

Letter from the Guest Editors

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The simple fact that this special issue is being published suggests that “we’ve come a long way, baby.” From obesity, vitamin D, and dietary intervention to interventional cardiology and maternal effects on cardiovascular risk in offspring, this issue includes more than a conventional discussion of heart disease in women and differentiates the dogma from the data. Of course, much remains to be explored.

Much of the sexual bias in risk, symptom presentation, and treatment outcome is likely due to pleiotropic effects of the sex steroids (estrogens, androgens, and progestins) on cells and tissues involved in the constellation of cardiovascular diseases. From a basic science standpoint, animal models have taught us much about sex differences in cell and tissue characteristics, particularly as they contribute to atherogenic mechanisms. Going forward, *in vitro* and *in vivo* models will be crucial to unraveling the genetics associated with sex differences. Whereas studies of single genes can be fruitful, more sophisticated approaches using microarrays and gene expression profiling such as the recent study by Mendelsohn and his colleagues [1] have greater potential for illuminating sex differences in vascular gene activation and are likely to have significant translational impact.

From a clinical perspective, the controversy surrounding postmenopausal hormone treatment continues as discussed in the editorials by Barrett-Connor and Wenger. The suggestion from the Women’s Health Initiative that estrogen intervention at or shortly after the menopause may be protective [2], now known as the

“critical timing” hypothesis, warrants further investigation. The Kronos Early Estrogen Prevention Study is designed to address this very question (see Miller et al. in this issue). Furthermore, the Women’s Ischemia Syndrome Evaluation Study has shed significant light on the vascular characteristics underlying the fact that women’s symptoms differ markedly from those of men, a critically important area of research [3]. In addition, there is much to be done to improve the pharmacologic treatment of women as reviewed by Oertelt-Prigone and Regitz-Zagrosek in this issue. Going forward, we anticipate that the data, the provocative questions, and the potential for future experimentation presented in this issue will translate into increased awareness and critical improvements in the prevention, diagnosis, and treatment of cardiovascular disease in women.

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