HHS Public Access

Author manuscript

Lancet Infect Dis. Author manuscript; available in PMC 2021 June 30.

Published in final edited form as:

Lancet Infect Dis. 2016 December ; 16(12): e310–e314. doi:10.1016/S1473-3099(16)30349-8.

Maternal immunisation: ethical issues

Marcel Verweij, **Philipp Lambach**, **Justin R Ortiz**, **Andreas Reis**

Section Communication, Philosophy and Technology, Department of Social Sciences, Wageningen University, Wageningen, Netherlands (Prof M Verweij PhD); and Initiative for Vaccine Research (P Lambach PhD, J R Ortiz MD) and Global Health Ethics Unit (A Reis MD), World Health Organization, Geneva, Switzerland

Abstract

There has been increased interest in the potential of maternal immunisation to protect maternal, fetal, and infant health. Maternal tetanus vaccination is part of routine antenatal care and immunisation campaigns in many countries, and it has played an important part in the reduction of maternal and neonatal tetanus. Additional vaccines that have been recommended for routine maternal immunisation include those for influenza and pertussis, and other vaccines are being developed. Maternal immunisation is controversial since regulators, professionals, and the public are often reluctant to accept pharmaceutical interventions during pregnancy. So far, little attention has been given to the ethics of vaccination during pregnancy. In this Personal View we argue that maternal immunisation should be offered in response to concrete, severe risks of disease for mother and child, and we explain how this requirement of serious risk can be used to guide ethical decision-making about maternal immunisation.

Introduction

Infectious diseases can pose a substantial risk for pregnant women and for fetal and newborn health. Pregnancy is an immunologically altered state that can render women more susceptible to infections than they are when they are not pregnant. Regular immunisation programmes offer protection against infections, but such vaccine-induced immunity can decrease over a lifetime. As a result, many women at the time they become pregnant might not have sufficient immunity against, for example, tetanus or pertussis. Furthermore, childhood immunisation could come too late to protect newborn infants—for example, the inactivated influenza vaccine should not be given to children younger than 6 months. In some cases, maternal immunisation can fill that gap: it offers direct protection to the pregnant woman; prevents disease transmission from mother to child; and leads to passive immunity for the newborn baby if antibodies are transferred to the fetus, or, after birth, via

Correspondence to: Prof Marcel Verweij, Section Communication, Philosophy, and Technology, Department of Social Sciences, Wageningen University, Hollandseweg 1, 6706KN Wageningen, Netherlands marcel.verweij@wur.nl.

Contributors

All authors drafted the outline of the manuscript. MV wrote the first versions; PL, JRO, and AR commented, made adjustments, and specifically took care of the technical, medical, and epidemiological aspects. MV compiled comments and wrote the prefinal version. All authors contributed to the final editing of the manuscript.

Declaration of interests

We declare no competing interests.

breast milk to the infant. In this way maternal immunisation can be a key element in maternal and child health care, and it is currently practised to protect against several diseases.

Maternal tetanus immunisation is part of routine antenatal care and immunisation campaigns in many countries. It has played a major part in reducing global neonatal mortality due to tetanus, from an estimated 787 000 neonates in 1988 to 49 000 neonates in 2013.[1,2] In the 2009 H1N1 influenza pandemic, pregnant women and infants were considered to be at high risk of hospital admission and complications, and many countries offered pandemic influenza vaccinations to pregnant women to reduce those risks. In 2012, WHO considered pregnant women the most important priority group for seasonal influenza immunisation programmes.[3] Finally, in recent years, several countries have recommended maternal pertussis immunisation as the best way to protect infants before they receive their first immunisations, given that infants are particularly susceptible to pertussis during the first weeks after birth.[4,5] Vaccines against group B streptococcus and respiratory syncytial virus are under development, and might have an important role in preventing serious infections in infants in the future.[6] If an effective vaccine against Zika virus is developed, it might well have a place in antenatal care in regions with high exposure to the virus. Other vaccines, such as those for hepatitis A and B, and meningococcal vaccines, might be considered during pregnancy under special circumstances—eg, if a woman has an increased risk of exposure to infection.[7]

Vaccine safety and precautions

A central ethical concern is that any vaccination programme should have a very high standard of safety, given that it involves a preventive procedure that is carried out in healthy people, some of whom might not get exposed to the infectious agent at all.[8] Such concerns about safety are reinforced during pregnancy because adverse effects could be harmful to the health of the mother and the future child. Commonly used vaccinations during pregnancy—namely inactivated influenza, pertussis, and tetanus—have not been shown to create an increased risk of adverse effects in infants.[7,9] Live attenuated vaccines are contraindicated just before or during pregnancy, but no adverse outcomes have been reported in cases in which live attenuated vaccines were administered to pregnant women inadvertently.[10–12] Results of studies in relation to the 2009 H1N1 influenza pandemic have also shown no harmful effects of the inactivated pandemic vaccines for mother or infant.[13] Widespread use of vaccines containing tetanus toxoid and tetanus-diphtheria in many countries has not produced any sign of possible harm to pregnant women or their fetuses.[7] Although most health jurisdictions only require passive reporting of adverse events following immunisation, and evidence about side-effects is limited, there is little reason to question the safety of these vaccinations during pregnancy.

Nevertheless, there is general reluctance towards pharmaceutical interventions during pregnancy, and regulators, researchers, and pharmaceutical companies often see pregnancy as an exclusion criterion in clinical trials. As a result, there is a lack of detailed evidence about the benefits and risks during pregnancy of otherwise widely accepted pharmaceutical interventions. Moreover, in clinical practice, regulators, health professionals, and pregnant

women tend to take the same precautionary approach to using medicines—including vaccinations—during pregnancy, which partly explains the relatively low vaccine uptake in some programmes for maternal immunisation in high-income countries.[14,15] This is in line with the precautionary principle, which states that if certain activities might potentially cause very serious and irreversible harm, precautionary measures are warranted, even if it is uncertain whether such harm can indeed occur.[16] Birth defects are generally considered to be a very severe harm, especially if they result from human actions or inactions. The precautionary principle might therefore offer some support for abstaining from vaccinations during pregnancy if substantial uncertainty exists about potential harmful effects of vaccination for the fetus.

As mentioned previously, there is reassuring evidence about the safety of several vaccinations during pregnancy, so decision-making concerning maternal immunisation is not necessarily a matter of dealing with uncertainty. Yet even when evidence about safety is not as decisive as one would hope, following the precautionary principle too strictly can be highly problematic, paralysing policies and inhibiting progress.[17,18] In the case of maternal and child health care, and of maternal immunisation more specifically, following the precautionary principle too strictly could mean that effective protection against a major threat will be foregone to avoid highly uncertain or rare adverse effects of vaccination. However, the risks of exposure to a specific pathogen, in specific circumstances, might well outweigh safety concerns, especially in low-income and middle-income countries where pregnant women and young children often face concrete and severe risk of infection, and where access to therapeutic care is limited. Somewhat paradoxically, the broadly accepted precautionary approach to using medicines during pregnancy could well result in increased risk rather than averted harm for women, fetuses, and neonates.[19] A responsible approach to maternal immunisation would involve weighing the magnitude of risk that can be averted by vaccination, and evidence about the safety of the vaccine in relation to fetal development. Evidence about vaccine safety can sometimes be limited, but not completely lacking. Reluctance towards preventive interventions in pregnancy makes sense, especially if the risks of infection are small, but it is unreasonable to follow a strict precautionary principle that requires a very high level of evidence about vaccine safety during pregnancy if the same principle prohibits research in pregnant women that could produce such evidence.

A more reasonable precautionary policy is to strengthen adverse event reporting systems and disease surveillance, and to ensure that maternal immunisation is only offered in response to concrete, severe risks of disease for mother and child. Rather than emphasising precautions in the face of limited uncertainty about safety, vaccination policies could indicate a minimum burden of disease or vaccine-preventable risk that justifies maternal immunisation. Such an approach would underline the importance of surveillance systems that provide evidence about the incidence of infectious diseases and the disease burden they cause in a given context.

Informed consent and voluntary participation

Informed consent is generally considered an essential element in ethically responsible health-care practices.[20] There are, however, several limitations to informed consent that

must be taken into account in the context of maternal immunisation. First, if informed consent is to enable women to make autonomous decisions about immunisation, then target groups should receive information about the goals, effectiveness, and risks and uncertainties of the vaccination, and it is assumed that they are capable of using this information to make their own choices. Women in different socioeconomic contexts and with different health-care experiences will often have very different informational needs about the disease and the safety and efficacy of the vaccine. Deliberate individual choice might be challenged by factors such as illiteracy, poor education, or lack of background information. Moreover, discussions, opinions, and statements that are easily available on the internet or within communities can include misinformation about immunisation that can lead to lack of trust in vaccination, unwarranted fear, or even refusal to be vaccinated.[21] As a result, it may also be diffi cult for health professionals to ascertain that the requirements of obtaining informed consent are met. As important as informed consent is in practice, it cannot always function to secure individual autonomy in health care.[20]

Second, it is not self-evident that public health interventions, including immunisation programmes, should satisfy the same explicit informed consent requirements that are commonly met in individual patient care or clinical trials. If vaccinations are offered in large-scale routine programmes, the possibilities of tailoring communication to each person's needs are limited. Protecting collective public health and equity might imply giving less importance to individual choice and autonomy in relation to immunisation, as happens when mandatory childhood immunisation programmes are considered necessary to secure herd protection and to protect the individual child against severe disease.[22,23] This is not to suggest that maternal immunisation programmes, likewise, should be mandatory. Mandatory maternal immunisation would involve a direct violation of a woman's right to control her own body that, arguably, can only be justified—if at all—if there is an immediate threat to her or others.[24] A topical illustration of this dilemma would occur if, in the future, a safe and effective Zika virus vaccine is licensed: should pregnant women in areas with a high Zika virus prevalence be permitted to refuse the vaccine? We would argue that in such a case, persuasive campaigns in which immunisation is offered in a routine, opting-out manner, are well justified. If women are aware of a concrete risk that their fetus could develop microcephaly or other abnormalities due to Zika virus, arguably few will opt out of immunisation. Yet compulsory vaccination of pregnant women could undermine trust in immunisation or antenatal care in general.

Some form of consent is therefore ethically desirable: women should at least understand that they are not forced to participate and have the opportunity to opt out. The possibilities of tailoring the informed consent process to each individual's informational needs and ascertaining that everyone is in the position to make an autonomous choice will be limited. Nevertheless, immunisation programmes should at least try to offer basic and reliable information about maternal immunisation to address the concerns of pregnant women as a group. Such information would ideally be tailored to the context of a particular setting.

Vaccinating mothers to protect their children

Maternal immunisation aims to protect either a pregnant woman, the fetus or infant, or both. In the case of tetanus immunisation there is a clear benefit to both mother and child. In some cases, however, maternal immunisation will offer protection against an infection that can pose a threat to the newborn child but less of one to the mother. Or it might be that there is clear evidence about a protective effect of maternal immunisation on child health, but less so in relation to maternal health. Side-effects mostly affecting pregnant women would result in an asymmetry of burdens and benefits of maternal immunisation that might be considered unfair. A related concern is the possibility that programmes focusing on neonatal health could involve an objectionably instrumental approach to maternal health, treating a woman as a "fetal container" rather than as an individual person who is to be respected in her own right.[24] Most pregnant women would endorse the goal of protecting the health of their fetus and future child, and would not object to maternal immunisation. They would see immunisation for the benefit of their child as neither unfair nor disrespectful. Yet if health professionals simply assume that pregnant women will accept immunisation for the sake of their children, they are not respecting them as individual people.

To some extent this problem is avoided by obtaining informed consent: if women understand the benefits and burdens and autonomously consent to immunisation, there are no grounds for the idea that maternal immunisation would be unfair or disrespectful. Yet, as discussed above, informed decision-making will often be difficult in this context, and consent is therefore not a panacea that resolves all problems of unfairness and instrumentalisation. Respectful, non-instrumental treatment of pregnant women is not only a matter of obtaining consent, but, first and foremost, of giving due care to their personal needs, concerns, and circumstances. Especially in low-income contexts, pregnant women face a variety of problems that affect their physical, mental, and social health. If such problems are neglected in focused programmes that emphasise the protection of newborn babies against a specific infection, it is not unreasonable for women to feel they are being treated merely as a means of promoting neonatal health. Many women worldwide only have one antenatal care visit, and provision of a new vaccine during that visit will leave less time for other important health-care needs. Ideally, maternal immunisation is integrated into comprehensive primary and perinatal care settings that offer a broad spectrum of disease prevention, health care, information, and advice to pregnant women and their families.[25,26] Local community involvement in the development, implementation, and evaluation of these programmes can ensure that priorities are set in line with local needs and values[27] so that maternal immunisation is neither unfair nor objectionably instrumental towards pregnant women.

Community involvement, trust, and integrated care

All ethical issues discussed so far support the involvement of local communities in the implementation of maternal immunisation programmes, and the integration of immunisation into primary maternal and child health care.[26,27] Active dialogue between pregnant women, health-care providers, and other relevant stakeholders in the community could enhance the receptiveness of pregnant women to vaccination, and this dialogue is necessary to take into account concerns about the necessity and safety of maternal immunisation. Taking the

perspectives of women seriously would contribute to the ethical justification and trustworthiness of the programme. Moreover, the integration of maternal immunisation into trusted primary maternal and child health services offers a stronger basis for informed consent, and for avoiding the treatment of pregnant women solely as a means of promoting newborn health. Where adequate antenatal care is lacking or weak, maternal immunisation can be implemented in vertical targeted campaigns, but these need to be shaped in ways that strengthen and do not undermine horizontal primary care services.

Additional complexities of influenza immunisation

Due to the seasonal character of influenza and the yearly changing vaccine formulations for the northern and southern hemispheres, maternal influenza immunisation faces additional technical complexities that are ethically relevant, affecting in particular low-income and middle-income countries in tropical regions. Tropical regions often have influenza seasonality that is different from seasonality in temperate regions, including extended seasons, multiple peaks of epidemics, or even year-round influenza circulation, which can require a year-round supply of maternal vaccinations. To ensure such a supply, it might be necessary to use vaccines that do not fully match the influenza strains circulating in the region at a particular time.[28] Consequently, vaccine recipients across different regions will not receive the same protection from vaccination, which might seem unfair. However, most if not all such differences are inevitable given the nature of influenza epidemiology and vaccine performance and availability. As long as there is sufficient evidence for considering influenza a serious threat to maternal and newborn health, and if decisions about which formulation to offer are based on attaining maximum protective effect with the available formulations, differential treatment is inevitable and justified. If there is a known mismatch between circulating influenza strains and the vaccine that can be offered, maternal immunisation is no longer ethically justified.

A further complication is that influenza vaccines have expiration dates that are based on the influenza seasons of the region for which they are produced. Tropical countries, however, can face year-round virus circulation, and to secure year-round immunisation sometimes the only vaccines that can be used have expired. Passing the expiration date does not mean that vaccines are unsafe or completely ineffective,[28] but it can easily lead to a misunderstanding that could undermine public trust in immunisation. The first ethical condition for immunisation is that it offers a reasonable prospect of protection against a substantial disease burden. A mismatch between an older vaccine and currently circulating influenza strains takes away the justification of immunisation. If, on the other hand, the previous season’s vaccines are expected to match at least some of the current strains in tropical countries, regulators have good moral reasons to extend the expiration date of such vaccines for those countries to promote equitable access to immunisation.

Yet another complication of maternal influenza immunisation concerns the timing of vaccination during pregnancy, which involves a compromise between maximising the protection of the mother or of the newborn baby. Vaccine delivery in the first trimester of pregnancy provides greater benefit to the mother than does vaccine delivery in the second and third trimesters, since she will be protected for a longer duration of her pregnancy.

Second or third trimester immunisation, however, will offer better protection for the infant.[28] This compromise is worsened in low-income settings where sometimes less than half of all pregnant women receive WHO-recommended minimum of four antenatal care visits.[29] If the influenza vaccine were to be delivered through antenatal care services, the functionality of the delivery system should be monitored to avoid missed opportunities for immunisation due to the unavailability of a vaccine. Where pregnant women might not be able to benefit from several antenatal care visits, it can be preferable to offer immunisation at the first—and possibly only—antenatal care visit during pregnancy, instead of aiming for higher levels of protection if vaccination were postponed to use the most recent formulation. Particularly in settings with limited access to antenatal care, immunisation can be offered as soon as pregnant women present for antenatal care, even if this is well before the peak of the influenza season.[28] These difficulties in relation to the timing of immunisation, especially in tropical middle-income and low-income countries, complicate policies that seek an optimum protective effect for mother and child. More research is desirable to further strengthen the evidentiary basis for maternal influenza immunisation in tropical regions.[30]

Conclusion

Pregnant women and newborn babies are susceptible to a range of health risks. Maternal immunisation programmes have an important role in improving maternal and child health given that, in many cases, immunisation is the most effective prevention against infectious diseases. Such programmes, however, raise a host of ethical issues that should be adequately addressed for intrinsic moral reasons but also to build and maintain trust.

Vaccinations that are commonly used during pregnancy—such as tetanus, inactivated influenza, and pertussis—have not been shown to create an increased risk of serious adverse effects, but in general some reluctance towards medical interventions in pregnancy is appropriate. This should not be a reason to follow a strict version of the precautionary principle, which would arguably reject any form of vaccination during pregnancy, but rather to ascertain that maternal immunisation is offered in response to a concrete, severe risk of disease for mother and child. Such a requirement underlines the importance of national surveillance systems that provide evidence about the incidence of vaccine-preventable infections and the disease burden among pregnant women and newborn infants. Community involvement and integration in regular antenatal care can help to prevent the diversion of attention, by maternal immunisation, from other, possibly greater health needs of pregnant women. This involvement also offers a stronger basis for informed consent and for avoiding treating pregnant women as if they are merely a means of promoting newborn health.

Acknowledgments

This study was funded by a grant from the World Health Organization’s Initiative for Vaccine Research. The authors would like to acknowledge the contributions of the Centers for Disease Control and Prevention (CDC), which provides financial support to the World Health Organization Initiative for Vaccine Research (U50 CK000431).

The authors received valuable feedback from WHO Public Health Ethics Consultation Group on a previous version of this work. PL, JRO, and AR work for WHO, but the views expressed in this publication do not necessarily represent the decisions, policy, or views of WHO.

References

1. WHO. Maternal and neonatal tetanus (MNT) elimination. 2015. http://www.who.int/immunization/diseases/MNTE_initiative/en/ (accessedDec 16, 2015).
2. Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet 2015; 385: 430–40. [PubMed: 25280870]
3. WHO Position Papers. Vaccines against influenza. Wkly Epidemiol Rec 2012; 87: 461–76.
4. Amirthalingam G, Andrews N, Campbell H, et al. Effectiveness of maternal pertussis vaccination in England: an observational study. Lancet 2014; 384: 1521–28. [PubMed: 25037990]
5. Gezondheidsraad. Vaccinatie tegen kinkhoest: doel en strategie. Den Haag: Gezondheidsraad. Report No: 2015/29. 2015. https://www.gezondheidsraad.nl/nl/taak-werkwijze/werkterrein/preventie/vaccinatie-tegen-kinkhoest-doel-en-strategie (accessed Sept 5, 2016).
6. Bassat Q Maternal immunization: An intelligent solution to reduce the hidden burden of group B streptococcus perinatal disease. J Trop Pediatr 2013; 59: 333–37. [PubMed: 24092698]
7. Keller-Stanislawski B, Englund JA, Kang G, et al. Safety of immunization during pregnancy: a review of the evidence of selected inactivated and live attenuated vaccines. Vaccine 2014; 32: 7057–64. [PubMed: 25285883]
8. Verweij M, Dawson A. Ethical principles for collective immunisation programmes. Vaccine 2004; 22: 3122–26. [PubMed: 15297064]
9. Lindsey B, Kampmann B, Jones C. Maternal immunization as a strategy to decrease susceptibility to infection in newborn infants. Curr Opin Infect Dis 2013; 26: 248–53. [PubMed: 23507974]
10. Castillo-Solórzano C, Reef SE, Morice A, et al. Rubella vaccination of unknowingly pregnant women during mass campaigns for rubella and congenital rubella syndrome elimination, the Americas 2001–2008. J Infect Dis 2011; 204 (suppl 2): S713–17. [PubMed: 21954271]
11. Moro PL, Broder K, Zheteyeva Y, et al. Adverse events in pregnant women following administration of trivalent inactivated influenza vaccine and live attenuated influenza vaccine in the Vaccine Adverse Event Reporting System, 1990–2009. Am J Obstet Gynecol 2011; 204: e1–7.
12. Nasidi A, Monath TP, Vandenberg J, et al. Yellow fever vaccination and pregnancy: a four-year prospective study. Trans R Soc Trop Med Hyg 1993; 87: 337–39. [PubMed: 8236412]
13. Pasternak B, Svanström H, Mølgaard-Nielsen D, et al. Risk of adverse fetal outcomes following administration of a pandemic influenza A(H1N1) vaccine during pregnancy. JAMA 2012; 308: 165–74. [PubMed: 22782418]
14. Yuen CYS, Tarrant M. Determinants of uptake of influenza vaccination among pregnant women—a systematic review. Vaccine 2014; 32: 4602–13. [PubMed: 24996123]
15. Wilson RJ, Paterson P, Jarrett C, Larson HJ. Understanding factors influencing vaccination acceptance during pregnancy globally: a literature review. Vaccine 2015; 33: 6420–29. [PubMed: 26320417]
16. Lewens T Taking sensible precautions. Lancet 2008; 371: 1992–93. [PubMed: 18561370]
17. Sunstein CR. Beyond the precautionary principle. Univ PA Law Rev 2003; 151: 1003–58.
18. Tubiana MConclusions. The precautionary principle: its advantages and risks. Bull Acad Natl Med 2000; 184: 969–93. [PubMed: 11077719]
19. Little MO. Treating important medical conditions during pregnancy. Enrolling pregnant women: issues in clinical research; Bethesda, MD: National Institutes of Health; 10 18, 2010: 23–26.
20. O'Neill O Some limits of informed consent. J Med Ethics 2003; 29: 4–7. [PubMed: 12569185]
21. Ruiz JB, Bell RA. Understanding vaccination resistance: vaccine search term selection bias and the valence of retrieved information. Vaccine 2014; 32: 5776–80. [PubMed: 25176640]
22. O'Neill O Informed consent and public health. Philos Trans R Soc Lond B Biol Sci 2004; 359: 1133–6. [PubMed: 15306401]
23. Nys TRV. Paternalism in public health care. Public Health Ethics 2008; 1: 64–72.
24. Purdy LM. Are pregnant women fetal containers? Bioethics 1990; 4: 273–91. [PubMed: 11649272]
25. Bhutta ZA, Black RE. Global maternal, newborn, and child health—so near and yet so far. N Engl J Med 2013; 369: 2226–35. [PubMed: 24304052]

26. Ekman B, Pathmanathan I, Liljestrand J. Integrating health interventions for women, newborn babies, and children: a framework for action. Lancet 2008; 372: 990–1000. [PubMed: 18790321]

27. Rosato M, Laverack G, Grabman LH, et al. Community participation: lessons for maternal, newborn, and child health. Lancet 2008; 372: 962–71. [PubMed: 18790319]

28. Lambach P, Alvarez AMR, Hirve S, et al. Considerations of strategies to provide influenza vaccine year round. Vaccine 2015; 33: 6493–98. [PubMed: 26319745]

29. WHO. World Health Statistics 2015. Geneva: World Health Organization, 2015. http://public.eblib.com/choice/publicfullrecord.aspx?p=2070501 (accessed Jan 14, 2016).

30. Savitz DA, Fell DB, Ortiz JR, Bhat N. Does influenza vaccination improve pregnancy outcome? Methodological issues and research needs. Vaccine 2015; 33: 6430–35. [PubMed: 26319740]