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The American Heart Association launched the Go Red for Women (*GoRedForWomen.org*) campaign in 2004 to increase awareness of cardiovascular disease (CVD) in women. A similar campaign called "Red Dress" has been sponsored by the National Heart, Lung, and Blood Institute and the Department of Health and Human Services. In the last five years, important strides have been made in raising awareness of the burden of CVD in women, yet fundamental gaps exist in our knowledge of the underlying biology, clinical presentation, and optimal treatment strategies of CVD in women. Younger women (20 to 39 years) tend to be protected from coronary heart disease, heart failure, stroke, and hypertension (Figure), yet CVD is more prevalent in older women relative to age-matched men (greater than 80 years). These differences appear to be attributable, in part, to the influence of sex hormones on the vasculature, platelets, and the expression of coagulation proteins.

See accompanying articles on pages 279, 284, 289

To mark the fifth anniversary of the Go Red for Women campaign, the current issue of *Arteriosclerosis, Thrombosis, and Vascular Biology* contains three articles focusing on CVD in women. The first article, by Kim and Venu[1] and entitled "The Status of Women in Cardiovascular Clinical Trials," describes efforts to increase the enrollment of women in cardiovascular clinical trials. In 1986, the National Institutes of Health adopted a policy for the inclusion of women in clinical research and, in 1993, this policy became federal law. However, despite these mandates and other initiatives, the number of women enrolled in cardiovascular clinical trials remains disappointingly low. For instance, women represented only 27% of patients enrolled in mixed-gender National Heart, Lung, and Blood Institute-sponsored cardiovascular trials published between 1997 and 2006. The underrepresentation of women in the trials may have profound implications for optimizing treatment strategies for CVD in women.

In the second article, Bailey and colleagues[2] summarize our current understanding of "Thrombosis and Antithrombotic Therapy in Women." Sex-based disparities in the presentation of arterial and venous thrombosis may relate to underlying differences in coagulation/fibrinolytic protein expression, platelet function, and patterns of vascular disease, which in turn translate into differences in clinical presentation. For example, women are more likely to suffer strokes in the setting of atrial fibrillation and may have subtle differences in the pathophysiology underlying acute coronary syndromes. Sex-based differences may also influence response to antithrombotic treatment. In a recent

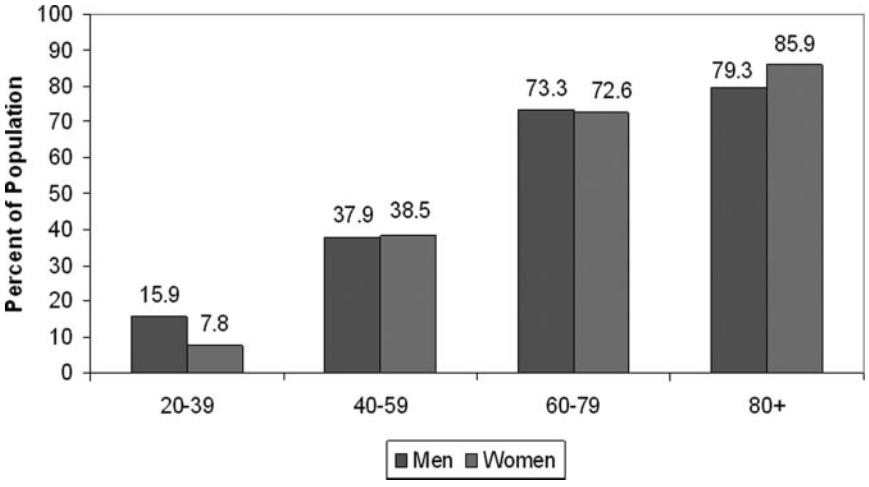

Figure. Prevalence of CVD in adults age 20 and older by age and sex (National Health and æExamination Survey: 2005–2006. Source: National Center for Health Statistics and National Heart Lung and Blood Institute. These data include coronary heart disease, heart failure, stroke, and hypertension. Original source: American Heart Association website http://www.americanheart.org/downloadable/heart/12293623845152009%20Stat%20charts%20for%20web1120%20v4.ppt.

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meta-analysis of primary prevention trials, aspirin reduced the risk of ischemic stroke but not myocardial infarction in women, whereas it reduced the risk of myocardial infarction but not ischemic stroke in men. Greater efforts are needed to encourage studies of drug interactions in woman, beginning with increased representation of woman in cardiovascular clinical trials.

In the last article, Xing and colleagues[3] address "Estrogen and Mechanisms of Vascular Protection." The greater age of women at the time of presentation of atherosclerotic coronary disease has been attributed to beneficial effects of estrogen. Yet, hormonal replacement therapy in older women (60 to 79 years) is associated with an increase risk of CVD. This article discusses the estrogen paradox and the "timing" hypothesis, which postulates that the antiinflammatory/vasoprotective effects of estrogen observed in young women are converted to proinflammatory/vasculotoxic effects in older women. Advances in understanding of the molecular mechanisms accounting for the effects of estrogen on the vasculature are reviewed, including the ability of estrogen to reduce inflammation by limiting oxidative stress and activation of the transcription factor NF-κB.

These three articles highlight the important advances that have been made in understanding sex-based differences in CVD that have been brought about in part by the efforts of the American Heart Association and the National Heart, Lung, and Blood Institute. We hope the series also serves to stimulate investigation aimed at elucidating the fundamental differences in pathophysiology of CVD in women and to promote translation of that knowledge into improved clinical outcomes.

Disclosures

None.

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