

medical examiner

Estrogen Uncovered

Have women been the unwitting victims of the medical establishment's experiment with hormones?

By Eliza McCarthy

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Hyperion Books recently published *The Greatest Experiment Ever Performed on Women: Exploding the Estrogen Myth*, by Barbara Seaman. Generally speaking, a new volume on estrogen would hardly merit a mention. After all, such books are a dime a dozen. On Amazon.com, for example, there are 448 books listed under "Women's Health, Menopause," and 95 under "Contraceptives, Oral."

But a book by Barbara Seaman on the topic is something special. Published in 1969, her first book, *The Doctors' Case Against the Pill*, caused an anti-estrogen sensation. At that time, the Food and Drug Administration had received reports of blood clots, strokes, and other less serious side effects, such as nausea, associated with the birth-control pill, but most doctors failed to mention these risks to their patients. Seaman's book, containing chapters such as "The Silence That Could Kill You," changed all that: After its publication, congressional hearings were called to discuss the then high-dose Pill; pharmaceutical companies subsequently lowered the Pill's concentrations of estrogen and its oft-ignored hormonal cousin, progesterin; the FDA also required that companies include those now-ubiquitous patient-information inserts listing a drug's potential risks.

All these years later, after writing several more books and co-founding the National Women's Health Network, a feminist activist group, Seaman is back to estrogen. It is a tumultuous time in the public life of the hormone: Last summer (in case you were hibernating or are a man) the government announced that it was halting a portion of its Women's Health Initiative, a 15-year study, in part devoted to investigating hormone use, of more than 100,000 postmenopausal women. In the WHI, it turned out, postmenopausal women taking hormone therapy containing both estrogen and progesterin ran a 24 percent increased risk for heart disease, even though hormones had been thought to protect the heart. The study also confirmed that combination therapy increases the risk for breast cancer by 24 percent; surprisingly, the hormones also doubled the risk for dementia, when they had been hypothesized to prevent cognitive decline. (Interestingly, no such risks have been discerned among women taking only estrogen; these women are still being tracked, with many doctors predicting the results will turn out to be similarly disappointing.)

As a result of the WHI findings and of the writings of estrogen skeptics like Seaman and Dr. Susan Love, the conventional wisdom on estrogen, particularly on postmenopausal hormone use, has recently been transformed: Whereas the hormones were once presented as potential lifesavers, they are now looked upon with intense suspicion. News anchor Ann Curry's reaction on a recent episode of *Today* is representative of the shift: "What accounts for this ... immoral positioning, immoral development?" she asked Seaman. "I think many of us are angry about what has transpired."

Seaman is angry, too. In her book, Seaman places the blame for what she calls the "dirty secrets" of estrogen's history on drug manufacturers and doctors who recommended hormone products for what they "hope or believe they can do, not for what they *know* the products can do," the marketers who sold the drugs with extravagant claims, and what she sees as the wimpy media that failed to adequately report data on negative side effects. As for the millions of women who've taken estrogen over the years, Seaman believes they were used as "lab animals."

The not so subtext of all these arguments is clear: The drug companies are reckless and greedy; the media are complicit; the patients are dupes. These are familiar tropes of health-care activism. But do these claims, in the case of estrogen, hold up?

As a skeptical health writer, I was ripe for proselytization. And Seaman's book does raise lots of good, if familiar, questions about the influence of money on estrogen-research and marketing. Still, Seaman's book did not convince me that all women should swear off estrogen products entirely. (Seaman says her goal isn't to inspire estrogen aversion, but with chapter titles like "Poison by Prescription" one has to wonder.) Nor did the book convince me that the medical establishment is incapable of improving its hormonal record. On the contrary, Seaman, perhaps unwittingly, tells the story of a medical establishment that has—admittedly with prodding from advocates like her—learned to look more

critically at the question of estrogen. We've come a long way from the early days of the Pill, when women were told, essentially, not to worry their pretty little heads about it, to the huge gold-standard clinical trial that is the WHI.

The book does include loads of fascinating research, particularly on the shoot-first-ask-questions-later development of hormonal drugs. Seaman writes of grisly hormone experiments done on prisoners at Auschwitz (according to Seaman's source, the prisoners' "rutabaga soup" was likely laced with estrogen); the development of the synthetic estrogen DES in England (DES was used by millions in the United States to "prevent miscarriage," when, horribly, it didn't—and exposed both the pregnant women and their children to serious health problems later in life); and the creation of the birth-control pill after tests conducted on what Seaman portrays as helplessly vulnerable Puerto Rican slum dwellers.

But Seaman's fixation on estrogenic details to the exclusion of other health data does her cause a weird kind of disservice. In using the word "experiment," Seaman implies that the many forms of estrogen—from the Pill to postmenopausal hormone therapy—have been foisted on women despite inadequate or even nonexistent evidence. In using the word "greatest," she suggests that this is the largest and worst of such "experiments" ever done unto women. But Seaman provides little context for these claims. Nowhere is there a comparison with other medical experiments like, say, the government's 40-year "Tuskegee Study of Untreated Syphilis in the Negro Male," in which researchers withheld known cures from sick men simply to observe the ailment's natural progression. OK, so the study was done on men, but it's a pretty good yardstick with which to measure nasty portions of medical history. Nor does she ever compare estrogen's safety profile with that of other drugs. While it's frightening that postmenopausal hormones could cause up to 6,000 more cases of breast cancer a year, let's put this number in perspective. One hundred thousand people may *die* annually in the hospital from adverse drug reactions. (And the truth is, postmenopausal hormones only raise an individual woman's yearly breast cancer risk—yours, mine—by one-tenth of 1 percent.)

Seaman also writes with an odd kind of childish faith that finding absolute Scientific Truth should be a piece of cake, and risk-free to boot. Yet before the 1960s, when government agencies enacted more stringent controls over drug experiments, some researchers—not just those working with hormones—experimented with a derring-do that would make us queasy today. For example: In 1941, after testing penicillin on a measly eight mice, English researchers tried it out on a man sick with septicemia. (After a brief rally, the man died.) A mere two years later, the drug was being mass-produced. Estrogen is clearly not the only drug that was put on the market before its benefits and dangers were known to an absolute certainty.

So what *do* we know for certain about estrogen-containing drugs?

We know that today's lower-dose contraceptive pills, patches, and injections are not as dangerous as the earlier version of the Pill. They do slightly increase the risk for blood clots and strokes—according to recent studies, an extra 1 to 3 women per 10,000 annually will develop a blood clot while on the Pill, and an extra 1 to 4 per 100,000 women will suffer a stroke, with smokers at particular risk. On breast cancer, some research, though not definitive, suggests that women on the Pill (particularly those who start the Pill before the age of 20) may have an increased risk of breast cancer, one that dissipates after they stop taking the drug. Yet women who take the Pill actually develop fewer ovarian and endometrial cancers. Besides, today's Pill is nearly 100 percent effective at preventing unwanted pregnancy, if taken faithfully.

As for postmenopausal hormones, Seaman's right that the hormones have only a very few clear-cut benefits: They do reliably quash menopausal hot flashes and may also alleviate vaginal dryness. But no one's studied a "safe" length of time to take the drug for these symptoms. Furthermore, the WHI found that despite hot-flash relief, women on hormones reported no better quality of life than women taking a dummy pill.

In light of this shaky rationale for hormone therapy, researchers are looking to other drugs to do some of what hormones were supposed to: It seems that the cholesterol-lowering drugs called statins may fit the bill—some clinical trials show that they reduce the risk of death from heart disease (even among people with normal cholesterol levels); they also may somehow reduce fracture risk, researchers speculate; and, at least in a test-tube, they keep breast-cancer cells from proliferating. But let's not get ahead of the data—if there's one message to glean from the estrogen saga, it's this.

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