**Letter to the Editor**

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**Cardiovascular Disease in Men**

In our recent article, we show that the excess risk of atherosclerotic cardiovascular disease (ASCVD) in men compared with women is evident only in the presence of hyperinsulinemia and at least one of the triad of glucose intolerance obesity and hypertension. Dr. Fontbonne, in her perceptive Editorial Comment, concludes that this observation must be connected with their androgenic hormonal profile.

The association of excess ASCVD in men with their sex hormone profile is a long-standing and logical contention. However, as we pointed out in our article, case-control and prospective studies yielded at best weak or indirect evidence of such an association. In contrast, studies of this kind in men have consistently revealed an association of ASCVD with hyperinsulinemia. In view of this, we would like to propose the following hypothesis.

For most of the history of mankind, man has been the hunter-gatherer, whereas the woman has tended to domestic chores. In these roles, men were much more exposed to physical danger. The "defense reaction," mediated by the autonomic nervous system, supposedly prepares the body to contend with such dangers. It has long been hypothesized that in urbanized society, the defense reaction leads to hypertension. Accordingly, environmental stressful stimuli in this society trigger this response and its resultant peripheral vasoconstricting hormonal effect, but there is no commensurate physical exertion needed to revert the body back to normal. Prominent metabolic changes associated with this response lead to elevated blood levels of glucose and free fatty acids. Landsberg's work in the last decade has shown that increased total caloric intake in general, and fat intake in particular, triggers a response that is very similar to the defense reaction, probably via the resulting hyperinsulinemia, whereas enhanced physical activity ameliorates this response.

Thus, the hormonal and metabolic changes that characterize the defense reaction and the environmental factors that trigger them are consistent not only with the development of hypertension but also with current concepts regarding etiology of obesity, glucose intolerance, dyslipoproteinemia, insulin resistance and ASCVD, or, in short, syndrome X.

We suggest that the androgenic hormonal profile has made the male sex more suitable for the role of hunter-gatherer through stronger musculature and bigger body build. However, irrespective of the individual hormonal profile, evolution favored men with a more effective defense reaction. This may have improved the survival of the male sex under traditional life-style but made them more prone to ASCVD in urbanized society.

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