Vaccines, pregnancy and ethics

History has shown the dangers posed by drugs that are untested in the pregnant population; yet these trials carry an inherent risk to women and vulnerable babies. George Winter debates the issue

In the late 1950s and early 1960s, the drug thalidomide was taken by pregnant women to counteract morning sickness—with the result that around 10 000 babies globally were born with limb deformities. Macklin (2010) not only observes that thalidomide had never been tested in pregnant women, but also suggests that: 'Had the drug been tested in very few women in a phase I or phase II clinical trial, the mutagenic effect would most likely have been discovered and the number of babies born with deformities would have been much smaller' (Macklin, 2010: 632).

This bold speculation exemplifies a utilitarian approach to ethics, which has at its core the intention of minimising the number of individuals exposed to a potential harm. But would it have been ethically right to have enrolled pregnant women in a clinical trial of thalidomide? If there is such a thing as 'objective' knowledge acquired through honest reasoning, it seems certain that if thalidomide had first been tested on 'very few women', as Macklin (2010) frames it, a public health catastrophe could have been prevented. Perhaps the unease that many of us would feel in adopting such a position is because of the difficulty in separating reason from innate values: in this case, an aversion to expose pregnant women to a possible mutagen.

As Verweij et al (2016) point out, there is a certain resistance to pharmaceutical interventions in pregnancy, with companies, researchers and regulators often deeming it unacceptable to include pregnant women in clinical trials. Yet, '[c]ommonly used vaccinations during pregnancy—namely inactivated influenza, pertussis, and tetanus—have not been shown to create an increased risk of adverse effects in infants (Verweij et al: e310).' Nevertheless, what some might see as an understandable reluctance to involve pregnant women in vaccine trials (for example) contributes to a paucity of evidence on the relative risks and benefits of pregnant women being exposed to a product that may well confer benefit.

Krubiner et al (2019) cite the example of hundreds of women who were inadvertently exposed to a live-attenuated rubella vaccine during pregnancy and who opted to terminate their pregnancies because they feared the vaccine may have harmed their babies. However, 'worries about vaccine-associated congenital rubella syndrome turned out to be unfounded, with not a single case documented from thousands of unintentional exposures worldwide' (Krubiner et al, 2019: 28).

Krubiner et al (2019) have presented 22 recommendations in a guidance document developed by the Pregnancy Research Ethics for Vaccines, Epidemics, and New Technologies (PREVENT) Working Group, a multidisciplinary, international team of experts in specialities that include bioethics, maternal immunisation, obstetrics and philosophy. Their intention is to 'provide a road map for the ethically responsible, socially just, and respectful inclusion of the interests of pregnant women in the development and deployment of vaccines against emerging pathogens' (Krubiner et al, 2019: 1).

This seems a reasonable approach, but where does it stand in relation to the precautionary principle, which has spread beyond its environmental origins to find expression in medicine where it is often invoked in areas such as public health? Might an over-reliance on the precautionary principle simply reflect the fact that we live in a risk-averse society, that might oppose high-quality research, such as that advocated by Krubiner et al (2019)? And given the prominence of evidence-based medicine, where does the 'better safe than sorry approach' embodied by the precautionary principle fit into a medical culture dedicated to proven scientific methods of risk evaluation?

The precautionary principle can take an ordinary notion of possibility and lead it down the philosophical garden path to meet 'logical' possibilities, where anything can happen 'in theory'. Therefore, it is logically possible that one day I shall read Proust in Russian; however, I know that this will never happen. By embracing what is logically possible, as well as what is practically possible, the precautionary principle could easily appear incoherent.

As midwifery evolves, my guess is that there will be an unfolding debate on the merits of pregnant women participating in vaccine trials, in which midwives may be asked by their peers—and perhaps by women and families in their care—for their views. It's a debate worth having. **BJM**

George F Winter
Freelance Writer; Fellow of the Institute of Biomedical Science

Krubiner CB, Faden RR, Karron RA et al. Pregnant women & vaccines against emerging epidemic threats: Ethics guidance for preparedness, research, and response. Vaccine. 2019. https://doi.org/10.1016/j.vaccine.2019.01.011

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