, and maternal infection. Therefore, it is very difficult to determine the optimal timing for vaccination during pregnancy. The concentration of fetal IgG in the late second and early third trimester is 25%–50% lower than the end of the third trimester. According to the published studies, later vaccination at 28–32 weeks of pregnancy provides the greatest protection to the infant. In line with that, preterm newborns have a lower level of IgG antibodies in comparison to term newborns. Decision should be considered individually to provide a wide window of opportunity (9). The efficacy of immune response towards vaccines is determined by the vaccine type. Four subclasses of IgG

antibodies are transformed across the placenta with different efficiency, with IgG1 being found in the highest concentration in cord blood, followed by IgG4, IgG3, and IgG2 (10). For instance, maternal immunization with polysaccharide vaccine, inducing predominately IgG2 and offer less protection against infections in comparison with a protein-conjugated vaccine, which elicits predominately IgG1 and IgG3. Secretory IgAs (sIgA) are thought to protect against diarrheal and respiratory pathogens through a variety of mechanisms, including immobilization, prevention of adhesion, or neutralization of toxins or virulence factors. Numerous clinical trials have identified significantly higher vaccine-specific sIgA in the breast milk of women vaccinated in the third trimester of pregnancy compared with unvaccinated women. These antibodies appear long-lived with elevated sIgA in the breast milk measured up to 7 months postpartum. As maternal vaccination strategies develop, it will be important to monitor the potential effects of vaccination on the composition of the breast milk; concerns have been raised about the potential blunting of infant immune responses to live oral vaccines from high breast milk sIgA; however further re-search is required to confirm these findings and understand the clinical implications (11–13).

### VACCINATION IN PREGNANCY

Since the early 19<sup>th</sup> century, vaccination in pregnancy has been observed to protect both mothers and newborns against smallpox, tetanus, and pertussis. Recently, the influenza pandemic in 2009 has raised the awareness of the importance of vaccination against influenza among pregnant women (14). One of the guidelines dealing with recommendations on the use of vaccines in pregnancy is the Advisory Committee on Immunization Practices (ACIP) from the United States of America. A group of experts from ACIP recommended that all pregnant women should be vaccinated with an inactivated influenza vaccine, inactive toxoid tetanus vaccine and pertussis. Pregnancy is not a contraindication or precaution to vaccination of Tetanus-diphtheria (Td), Hepatitis B, Meningococcal polysaccharide and routine vaccination should be applied to pregnant women. Vaccination using Hepatitis A vaccine, Inactivated polio vaccine (IPV), or yellow fever vaccine (in case of travel to an area where exposure is likely), rabies vaccine (eg, after possible exposure) should be deferred and the vaccine should only be given when benefits outweigh risks. Vaccines such as Measles, Mumps and Rubella MMR, varicella vaccine, and live-attenuated influenza vaccine should not be administered to pregnant women (15,16).

### References

1. <https://www.who.int/news-room/fact-sheets/detail/immunization-coverage> (last accessed 08.02.2026)
2. <https://vaccineknowledge.ox.ac.uk/herd-immunity> (last accesses 08.02.2026)
3. Psarris A, Sindos M, Daskalakis G, Chondrogianni ME, Panayiotou S, Antsaklis P, Loutradis D. Immunizations during pregnancy: How, when and why. *Eur J Obstet Gynecol Reprod Biol.* 2019;240:29–35. doi: 10.1016/j.ejogrb.2019.06.019
4. Kollmann TR, Marchant A, Way SS. Vaccination strategies to enhance immunity in neonates. *Science.* 2020;368(6491):612–615. doi: 10.1126/science.aaz9447
5. Morein B, Abusugra I, Blomqvist G. Immunity in neonates. *Vet Immunol Immunopathol.* 2002;87(3–4):207–213. doi: 10.1016/s0165-2427(02)00078-8
6. Lacković M, Mihajlović S, Bakić T, Marina Lj, Stefan Šojat A, Ilić A, Rovčanin M, F Mošković F, Filipović I. Imunski sistem u trudnoći. *Prev Ped.* 2020; 6(1–2): 37–40

7. Munoz FM, Jamieson DJ. Maternal Immunization. *Obstet Gynecol.* 2019;133(4):739-753. doi: 10.1097/AOG.0000000000003161
8. Pellegrini C, McCabe ER. Maternal immunization at the crossroads. *Vaccine.* 2015;33(47):6501-6502. doi: 10.1016/j.vaccine.2015.06.118
9. Álvarez Aldeán J, José Álvarez García F, de la Calle Fernández-Miranda M, Figueras Falcón T, Iofrio de Arce A, López Rojano M, Rivero Calle I, Suy Franch A. Vaccination in pregnancy. Consensus document of the CAV-AEP and the SEGO. *An Pediatr (Engl Ed).* 2024;100(4):268-274. doi: 10.1016/j.anpede.2024.02.014
10. Sealey KL, Belcher T, Preston A (2016) Bordetella pertussis epidemiology and evolution in the light of pertussis resurgence. *Infect Genet Evol.* 40:136–143.
11. Etti M, Calvert A, Galiza E, Lim S, Khalil A, Le Doare K, Heath PT. 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
12. Trifunović Kubat J, Sazdanović P, Mihajlović S, Filipović I, Mošković F. COVID19 kod trudnica. *Prev Ped.* 2022;8(1-2):8-11.
13. Filipović I, Živković Z, Zdjelar S, Ostojić O, Mihajlović S. Infekcija SARS CoV-2 u neonatalnom uzrastu. *Prev Ped.* 2022;8(1-2):12-15.
14. Munoz FM, Jamieson DJ. Maternal Immunization. *Obstet Gynecol.* 2019;133(4):739-753. doi: 10.1097/AOG.0000000000003161
15. Santilli V, Sgrulletti M, Costagliola G, Beni A, Mastrototaro MF, Montin D, Rizzo C, Martire B, Miraglia Del Giudice M, Moschese V; Italian Society of Pediatric Allergy and Immunology (SIAIP) Vaccine Committee. Maternal Immunization: Current Evidence, Progress, and Challenges. *Vaccines (Basel).* 2025;13(5):450. doi: 10.3390/vaccines13050450
16. Cairns A, Hogan J, Mackillop L. Vaccinations in pregnancy. *Obstet Gynaecol Reprod Med.* 2022;32(8):163-171. doi: 10.1016/j.ogrm.2022.05.001