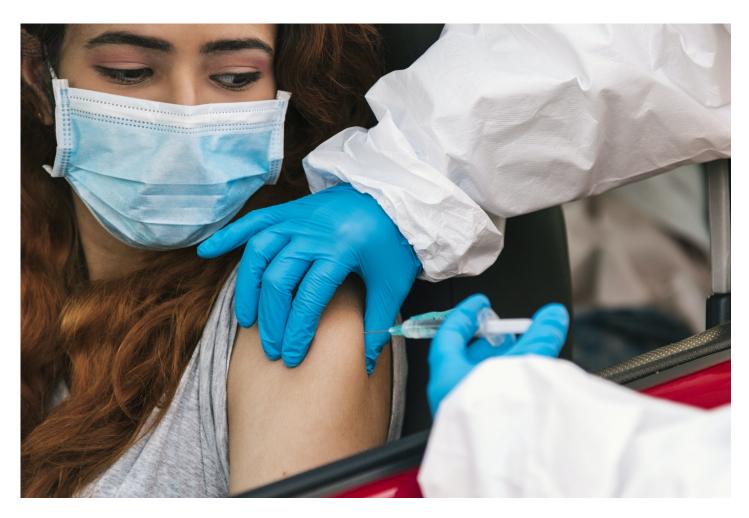


The COVID-19 vaccine and menstrual irregularities. Exploring potential mechanisms.



Dr. Jen Gunter Apr 11 ♡ 46 □ 7 &



There are an increasing number of reports surfacing online of changes in the menstrual cycle shortly after COVID vaccination, either bleeding that appeared earlier than expected (a few days after the vaccine), was heavier than expected, and/or more painful than expected.

This was first formally covered by The Lily, and the article pointed out the impact of vaccines on menstruation isn't typically tracked in studies. Bleeding that is heavy enough to require a trip to the emergency room would be picked up in most vaccine studies, but not an early period, breakthrough bleeding, a heavier period, or a more painful one. This lack of information is maddening. Not because I think there is anything harmful happening to the uterus post vaccination, but because this is something we should understand. And, people like to be warned of side effects in advance. For example, I warn my patients that steroid injections can cause irregular periods, so if that happens, my patients are not upset or surprised.

Imagine if you didn't know that fever could be a vaccine side effect? You might be concerned that something untoward was happening to your body when all you were experiencing was a typical post vaccine fever. That is exactly the same with menstrual irregularities.

It is possible that side effects may even vary depending on when the vaccine is given during the menstrual cycle. I found this study from 1987 that suggests side effects with the Rubella vaccine were the highest when the vaccine was administered during the luteal phase (second half of the menstrual cycle). I understand that right now most people get the vaccine slot they get, so even if optimal menstrual timing to minimize side effects existed, taking advantage of that might not be possible. Then again, who knows? Without the data it isn't possible to say much of anything.

I wondered if the data on menstruation had been tracked in the studies, but wasn't reported. So, I emailed one of the principal investigators from Pfizer to see if they tracked the data for their COVID-19 vaccine and just didn't report it, but I didn't hear back.

Striking out, I thought perhaps if *anyone* had tracked menstrual data in *any* vaccine study it would have been Merck and *Gardasil*, the human papillomavirus or HPV vaccine, as the initial target population was teenage girls. So I contacted Merck...and didn't hear back. I also contacted Dr. Kevin Ault, who was involved with the initial Gardasil studies, and he responded immediately. And no, he couldn't find any data either. Kevin is a great guy, and worth a follow on Twitter.

Undeterred, I started weeding through post HPV vaccine surveillance studies. These are the studies published after a vaccine is approved to look for side effects and complications that may have been missed in the initial trials. Eventually, I found one that included menstrual irregularities. This study was from Japan, where the HPV vaccine had been temporarily halted several years ago due to fear of side effects (fears later disproven). The Japanese Ministry of Health, Labour and Welfare (MHLW) insisted on a deeper dive into possible vaccine side effects before relaunching the program.

In this study, researchers surveyed almost 30,000 people who had received the vaccine as teens to find out what symptoms might be more common among those who had received the HPV

vaccine compared with those who had not. Among the list of questions asked? Irregular menstrual periods and an abnormal amount of menstrual bleeding. Eureka!

This study is retrospective, meaning the researchers asked the participants to remember what had happened to them several years before. Not as good as following them in real time (meaning a prospective study), but they also surveyed an unvaccinated control group, so that was helpful.

Of the 24 symptoms surveyed, the most common identified among those who were vaccinated were menstrual irregularities and heavy menstrual bleeding. However, these were also the most common symptoms reported by the unvaccinated teens. Teens have a higher incidence of menstrual irregularities and heavy menstrual bleeding, so some caution is required in interpreting these results. When controlling for variables, the data identified a possible link between three menstrual symptoms and the HPV vaccine: "persistent abnormal amounts of menstrual bleeding" or "irregular menstruation."

As this is a retrospective study, there are a lot of inherent issues. There could be recall bias, meaning people who received the vaccination may be more likely to remember symptoms such as abnormal bleeding compared with those who received placebo. People who received the vaccine may also have had more health problems, and hence were more likely to have abnormal bleeding. The emotional stress of receiving the vaccine could also impact menstruation. Regardless, this study supports a link between vaccinations and menstrual irregularity. Not all vaccines trigger the immune system in the same way, so the data here may not apply to the COVID-19 vaccines.

Before we get to the COVID-19 vaccine and menstrual irregularity, it's important to be very clear that there has been no link identified between the HPV vaccine and infertility or miscarriage. If the vaccine were damaging the lining of the uterus (endometrium) we would see that downstream effect.

How might the COVID-19 vaccine be linked with menstrual irregularity?

There are several possibilities. First, let's review a quick primer on periods.

Complex signaling from the brain triggers follicles (eggs and their surrounding tissue) to start developing. Several follicles are recruited and they produce increasing amounts of estrogen. Typically, one follicle becomes dominant and the others disappear. The estrogen produced by the larger group of follicles and then by the dominant follicle builds the lining of the uterus. With ovulation, the hormone progesterone is released, stabilizing the lining of the uterus and preparing it for a potential pregnancy. If there is no pregnancy, the progesterone is withdrawn and the lining is destabilized and comes out as menstrual blood.

The three ways the COVID-19 vaccine could potentially impact menstruation are:

- Impact on the chemical messaging from the brain to the ovaries.
- Impact on the chemical messaging from the ovaries to the uterus.
- Impact that directly affects the lining of the uterus

These effects could be from the vaccine itself, the immune system response to the vaccine, or potentially related to fever or feeling unwell from the vaccine or stress related to vaccination.

Interrupting the signaling from brain to ovary in the first half of the cycle would slow or stop estrogen production. While this might delay a cycle or lead to a skipped period, it wouldn't likely cause bleeding within a few days of the vaccine. Even a surge of estrogen wouldn't likely trigger bleeding. Similarly, any direct impact on the ovary in the first half of the cycle is more likely to delay a period. It would likely take halting progesterone to trigger a period. This would require inflammation that damaged the corpus luteum in the ovary enough to stop production of progesterone and that seems an unlikely mechanism.

I believe the most likely mechanism for bleeding within a few days of the vaccine is due to an impact on the lining of the uterus (endometrium), since the endometrium is part of the immune system. The endometrium is involved with maintaining the microbiome of the endometrium (yes, there is one), defending against infectious insults, menstruation, as well the complex immune system interactions required for implantation of the embryo and early development of the placenta.

So how might this happen?

One Possibility: It's not happening. There is no link, it just looks like there is.

This does not mean that the people reporting irregular menstruation are making it up, rather, they are having menstrual irregularities that are being erroneously attributed to the vaccine. It's possible that people with medical conditions associated with menstrual irregularities are receiving their vaccine sooner or those receiving the vaccine sooner are more likely to be observant of their menstrual cycles. People with a history of menstrual irregularities may be

more likely to track their cycles and others may be paying closer attention to their periods so they are noticing irregularities they may have previously ignored. Basically, this boils down to a sampling or a reporting error.

This is the kind of thing that would have been sorted out in the prospective studies if the rates of menstrual irregularities were the same or different in the vaccine and placebo groups.

Another possibility: An indirect link.

It's possible the stress of getting vaccinated—some people have reported a lot of issues accessing vaccines—or the abject relief at being vaccinated is having an effect. Stress affects the immune response and theoretically this could impact the lining of the uterus. It could also affect signaling from the brain, but that is more likely to delay a period than trigger one.

The third possibility: A Direct Effect on the Endometrium From Vaccination

There are a lot of complex immune system interactions in the lining of the uterus that are also involved in menstruation. Here are some possibilities:

- Nitric Oxide. Nitric oxide is produced when the immune system is activated (e.g. by a vaccine) and it also plays a role in menstruation by causing tissue breakdown, relaxing blood vessels, and reducing how platelets clot. This mechanism was suggested to me by my favorite RNA biologist, Rob Swanda. (If you are not following him on Instagram or Twitter (or both!), you are missing out.).
- Mast Cells. Mast cells are proinflammatory mediators that are part of the immune system and are also involved in menstruation. In the uterus, mast cell activation causes spasm of arteries that supply the lining of the uterus as well as trigger enzymes that break down the lining of the uterus, both mechanisms that cause bleeding. Vaccines can trigger the release of mast cells.
- Toll-Like Receptor Signaling. Toll-like receptors or Tlrs are involved in the innate immune system, meaning nonspecific defenses such as found in the endometrium. They are also involved in menstruation. Tlrs are very sensitive alarms. According to Dr. Peter Hoetez, a noted expert on vaccines, Tlr-7 is particularly sensitive to singlestranded RNA and COVID-19 is a single stranded RNA virus. The Pfizer and Moderna vaccines are single stranded RNA vaccines and the Johnson & Johnson vaccine is double stranded DNA, so if there were any difference between the RNA and DNA vaccines it might support a Tlr-7 theory. Tlr-4 is also involved in menstruation. The

RNA vaccines or the inflammatory response from the vaccines might directly trigger bleeding via activation of toll-like receptor signaling.

These are all theories, but it does seem to me that if an effect exists it is likely via inflammation on the endometrium that triggers menstruation via shared mechanisms.

I'll also add that the impact on the endometrium via shared immune mechanisms could also explain a more painful period. It might also explain flares in pain from endometriosis as there is some evidence of disordered inflammatory mechanisms in endometriosis implants.

Why Don't We Have More Answers?

The lack of data regarding menstrual cycles and vaccines is infuriating. I am not concerned about downstream effects regarding infertility or recurrent miscarriages as this has been wellstudied for a variety of vaccines. But knowing about menstrual irregularity is as important as knowing about fever.

We are missing a lot of data because it seems menstrual effects didn't seem worth studying, and *worth* is doing a lot of heavy lifting here. But it's also important to acknowledge that finding answers could be challenging. Ideally, we'd like menstrual cycle data from two or more months running into the study and not everyone has that. And if an effect on menstruation were seen, to really understand what was happening people would likely need to volunteer to have biopsies taken from the lining of their uterus post vaccine. Blood work can only take you so far here.

In Summary

It is important to put any potential vaccine side effects in perspective. Actually catching COVID-19 has a very good chance of messing with your menstrual cycle via a variety of mechanisms.

There is no data to support any impact on fertility or miscarriages from any COVID-19 vaccine. Here is some data from the CDC on infertility. Given the potential damaging effects, both short and long term, of getting COVID-19, the best way to protect your overall health and your menstrual cycle is to get vaccinated.

Hopefully, over time we will learn more. If there is an effect on menstruation—and biologically an effect is plausible—I personally believe the most likely mechanism is an impact on the endometrium from immune system activation. This could also explain changes in pain.

In the meantime, think of potential menstrual irregularities as a vaccine side effect like fever, it's a sign the immune system is being activated. And in the same way that fever doesn't make people permanently hot after a vaccine, menstrual irregularities will not be permanent either.

Addendum:

Since posting this several women on the pill or using the Mirena (hormonal) IUD have contacted me to tell me they have had abnormal bleeding. This definitely supports and endometrial mechanism.

Update: Dr. Kate Clancy has a study that was approved a few days ago to survey menstrual experiences post COVID-19 vaccination. The link is here. https://redcap.healthinstitute.illinois.edu/surveys/index.php?s=LL8TKKC8DP

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1

Barbara Aug 11

Dr. Jen Gunter, my name is Barbara, I am Italian and I am a health worker, suffering from endometriosis, I have undergone several operations for the presence of ovarian cysts and important abdominal adhesions, fibroids and uterine polyps that they have been removed and following the operations; I have developed pelvic varicles.

I am waiting for a further intervention (the fifth). I also suffer from autoimmune thyroiditis.

At the moment I have not been vaccinated against covid 19, I am obliged by decree law but I am afraid of worsening my symptomatological and pathological situation.

Could you please give me the directions on how to behave?

Thank you.

Reply



mpp Apr 12

Thank you so much for this!!! I feel like crying tears of joy that I found your blog. I have been strategizing when I should time my vaccination based on my cycle and all the symptoms I'm have in general and how sensitive it is. I wish there was more data and I'm so glad that a study was approved.

For clarity - does the J and J vaccine not effect Tlrs? (In theory of course)

Thank you again for this enlightening post.

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1 reply by Dr. Jen Gunter

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