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BOOK REVIEWS

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Barbara Seaman. *The Greatest Experiment Ever Performed on Women: Exploding the Estrogen Myth*. New York: Hyperion Books, 2003. xv+332 pp. \$24.95 cloth.

Little more than a year ago, a post-menopausal woman visiting her internist would more than likely have been strongly advised to go on hormone replacement therapy (HRT). Women who expressed skepticism about the new hormone regime, prescribed mainly as a preventive regimen, were looked upon as medical Luddites. Advertisements, magazines, and drug company communications to physicians described estrogen replacement as a way to treat hot flashes, to prevent osteoporosis, dementia, Alzheimer's and heart diseases, and in general to protect women from the natural effects of aging. How could women refuse HRT intervention in the face of all the medical evidence?

And then one report toppled the whole house of cards. In the summer of 2002, a large federal study of hormone replacement therapy was halted after five years, when the researchers learned that women who were treated with hormones (a combined therapy of estrogen and progestin) had more cases of breast cancer than those on placebo. In addition, women on HRT had more strokes, more blood clots in veins and lungs, and more heart disease compared to those who were not on the therapy. On the positive side they had fewer hip and spinal fractures and fewer colorectal cancers. The new study created confusion in the medical establishment and cognitive dissonance among women who couldn't decide whether to trust or distrust their health care providers. This was just the latest episode in a long and troubled history of hormone therapies prescribed for women beginning in the 1940s, when the first synthetic estrogen, diethylstilbestrol (DES) was approved for use by pregnant women.

Barbara Seaman, the author of *The Greatest Experiment Ever Performed on Women* is a well-published journalist and author, who has written extensively on women's health. She is also co-founder of the influential National Women's Health Network, an organization dedicated to providing reliable information to women so that they can make informed decisions about their health.

Written primarily for a lay audience, the book provides an overview of the role of hormones in the treatment of women, a narrative that begins in the early part of the 20th century and takes us to the present. According to Seaman, the "greatest experiment," which she refers to in the book's title, began in England in 1938 and has continued to the present day. In her account, "A British biochemist, desperate to prevent Nazi Germany from cornering the world market on synthetic sex hormones, published his formula for a cheap and powerful oral estrogen" (p. 4). From that point on, drug companies have been aggressively producing and marketing hormone formularies designed specifically for women. The history of hormones in clinical practice has many twists and turns. Even before synthetic estrogens were produced, hormones were extracted from animals and injected into humans with the hope that they might improve an individual's vigor and slow down the effects of aging.

The book begins as if it were going to proceed historically, but then it turns to topical discussions on issues such as the birth control pill, bone health, heart disease, and endocrine disrupters. But the book

also highlights personalities such as FDA reformer, Senator Gaylord Nelson, and influential physician-author Robert Wilson who wrote *Feminine Forever*. Linear readers may find the discontinuous historical organization of the book somewhat distracting. For example, the discussion about Sir Charles Dodds, who first created a synthetic form of estrogen, appears in early chapters and then again well into the book, breaking the continuity in the discussion of an important scientific figure in the history of hormone development.

Central themes of the book are that women have been misled about hormone therapies and that there have been good docs and bad docs in the history of medical endocrinology. Much of the book's narrative is about how this happened, rather than why. There are many cautionary tales and some suggestions for women about what they should know when they talk to clinicians about hormone replacement. Seaman emphasizes that even the most limited results from clinical trials can prompt drug companies to go full throttle toward Food and Drug Administration approval of a product. "Medical policy in estrogen has been to shoot first and apologize later" (p. 5).

Preventive, rather than restorative or therapeutic pharmacology has been one of the fastest growing markets for drugs, vitamins, and supplements. In seeking to exploit these new markets, the pharmaceutical industry deceived millions of women, according to Seaman.

While it can be demonstrated that hormone therapy treats hot flashes and helps maintain bone mass, it was never proven to be helpful in preventing or treating heart disease . . . but for "reasons not fully understood," menopausal and postmenopausal women were led to believe otherwise . . . For that, all women have a right to be truly, righteously mad. (p. 168)

The author exhibits a somewhat dualistic attitude toward science and medical practitioners. She shows respect and even dependency on good scientific studies. But she also harbors a deep skepticism of scientists and physicians who have cozy relationships with drug companies. She writes that "the very people profiting from osteoporosis's status as a disease are the ones defining it as such presents a difficult ethic to be sure" (p. 172). One can only ask, why has so much reputable and peer-reviewed science resulted in such error-laden clinical applications? This central question is left unanalyzed and unresolved.

The book justifiably avoids reviewing the ponderous science that

surrounds any issue. Instead, the author selects out a few choice examples that raise fundamental questions about evidence-based medicine. For example, a 1998 study published in the *Journal of the American Medical Association* reported that in a group of about 2,700 women who had experienced a heart attack, those who had taken estrogen had higher mortality and additional heart attacks compared to those who were not taking the hormone. Despite these findings, and without definitive proof of the efficacy of hormone treatments, women continued to be advised to use estrogen for general postmenopausal health.

Seaman's account suggests that the belief in estrogen's preventative and restorative effects were deeply entrenched in the lore of clinical endocrinology. New data signifying otherwise were usually met with a high degree of skepticism. Even after the 2002 study, some medical researchers are calling for another large clinical trial to ascertain whether the negative effect of estrogen on cardiac health was an artifact of the study.

The book gives us little useful analysis of the microforces at work that protect the dominant view, namely, that exogenous estrogen will protect against disease and that medicine is capable of extending the life of healthy individuals by preventive drug interventions.

After reading her book, you may ask, as I had, is this the way our clinical system is supposed to behave? Is this what evidence-based medicine is like? Do we have the best possible free-market drug development system in the world? I myself believe there is more to offer consumers. Seaman gives us few clues on how to reform a system that is infused with conflicts of interest. "Big Pharma" is rapidly becoming a vertically integrated industry. It pays for research, owns the data, often dictates to researchers what gets published, pays for ghost-written articles, markets directly to consumers, purchases journal supplements, keeps academic scientists on healthy consultant lines, supports the education and sometimes the vacations of physicians, and influences public policy through donations to election campaigns and sophisticated lobbying.

The impression I get from reading Seaman's probing exposé is that the system of drug development appears untouchable. The author sees hope for reform in health consumers who are better informed, less dependant on the advice from physicians, and more resistant to the influence of pharmaceutical company advertisements. She confides, "I would never again trust a doctor blindly" (p. 118). Here is where the results of my studies of these issues have led me to a different con-

clusion. Rather than suggesting to consumers that they reach their own conclusions by becoming more informed about drug testing (learn about MedLine or become involved with a consumer health network), it seems to me that we should begin by addressing the egregious conflicts of interest in the current system—between Big Pharma, clinical investigators, the journals, and FDA. We need to create a firewall between drug development and drug testing and approval. Evidence-based medicine will not be our solution if we lose our trust in how the evidence is produced. Seaman's book is a reminder that what we believe is progress in drug development is sometimes an opportunistic construction powered by financial interests. And while science will eventually correct itself, it would be desirable to reform the system of drug evaluation, testing, physician education, and advertising so that drug hypotheses can be corrected early enough to avoid human casualties and broken dreams.

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