It is well established that important differences exist between women and men with regard to the function and diseases of the cardiovascular system. Women appear to be protected from the most common form of cardiovascular disease, coronary heart disease, when compared to men. The reason(s) for this apparent protection in women are not fully understood and may not solely be related to hormonal differences. Data generated from epidemiological studies and basic science research about steroid hormone receptors and ion channels in cells provide evidence for distinct differences with regard to gender. Despite a wealth of surrogate endpoint and observational data suggesting hormones may play a cardioprotective role in women, clinical trials have yielded unexpected findings and at this time do not provide evidence to assert that hormone replacement therapy reduces the risk of cardiovascular events in women. We hope that this series of articles in the Spotlight issue will highlight some of the interesting gender differences in cardiovascular disease. We are pleased to present both invited reviews and original data.

The issue is divided into five sections covering a number of topics:

1. Gender and risk factors for cardiovascular disease

The issue begins with an overview of coronary heart disease comparing differences in risk factors between men and women, with an emphasis on menopause and cardiovascular risk [1]. It is salutary to consider that most women are unaware that, particularly in later ages, their risk of suffering from or dying of coronary heart disease is greater than any other disease process. The specific effect of age is discussed and gender differences in plasma lipids are highlighted to explain some of the differences [2]. Wenger [3] summarises current issues in the presentation, investigation and treatment of coronary heart disease in women and focuses on the specific management and assessment of coronary heart disease in women. Cigarette smoking as a risk factor for coronary heart disease in women is reviewed by Bolego et al. [4] reminding us that it is more detrimental in women than men. The importance of education for preventive efforts is stressed. The effect of a recently recognised cardiovascular risk factor, homocysteine is reviewed by Dimitrova et al. [5] and the same group demonstrates the beneficial effect of oestrogen on homocysteine-induced endothelial injury in male rats [6]. The mechanisms appear to involve glutathione and glucose-6-phosphate dehydrogenase activity.

2. Endothelial function, atherosclerosis and coronary artery function

There is a wealth of information on the effect of gonadal hormones, endothelial function and vascular reactivity reviewed by Sader and Celermajer [7]. An original paper by Chan et al. [10] describes how isoproterenol enhances estradiol-induced relaxation via endothelium-derived nitric oxide and cyclic-AMP, a novel mechanism. Nakano et al. [11] discuss the effect of oestrogen on platelet function in postmenopausal women. One of the possible detrimental effects of oestrogen on the cardiovascular system is an adverse action on prothrombosis. These authors report an anti aggregatory effect on platelets supporting a potential beneficial action. One facet of the effect of gender is the importance of gonadal hormones in the development of cardiovascular disease, particularly atheroma progression.
5. Gender and electrophysiology

The electrophysiological actions of hormones are discussed in an up-to-date review of the influence of gender and gonadal hormones on ventricular repolarization and arrhythmias by Pham and Rosen [21]. Original basic data on the effects of gonadal hormones on transmural dispersion of calcium currents in rabbit myocytes using patch clamp techniques are also presented [22]. The effect of gender on repolarization in ventricular myocytes is presented by Wu and Anderson [23], and finally, an original paper by Conrath et al. [24] describes gender differences in the long QT syndrome and the effects of beta-blockade.

This Spotlight on Gender issue should be thought provoking and we are delighted that we are able to publish original data as well as reviews on important cardiovascular gender related topics. Women have often been excluded from large cardiovascular trials, but recent efforts to address gender specific health issues has dramatically improved the amount of data available to help guide physicians to optimise the cardiovascular health of their female patients. Further research is needed, as there are important questions, which still need to be answered with regard to the complex interplay between gender, hormones and function of the cardiovascular system.

References


Mikkola and Clarkson review data from both human and animal studies [8]. They emphasise important issues such as oestrogen and progestogen combinations, effects on plasma lipids and lipoproteins and suggest the potential for early initiation of gonadal hormones, lower doses of hormones and different combinations of hormones to interact beneficially on the development of atherosclerosis. One hypothesis that has been advanced to explain the discrepant findings between clinical trials and other forms of evidence is that the trials completed to date have treated women who are decades past the menopause. It may be that to be effective, therapy needs to be initiated closer to the time of menopause or before vascular disease is well established. The diversity of the effects of sex steroids on cellular function is emphasised in a paper by Stork et al. [12] showing that oestrogen in postmenopausal women reduces levels of monocyte chemotacttractant protein-I. This is another potential mechanism by which oestrogen may reduce atheroma development. Elegant studies by White et al. [13] demonstrate direct cellular effects of oestrogen on calcium gating in isolated human coronary smooth muscle. A mouse model of ischaemia-reperfusion myocardial injury and the role of gender in this process is presented by Cross et al. [14] in an original paper. Finally a cardiological condition although rare, but which is most common in postmenopausal females, cardiac Syndrome X, is reviewed by Kaski [9].

3. The autonomic nervous system, renin–angiotensin system and hypertension

Gonadal hormones impact on other systems allied to cardiovascular function such as the renin–angiotensin system and the autonomic nervous system. The influence of gender on these systems is reviewed by Fisher et al. [15] and Dart et al. [16]. The importance of gender and sex hormones on blood pressure is reviewed by Dubey et al. [17].

4. Gender and the myocardium

In addition to important actions on the vasculature, gonadal hormones influence the myocardium. Myocardial cells have functional oestrogen receptors and the important regulatory effect of oestrogen on the myocardium is reviewed by Babiker et al. [18]. Women appear to have a lower prevalence and better prognosis of heart failure compared to men, as described by Luchner et al. by utilising the MONICA database to assess gender differences in parameters of left ventricular size and function [19]. Cardiac fibroblast proliferation and the effects of oestrogen and progesterone is investigated in an original paper by Mercier et al. [20].


