The Pros and Cons of Estrogen (estradiol) therapy

“You want me to start on estrogen therapy? But I thought that estrogen therapy was “forbidden” now and would trigger breast cancer? And I’ve heard of other risks, such as blood clots, etc., that are increased with estrogen therapy – is this true?”

Well, as with any prescription medication, there are risks and benefits in using estrogen therapy. And while we can’t guarantee that you won’t develop breast cancer on estrogen therapy, the risks are very low. There is a lot of hype and misinformation in the media currently about HRT (hormone replacement therapy). Much of the misinformation is an overgeneralization error. The WHI (the Women’s Health Initiative) study, which is the study that much of the media is quoting, studied Premarin and Prempro. Premarin is an estrogen that is obtained from horse urine, not the physiological human estrogen (Estrace or estradiol) that we recommend. Prempro is a combination of Premarin and Provera (medroxyprogesterone – a type of progesterone hormone). The investigators did not study Estrace (estradiol) at all. Prescription Estrace (estradiol) is the same, physiological copy of the estradiol that your ovaries make (or used to make). And, interestingly, they didn’t find any increase in the risk of developing breast cancer with just Premarin (the estrogen derived from horses, without the progesterone component). However, with the combination PremPro medication they did see a slight increase in the incidence of breast cancer, and a worsened risk of heart disease and strokes. But it was a very slight increase in the total incidence of breast cancer – 38 cases out of 10,000 women per year taking PremPro, vs. 30 out of 10,000 in women who didn’t use PremPro.

Since they did not study estradiol at all, and since the Premarin by itself did not raise the breast cancer risk, one cannot say that all estrogen replacement therapy causes breast cancer. Many other studies have NOT been able to show a link between estradiol use and any increased risk of breast cancer. And, in fact, some studies have shown a reduced risk of breast cancer with estrogen only medications.

This WHI study suggests that the progesterone component of the PremPro may be raising the risk of breast cancer more than the estrogen component. Those of you who still have a uterus (who haven’t had a hysterectomy), do require combination therapy with estradiol and some type of progesterone. This is done to prevent the small increased risk of developing uterine cancer that is seen with any type of estrogen therapy. Studies have not been conclusive about whether Prometrium (one of our favorite progesterone therapies), or Progesterone skin creams, have been linked to a definite increase in the chance of developing breast cancer. More research is needed to determine the absolute risk of taking progesterone products. At this point though, we still need to continue to protect women who still have their uterus by having them take a progesterone medication with their estradiol. Once again, this should erase any increased chance of developing uterine cancer. We’ll continue to recommend this progesterone treatment until we get further scientific evidence that puts the breast cancer and uterine cancer risks in perspective.
If you think about it, with estradiol therapy we are just taking you back to the same risk of breast cancer that you would have had when your ovaries were making estradiol. It is true that there is a slight increase in the chance of developing breast cancer with longer exposure to female hormones, so that risk must be taken into account. We know that women who start their menstrual cycles early or who have a later menopause have a slightly higher risk of developing breast cancer. But we are not adding any additional risk above and beyond that “natural”, baseline risk. And, if the risk is actually from the progesterone component, then we are not even taking you back to your previous “natural” risk with estradiol therapy! (In those of you who can just take the estradiol by itself anyway).

And what if you’ve already had breast cancer? Should you use estradiol? That is a difficult question. Some studies have indeed shown an increase in recurrent breast cancer with estrogen products. However, other studies have not been conclusive, and some European doctors do routinely give estrogen to their patients who are recovering from breast cancer treatments. Once again we wonder if the progesterone component is the causative agent. We would suggest that you have long discussions with your endocrinologist, primary care doctor, and your oncologist about your specific risks. We certainly wouldn’t recommend it unless there was some pressing reason to do so, like uncontrolled, severe hot flashes. And we certainly would use other osteoporosis medications first before we prescribed estradiol.

What are the benefits of estradiol replacement therapy? Two of the most common symptoms that can be successfully treated with estradiol are hot flashes and vaginal dryness/pain (and this can alleviate some sexual difficulties and pain with sex). Many women also find it helpful in treating urinary incontinence and in stabilizing the depression and mood swings that can sometimes be triggered by menopause. It is also helpful in treating or preventing osteoporosis. It has been shown to reduce the risk of fracturing a bone. And, interestingly, it has been shown to lower the risk of colon cancer. Researchers did see that women on estrogen therapy reported less arthritis/joint pain and less stiffness overall. We still believe that estradiol is beneficial in improving cholesterol levels and delaying or preventing heart disease. The WHI study found an increased risk of heart attacks and strokes with PremPro, but remember again, that this was with PremPro, not estradiol.

We also have seen an improvement in memory and mental functioning. Many media sources and doctors quote that the WHI study proved that estrogen therapy doesn’t prevent dementia and actually may hasten dementia, but this is blatantly false. Women in the Premarin-only part of the study did show signs of memory improvement. And some studies have shown that the earlier a menopausal woman uses supplemental estrogen, the better the results as far as preserving memory and cognitive function as they age.

What are the other risks of estradiol replacement therapy? Well, we’ve explored the breast cancer risk above. And, to reiterate, there have NOT been any studies with any conclusive evidence linking estradiol with an increased chance of developing breast cancer.
There is a clot risk, especially in women who smoke. So if you are a smoker you need to decide whether the clot risk is significant enough to not start estradiol therapy, or, even better, give up the cigarettes. The clot risk includes DVTs (deep venous thrombosis), which are blood clots in the deep veins in the lower legs; and also includes a higher incidence of strokes. There might be some protective effect, or offset of the clot/stroke risk, by taking aspirin. Please discuss this issue with your doctors, and don’t take aspirin without first consulting with your doctors. Women who have had significant problems with blood clots or strokes in the past need to discuss the risks of HRT with their doctors, and see if the risk is too high, or see if there are other therapies, or life-style changes, that could lower that risk.

There can be annoying side-effects of breast tenderness or vaginal/uterine bleeding. These side-effects usually mean that the woman is being overdosed, though, and their estradiol dose should be reduced. Yes, this means that you do need to get follow-up estradiol levels checked periodically, to see if your dose needs adjusting.

Researchers did see an increased chance of gallbladder problems with estrogen therapy. We don’t know how much of an impact that weight and diet had in increasing this risk.

No study has been able to prove that there is any link between estradiol use and an increased risk of heart attacks, as opposed to the increased cardiac risk seen with PremPro.

If you are a relatively healthy woman, without previous breast cancer, or without significant clot risks, the absolute risk of any kind of adverse event is extremely low, so don’t allow anyone to inappropriately scare you away from your estradiol therapy.