Book Review

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The X in Sex: How the X Chromosome Controls our Lives. By David Bainbridge. Cambridge, MA: Harvard University Press, 2003. Pp. 205. $22.95 hardcover, $14.95 paperback.

David Bainbridge, the author of *The X in Sex: How the X Chromosome Controls our Lives,* is a Fellow, Tutor, and Director of Studies in Veterinary Anatomy at St. Catherine's College, the University of Cambridge. His earlier attempt to popularize science, *Making Babies: The Science of Pregnancy* (published in 2001 by Harvard University Press), was stimulated by the birth of his son. He has sufficient knowledge, as well as the extraordinary ability to communicate it in a breezy, highly readable fashion that is both entertaining and informative. The present book demands little effort to comprehend and deals with important subjects not usually discussed in the popular press—that is, the genetic basis of sex differences and X inactivation. That said, *The X in Sex*—like his previous book—is not comprehensive. Instead, it is a somewhat superficial treatment of material selected for its entertainment value, often the titillating tidbits worthy of discussion on popular talk shows and at cocktail parties. His dedication of the book to his son Edward, "Thanks for taking the Y off my hands, I wasn't using it much anyway. And if you have complaints about the X, blame your mother," may give some idea of his style and the truth inherent in what he has glibly written.

The book consists of a two-page prologue, three chapters, an epilogue, a glossary, an index, and a suggested reading list. The prologue introduces a 6-wk-old embryo not yet a member of one sex or the other. Although Bainbridge knows the role of the Y chromosome, he implies that it is the "little nugget of life called the X" that is responsible for "the spark of sexuality that makes a child a boy or a girl" (p. 2).

Chapter 1, titled "Making a Difference," first considers Herman Henking's observations of the testicle of the insect Pyrrhocoris, in which he noted "a wallflower chromosome" that did not participate in "the two-part chromosomal dance" (p. 5), and he called it "X," for extra chromosome. Then Bainbridge proceeds to discuss the essence of man and woman, "impregnator and gestator" (p. 5), as well as Aristotle's concept of the origin of the sexes and Democritus's theory on how it is inherited. Next comes the reason "Y" (his pun, not mine). What follows is a discussion of Mendel, Darwin, and McClung and the discovery of the "macho" Y chromosome of the mealworm by Nettie Stevens at Bryn Mawr College. Since I had never heard of her (the credit usually goes to E. B. Wilson, who independently discovered sex chromosomes the same year), it was delightful to learn that it was she who discovered that the smaller of the sex chromosomes was the male-sex determinant. Bainbridge reassures us not to worry, because "the X is a bold full size *bone fide* chromosome, whereas the Y is a sad shrunken vestigial thing…the X has hidden depths, and a very special place in controlling our lives…and [is] the most compelling little scrap of stuff in existence" (p. 15). After a discussion of the role of *Sry* in male differentiation, he asks whether girls are just an afterthought. He also asks us to think about sex as a *restaurant,* with the smoking area being a boy (XY) and the nonsmoking area being a girl (XX), as a rather complicated way of explaining how the Y determines maleness. His explanation of the female default pathway and the chain reaction leading to maleness is quite nice. After whizzing through reproduction in sea worms, honeybees, flies, and moles, and even ZW chromosomes in birds, he relates the saga of the "sad divorce of X and Y" and the deterioration of the Y chromosome (p. 56). He ends with a description of our X chromosome, including its helical DNA structure, calling it "a two inch–long string of code that is wrapped up tight" (p. 68). In the figure showing the X and Y chromosomes, the Y is upside down, with the q arm on top (p. 66).

Chapter 2, titled "The Duke of Kent's Testicles," is the amusing shaggy-dog tale of *hemophilia A* in the royal family and is as good a description of the inheritance of this gene as you will find anywhere. Also included is the reason why males are more susceptible to hemophilia than females, which he calls "the curse of the lone X" (p. 89). This chapter ends with shorter discussions of the "vulnerable giant" (the dystrophin gene) (p. 89) and color blindness. In the Interlude, titled "How sexy is X," he points out that the X and Y are "seething with latent sexuality" (p. 121), with both chromosomes enriched with reproduction-related genes, including the X-linked gene for prostate cancer. A few of his statements may not be justified, and, unfortunately, there are no citations.

Chapter 3 is titled "The Double Life of Women." Starting out with the fact that women (including the Virgin Mary) are unnecessarily complex—at least to men—he proceeds to discuss the discovery of sex chromatin, its recognition as an X chromosome by Ohno, the X-inactivation hypothesis of Mary Lyon, and, finally, calico cats. It then becomes clear that "the double life of women" refers to their X-chromosome mosaicism: "A woman is a double creature" (p. 135). The description of the X-inactivation phenomenon is generally accurate and comprehensible, even for a reader with only a little knowledge of genetics. He also discusses the *Xist* gene quite well, but, in his figure (p. 138), the arrow pointing to this gene on the X chromosome is not in the right place. What follows is a discussion of random versus paternal inactivation, including the fact that, in mouse embryos, slightly more cells switch off

the maternal X than the paternal X. I was not familiar with this finding. Bainbridge suggests that silencing the father's X-linked genes in placental tissue is a means of protecting the female fetus from rejection in utero. That is not a bad teleological explanation for paternal X inactivation in the mouse placenta, but it is inappropriate for humans, who express paternal X genes in their placentas, which he fails to mention. Yet, he does present the idea that X-linked genes in both sexes may be hypertranscribed as a means to avoid monosomy X. Also included are excellent discussions of discordant identical twins, skewed X inactivation, and why autoimmune disease might be more prevalent in females. The topic presented in more detail than it deserves is the poorly supported hypothesis of X-chromosome imprinting in Turner syndrome, including the author's hypothetical "*girly behavior gene*"—active only on the paternal X—that makes females behave like "daddy's girls" (p.167).

In brief, this is not the most balanced or rigorous book on either sex or the X chromosome. However, it is worth reading and fills a void that is best appreciated by reading it. For the subjects that are presented, it is a good source of information, most of which is accurate enough. I would consider recommending it to patients with X-linked diseases or to their parents, to help them understand the disorder. I would also recommend it to those of us who teach this subject, for ideas on how to better communicate it to our students. Other audiences for the book might be high school students, undergraduates, and even medical students who are learning about X-chromosome inheritance and sex differentiation—as a supplement to their biology text—with the hope that it might seduce them to read more about it.

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