



Department of Metabolism, Digestion and Reproduction, Imperial College London, London, UK

v.male@imperial.ac.uk

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Menstruation and covid-19 vaccination

Latest evidence is limited but reassuring

Victoria Male *lecturer in reproductive immunology*

Vaccination against covid-19 provides protection against the potentially serious consequences of SARS-CoV2 infection, but as the vaccines were rolled out into younger age groups, clinicians were increasingly approached by patients worried that the vaccine had caused a change to their periods.

More than 36 000 reports of menstrual changes or unexpected vaginal bleeding following covid-19 vaccination have so far been made to the yellow card surveillance scheme run by the UK Medicine and Healthcare Products Regulatory Agency (MHRA).¹ But as cycles vary naturally and the MHRA does not collect comparison data from unvaccinated people, these data cannot be used to establish whether menstrual changes increase after vaccination. A similar signal appeared in the US vaccine adverse event reporting system (VAERS), and as a result the National Institutes of Health allocated \$1.67m (£1.2m; €1.4m) for research into a possible connection.²

The first of these studies has now reported.³ The authors took advantage of an existing dataset from a menstrual cycle tracking app: 3959 Americans logged at least six consecutive cycles; 2403 of them were vaccinated and the remainder acted as a control group. In adjusted models, the first dose of vaccine had no effect on timing of the subsequent period, while the second dose was associated with a delay of 0.45 days (98.75% confidence interval 0.06 to 0.84).

Most affected were the 358 individuals who received both doses of the vaccine in the same cycle, experiencing a 2.32 day (98.75% CI 1.59 to 3.04) delay to their next period. Among this group, 10.6% experienced a change in cycle length of more than 8 days, which is considered clinically significant,⁴ compared with 4.3% in the unvaccinated cohort ($P < 0.001$). In all groups, cycle lengths returned to normal by two cycles after vaccination.

A study from the Norwegian Institute of Public Health asked a pre-existing cohort of 5688 Norwegians whether they had experienced specific menstrual changes (such as unexpected breakthrough bleeding or worse than normal period pain) in the cycles before and after each vaccine dose.⁵ The high level of variation in normal cycles is underlined by the finding that 37.8% of participants reported at least one change from normal even in pre-vaccination cycles. The study identified heavier than normal bleeding as the change most associated with vaccination (first dose: relative risk 1.9, 95% confidence interval 1.69 to 2.13; second dose: 1.84, 1.66 to 2.03).

The findings from both these studies are reassuring: changes to the menstrual cycle do occur following vaccination, but they are small compared with natural

variation and quickly reverse. But how applicable are these results to the UK? Unlike the US and Norway, where the interval between the first two vaccine doses is 3-4 weeks, the interval in the UK is 8 weeks. Under the UK vaccination schedule, it is therefore impossible to receive both doses of the vaccine in the same cycle, and this may mean that the changes observed in the US and Norway do not occur here. A study using data from UK users of the same menstrual cycle tracking app as in the US study is expected to clarify this point soon. In the interim, the MHRA says that current evidence does not support a link between changes to menstrual periods and covid vaccination in the UK, and it continues to advise that anyone noticing a change to their periods that persists over several of cycles, or who has any new vaginal bleeding after the menopause, be treated according to the usual clinical pathways.¹

Unanswered questions

Taking advantage of pre-existing datasets and cohorts means we have been able to make progress on these questions in a short time, but there is still much to learn. Scientifically, it will be important to characterise the mechanism by which post-vaccination menstrual changes occur. Medically, we must also determine whether any group is particularly vulnerable—for example, those with pre-existing gynaecological conditions—so they can be counselled appropriately. There is already evidence that covid infection can alter periods,^{6,7} but better defining the extent and persistence of these changes will also be important in counselling women on the risks and benefits of vaccination.

Much of the public concern around this issue arises from misinformation that covid-19 vaccines cause female infertility.⁸ Although we already have evidence that this is not the case, it comes from the clinical trials, in which pregnancy rates were extremely low because participants were using contraception,^{9,10} and fertility clinics, where users do not necessarily reflect the broader population.¹¹⁻¹⁴ Studies of pregnancy rates in couples trying to conceive through intercourse are needed, and they should also include analyses of the effects of having covid-19, because evidence suggests that infection may reduce sperm count and quality.¹⁵ A deeper understanding of the effects of both infection and vaccination on fertility will enable better counselling of patients for whom this is of particular concern.

The work that has been done represents a step in the right direction, but the fact that it has taken us so long to get here reflects the low priority with which menstrual and reproductive health is often treated in medical research. The widespread interest in this

topic highlights how pressing a concern this is for the public. It's time we started listening to them.

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