Stopping Depo-Provera: Why and what to do about adverse experiences

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Laura Wershler interviews Ask Jerilynn, clinician-scientist and endocrinologist

With 250 comments - and counting - to my year-old post Coming off Depo-Provera is a women's worst nightmare (April 4, 2012) I thought it was time to revisit this topic.

That blog post has become a forum for women to share their negative experiences with stopping Depo-Provera (also called "the shot," or Depo), the four-times-a-year contraceptive injection. (Commenters reporting positive experiences have been extremely rare.) Many women have experienced distressing effects either while taking Depo and/or after stopping it. They report that health-care professionals seem unable to explain their problems or to offer effective solutions. What is puzzling for many is why they are experiencing symptoms like sore breasts, heavy and ongoing bleeding (or not getting flow back at all), digestive problems, weight gain and mood issues when they stop Depo.

This post aims to briefly explain how Depo works to prevent pregnancy, its common side effects and, most importantly, why and what to do about adverse experiences when stopping it.

What follows is my interview with Dr. Jerilynn C. Prior, Society for Menstrual Cycle Research board member, professor of endocrinology at the University of British Columbia, and scientific director of the Centre for Menstrual Cycle and Ovulation Research (CeMCOR) Section 1 explains how Depo-Provera works and what causes its side effects. Section 2 explains the symptoms women are experiencing after stopping the drug.

1) Taking Depo-Provera: How it works and established side effects

Laura Wershler (LW): Dr. Prior, what is Depo-Provera® and how does it prevent pregnancy?

Ask Jerilynn: The term, "depo" means a deposit or injection and Provera is a common brand name of the most frequently used synthetic progestin in North America, medroxyprogesterone acetate (MPA). Depo is a shot of MPA given every three months in the large dose of 150 mg. Depo prevents pregnancy by "drying up" the cervical mucus so sperm have trouble swimming, by thinning the endometrium (uterine lining) so a fertilized egg can't implant and primarily by suppressing the hypothalamic and pituitary signals that coordinate the menstrual cycle. That means a woman's own hormone levels become almost as low as in menopause, with very low progesterone and lowered estrogen levels.

LW: Could you explain the hormonal changes behind the several established side effects of Depo? Let's start with bleeding issues including spotting, unpredictable or non-stop bleeding that can last for several months before, in most women, leading to amenorrhea (no menstrual period).

Ask Jerilynn: It is not entirely clear, but probably the initial unpredictable bleeding relates to how long it takes for this big hormone injection to suppress women's own estrogen levels. The other reason is that where the endometrium has gotten thin it is more likely to break down and bleed. These unpredictable flow side-effects of Depo are something that women should expect

and plan for since they occur in the early days of use for every woman. After the first year of Depo (depending on the age and weight of the woman) about a third of women will have no more bleeding.

LW: What about headaches and depression?

Ask Jerilynn: It is not clear why headaches increase on Depo—they tend not to be serious migraine headaches but are more stress type. Perhaps they are related to the higher stress hormones the body makes whenever estrogen levels drop. Unfortunately, headaches tend to increase over time, rather than getting better as the not-so-funny bleeding does.

The reasons for depression are mysterious to me but this is an important adverse effect. I believe that anyone who has previously had an episode of depression (whether diagnosed or not, but sufficient to interfere with life and work) should avoid Depo.

LW: Although there has been little discussion about bone health concerns on the previous blog post, I think we should address the fact that Depo causes bone loss. How does it do this?

Ask Jerilynn: As we discussed, Depo causes estrogen levels to drop. Dropping estrogen levels always cause bone loss. Several randomized, blinded studies for example, have shown that if women taking Depo wear an estrogen patch, compared with a placebo patch, they don't lose bone. (That was a test of the cause of bone loss but isn't a good strategy during Depo because it might prevent its contraceptive effectiveness).

The bone loss concern is now decreased because we know that women, on average, regain all of that lost bone as they stop taking Depo. MPA, like progesterone, stimulates new bone to form but this formation is not visible while bone loss is high (as in, while taking Depo). The increase in bone density on stopping Depo is because rising estrogen levels prevent bone loss and the increased bone formation then becomes visible.

I have tended to think the bone loss is not an important problem because the bone density returns to normal. However, women at osteoporosis risk do have more broken bones while on Depo. Therefore I recommend that all woman choosing Depo for contraception have at least three high calcium (dairy or calcium-fortified) foods per day (or take one 500 mg calcium pill with a meal and the other at bedtime) plus also 2000 IU of vitamin D3 daily.

It is probably wise for teens to avoid Depo if they have a personal history of amenorrhea (no flow for three or more months), or a close relative (mother, grandfather or sister) who had a broken bone without a major fall. (Note: For more life cycle specific information about preventing bone loss click here.)

LW: Weight gain has caused grief for many women taking Depo. What's going on?

Ask Jerilynn: The suppression of women's estrogen production likely causes the weight gain on Depo (that averages 2 kg or five pounds in the first year). A similar weight gain occurs in women or in animals when their ovaries are removed. It is probably the body's way of trying to increase fat (that can convert male and stress hormones into estrogen) and thus to prevent the rapid bone loss that happens when estrogen levels drop.

LW: Another reported effect of Depo is digestive problems. I've read that abdominal distress including cramps, bloating and constipation are common because Depo loosens the tone of the muscles in the gastrointestinal tract. Can you comment on this?

Ask Jerilynn: I don't really understand this. What I do know is that abdominal problems are common in general for women and haven't shown up as significantly different between women on Depo or placebo in trials of Depo. I suspect, again, that the drop in estrogen level triggers stress hormones that cause crampy gut pain and changes in bowel habits.

2) Stopping Depo-Provera: What is causing adverse effects and what to do about them

LW: Thanks for explaining the side effects women experience while taking Depo. What happens and why are women miserable when they stop it?

Ask Jerilynn: First let me say that I have looked in the recent medical literature and been unable to find any studies of women's experiences on stopping Depo. One would surely hope that drug regulatory bodies have required research on the return to fertility in women taking Depo.

Here's what I think is happening, and I've formed this understanding based on what women described in their posts: Women's reproduction has been suppressed by Depo for months or years. This means that (figuratively speaking) the hypothalamus, pituitary and ovaries have 'forgotten how' to coordinate their usual complex and amazing feedback needed for normal ovulatory menstrual cycles.

However, our bodies are programmed to work hard to regain reproduction so there is a kind of rebound over-stimulation of estrogen levels (the easiest hormone to get the ovary to produce). The result is erratic but high estrogen levels causing nausea, sore breasts, fluid retention and abdominal bloating, mood swings and heavy or prolonged vaginal bleeding.

With high estrogen levels and weight gain, plus the "hypothalamic incoordination," ovulation doesn't occur and therefore no progesterone is produced. Progesterone – the hormone produced after ovulation in normal menstrual cycles – is needed to counterbalance the high estrogen levels. I believe that it is this estrogen-progesterone imbalance that is leading to all these miserable symptoms.

LW: Many women who have shared their experiences on my previous post also seem very concerned by the delayed return to normal menstrual cycles, with some experiencing no bleeding for months. Others seem to have flooding and continual flow. What's up?

Ask Jerilynn: We'd have to study this to be sure, but I suspect that the women who have no flow for months on stopping Depo likely are younger, have gained the least weight and are under the most situational/emotional/physical stress. On the other hand, those who have heavy and/or prolonged vaginal bleeding are likely older (and often perimenopausal—when ovarian hypothalamic coordination has normally become dysfunctional) and have usually gained more weight.

Therefore I believe that the varying responses in vaginal bleeding depend on whether women were on the young-thin-stressed side when starting and stopping Depo versus normal to now

overweight or obese. Another possibility is that women have become perimenopausal during their years on Depo. Thus when they stop Depo they are now in a symptomatic perimenopause that the Depo was preventing or treating.

LW: Some women have noted extreme weight gain upon stopping Depo. Can you explain why this might be happening?

Ask Jerilynn: If estrogen levels are high and progesterone levels are low, the natural result is inappropriate hunger and weight gain. Progesterone levels following ovulation make women burn about 300 more calories a day, which obviously helps prevent weight gain. I think this weight gain side-effect of stopping is also due "estrogen dominance."

LW: Another common experience that disturbs women as they stop taking Depo-Provera is extremely sore breasts. What causes this?

Ask Jerilynn: This is directly caused by the "estrogen overdrive" as the body tries to recover from the suppression caused by Depo. Sore breasts tell us that our estrogen levels are higher than the highest normal mid-cycle estrogen peak. If it is sore when you press your palm onto your nipple, you don't need a blood/urine/saliva test to know your own estrogen is higher than it ever should be in the normal cycle.

LW: Why are some women getting acne or pimples on their face and backs?

Ask Jerilynn: Whenever women are overweight and not making enough progesterone (because they are not ovulating) the body makes more male hormones that lead to oily skin and acne.

LW: What about the hot flushes that some women are experiencing? These symptoms are typically associated with perimenopause, the transition to menopause.

Ask Jerilynn: Yes. Some women who have become perimenopausal while on Depo will have had their hot flushes and night sweats effectively treated by the progestin. Therefore, when they stop, they experience the symptoms of perimenopause including night sweats and daytime hot flushes.

That brings me to another educated guess—many women stop Depo in their 30s and 40s because they want to have a family or because their doctors advise them to. They may already be starting into perimenopause but the signs, such as hot flushes, are masked while on Depo. However, off Depo the estrogen swings (that may be high both because of stopping Depo and because of changes related to perimenopause) cause hot flushes and night sweats. If you'd like more information about perimenopause here's a recent open-access scientific review.

Heavy flow is one of the most common experiences of early perimenopause that at least a quarter of all women experience. When you add the estrogen excess production on stopping Depo to perimenopause ("Estrogen's Storm Season") you get really, REALLY heavy flow. No wonder women are so frustrated and doctors are so puzzled.

LW: Many women are told to just "wait it out." This could mean months of not ovulating, ages without a menstrual period, or putting up with flooding menstruation. Do you think that's a good idea? If not, what would you suggest?

Ask Jerilynn: Based on what I'm guessing is going on hormonally, and also on a woman's age, her desire or not for pregnancy, and on her current body mass index, here are some suggestions:

Heavy vaginal bleeding: My first suggestion—something every woman should know— is ibuprofen. One tablet four times on every heavy-flow day, decreases flow by almost a half. See this article about how to manage flooding or heavy vaginal bleeding. You can take ibuprofen on your own and track your own cycles by downloading and completing the Daily Perimenopause Diary.

Having such a record will help your health care provider to understand what you are experiencing as well as allowing you to know for yourself what is going on. If ibuprofen does not sufficiently decrease heavy flow so you can cope, you will likely need to ask your physician's help. You will need a prescription in order to take what I next recommend, cyclic or daily progesterone. What works best is to print out this information sheet for on Cyclic Progesterone Therapy, one for yourself to stick somewhere obvious and one to take to your doctor.

However, if your flow has been so heavy and long that you already have iron loss anemia (commonly called a "low blood count"), have had continuous flow for over a month, or are bleeding enough to become dizzy when standing, you need a more powerful solution than cyclic progesterone. The answer is progesterone every day for three months (plus ibuprofen on every heavy flow day). I've written this article on heavy flow to take to your family doctor.

No flow for three months after stopping Depo: I suggest starting to take natural, bio-identical progesterone (see Cyclic Progesterone Therapy) for two weeks and stop for two weeks. Don't be discouraged if you don't get a period when you stop it. Just keep doing that two weeks "on" and two weeks "off" progesterone until your flow returns. Even without flow, this treatment will increase bone density (based on a trial we did years ago).

If, in the course of taking cyclic progesterone you start getting irregular flow, follow the instructions (and picture) in that handout carefully. Most of all, think of this as restoring a normal balance of your own hormones and ovulatory menstrual cycles.

When you start noticing stretchy mucus about the middle of the month, this means your estrogen levels are recovering. Now you can actively start working on becoming pregnant, if this is your desire. You will take the progesterone for two weeks or fourteen days but start checking for your urinary LH peak (with a fertility kit you can buy over the counter) in the evening when you notice stretchy vaginal mucus. Only begin the progesterone after you see the LH peak (a positive test) or after the stretchy mucus decreases. The reason is that if you take the progesterone too early it could suppress that necessary LH peak.

Sore breasts, bloating and/or nausea: These symptoms mean high estrogen levels, usually without any or enough progesterone. Increasing exercise, increasing vegetables and fruits, and decreasing junk/snacks and desserts (except fruit) will decrease estrogen levels in premenopausal women. Although I can't promise that for women in perimenopause, it will certainly help you feel better. After you've started on these lifestyle changes, I'd suggest

beginning cyclic progesterone 14 days after the start of a flow or any time if you are not getting flow regularly. Follow the suggestions about how to take progesterone on the Cyclic Progesterone Therapy. If sore breasts get better but still persist, you can also try (gradually) decreasing your caffeine and alcohol intakes.

Hot flushes and night sweats: To start, I think it is important to realize that the experience of hot flushes or night sweats means you are in perimenopause. So, although it is not much help, you can blame some of what you are experiencing on perimenopause instead of just on stopping Depo!

CeMCOR recently proved that progesterone is effective for treatment of menopausal hot flushes in a randomized, placebo-controlled trial. We are now testing its effectiveness for perimenopausal hot flushes in a similar controlled study. If you live anywhere in Canada, you could potentially participate.

If, as is typical in very early perimenopause, you are waking at night feeling hot (and often sweaty or irritable) on only a few nights a month, and usually around flow, then cyclic progesterone works. Take it for 14 days, but if you typically have night sweats on the first few nights of flow, continue it a few more days.

However, if hot flushes are coming day and night and are troublesome any old time, then take progesterone daily instead of cyclically.

LW: This information will certainly help the many women who are having these experiences. Is there anything else you want to add about Depo-Provera?

Ask Jerilynn: I would like to say, perhaps belatedly, that Depo is an effective contraceptive that I feel women should have the option to choose. (Here I may differ from Laura!) Those of you who know me (and CeMCOR) realize that my goal in life is to help every woman achieve normal, ovulatory menstrual cycles. However, not every woman is — because of living conditions, partner attitudes or general life chaos — to manage barrier birth control methods that support ovulatory cycles. For women who should not take estrogen-based hormonal birth control (past blood clot, liver problems, heart problems, severe migraines, smoking, or over age 35) Depo may be an effective and valued contraceptive. Here's a quote from one post, *"I too was on the depo, for 11 years actually during this time I loved it…no periods, no PMS awesome. . . ."*

LW: Point taken. I agree women should have access to Depo-Provera for the reasons you mention. But, what that commenter wrote next was: *"My god what happened post depo I never ever thought I would go through…throbbing sore breasts to the point I couldn't even touch them, night sweats (a year) anxiety, major bloating, nausea, withdrawal from social events, weight gain mid section and boobs…I hated life!!!!"* I think this is the "nightmare" scenario I was referring to in the title of last April's post. Let's hope your suggestions above are helpful for her and everyone who has commented, or will comment, on last year's post.

What I find unacceptable is the lack of information women have about how this drug works and what its effects are both during and after use, as well as the lack of assistance available from healthcare providers in recovering from the drug. Thank you so much for explaining some of

what is going on for the women who've been sharing their experiences here at ***re:Cycling***, and for offering suggestions to help in their recovery from Depo-Provera.

Note to readers: Please feel free to share this interview with other women and health-care professionals who may find the content of value.

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