



## Editor's Comments

### Sex-Based Differences in Cardiovascular Diseases: Political or Biological?

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Currently an area of intense interest, it has long been recognized that important sex-specific differences exist for many cardiovascular problems with respect to epidemiologic features, disease development, clinical features, and outcomes. Examples of conditions more prevalent in women than in men are congenital ostium secundum atrial septal defects (still sometimes first recognized in adult life), patent ductus arteriosus, rheumatic valvular heart disease, mitral valve prolapse, primary pulmonary hypertension, and susceptibility to pro-arrhythmic effects of antiarrhythmic medications. It is noteworthy that concern about underappreciation of the importance of heart conditions in women is only a recent phenomenon. This delay is probably a consequence of the tendency by lay persons to think synonymously of *CHD* and *cardiovascular disease*, since CHD is the most prevalent cardiovascular disease.

The Perspective article about rheumatic fever in this issue<sup>1</sup> includes insightful observations by a physician with long experience and interest in rheumatic fever. Rheumatic fever itself has no major sex predilection, as confirmed by the 1945 article. Yet it is well known, and still without explanation, that chronic cardiac valvular sequelae, especially mitral disease, is more common in women, having about a 2/1 female/male prevalence. Because rheumatic heart disease, still common in undeveloped countries, often involves women in the childbearing age, much of the substantial older literature concerns complications and management during pregnancy and lactation. A MEDLINE search of the linkage of "rheumatic heart disease" and "sex differences" yielded only one article, indicating that this aspect has been of little interest in recent decades.

By contrast, a MEDLINE search of "coronary heart disease" and "sex differences" yielded 427 articles in the recent literature. This discrepancy became an issue about ten years ago, largely because of the fact that most clinical trials of CHD management before 1990 inappropriately involved only or almost only men. This difference in reporting was a consequence, most likely, of the fact that CHD develops earlier in men and probably was truly more prevalent in men before recent extension of life expectancy. It is now clear that total CHD mortality is equally prevalent in the sexes. The regrettable clinical trial disparity has probably been fully corrected, largely through the efforts of the NIH Office of Research on Women's Health.

In the Summer 2000 issue of *The Permanente Journal*, the first women's health issue, an article presented Kaiser Permanente data which showed that a substantial proportion (18%) of women hospitalized for CHD have no known major CHD risk factors at the time of diagnosis.<sup>2</sup> Because known risk factors have sometimes been given more importance in women than in men when assessing the likelihood of a coronary diagnosis, these data reemphasize the fact that total clinical evaluation in suspected CHD should always be the prime approach. Sex differences may exist in relative strength of specific risk factors to CHD development; but, if so, such differences play little role in initial assessment of symptoms that might represent a CHD episode.

Biologically determined sex-related CHD differences certainly exist. One probable example is detailed in this issue in an article entitled "Sex-based differences in causes of hospitalization for coronary heart disease." These Kaiser Permanente data show that men are more likely to have an acute myocardial infarction as the initial CHD presentation while women are more likely to have angina (unstable or stable). This sex difference in clinical CHD presentation, which was also found in the Framingham Heart Study, has implications for understanding CHD pathogenesis as well as for management decisions.

It is beyond the scope of these comments to exhaustively discuss the debates about possible sex differences with respect to diagnostic evaluation, disparities in either treatment or prognosis, and prevalence of nonatherosclerotic coronary syndromes or of noncardiac syndromes that mimic CHD problems. All of these areas are pertinent both to various forms of bias and possible biological sex-based differences in CHD manifestations. Differences have been found between the sexes in sensitivity, specificity, and predictive value of the various noninvasive tests, based substantially on age-specific differences in pretest likelihood of a CHD diagnosis. Disparities in management seem to mostly disappear when disease severity is controlled for.

Possible differences in management related to the misperception that this is a "male" disease have become a potent political issue. The following statement illustrates one type of material that has appeared in the public media: "Even some doctors still think of heart disease as primarily a man's problem. Studies have found that doctors provide women with less testing, less follow-up, less treatment, and less surgery. That may partly explain why once heart disease does strike, it's far deadlier for women."<sup>3</sup> It is not surprising that cardiologists occasionally see women who, having heard of possible sex bias, press, on this basis, for diagnostic and therapeutic procedures (including even coronary arteriography CABG). It is a given that physician bias should never play a role in medical decisions. Neither should patient demand, whatever the basis, influence decisions to perform inappropriate tests or procedures.

Thus, the answer to the query in the title is "both." Important sex-related disparities in CHD and other cardiovascular problems are a fact, as is the case in many medical fields of interest. The political aspect has driven much productive and thought-provoking research. All considered, this has had a constructive influence on medical practice and on women's health. ♦

#### References

1. Sellers AL, Levine EB. Acute rheumatic fever in adults. *Perm Found Med Bull* 1945;3:81-6. Commentary by Fessel WJ. *Perm J* 2000;4(4):30-5.
2. Petitti DB, Sidney S, Quesenberry CP, Klatsky AL. Likelihood that a woman will have no major risk factors at the time of a first myocardial infarction or stroke. *Perm J* 2000;4(3):35-8.
3. Perlmutter C. The heart of the matter. *Prevention* 1998 Feb;50(2):100-11.