Cardiovascular benefits of HRT

Beneficial effects of oestrogen on metabolic risk factors for coronary heart disease (CHD), as well as on arterial function and on surrogate clinical markers of CHD, have been widely demonstrated. Thus hormone replacement therapy (HRT) should benefit CHD in postmenopausal women. Observational studies have consistently shown a benefit of HRT on CHD prevention, although it has been noted that the biggest beneficial impact has been seen in those women who initiated HRT close to the menopause. However, randomised clinical trials of HRT did not show any significant benefit on CHD, and there was even a report of harm from the initial publication of the Women’s Health Initiative (WHI). This has led to the abandonment of HRT for prevention of CHD by cardiologists and other physicians, but they have failed to realise the shortcomings in the interpretation of the data. Firstly, the WHI finding of a significant increase in CHD events was published in the preliminary analysis of their data of combined estrogen-progestogen HRT, and subsequent publications of the complete data did not confirm this. Indeed, there was a non-significant decrease in events seen with estrogen-alone HRT. Secondly, most randomised trials using defined clinical events as outcomes have studied just one dose of one HRT regimen, a dose inappropriately high with the average starting age of the participants being in their mid-sixties. In contrast, the observational population studies that do show benefit largely comprise women starting on HRT around the age of menopause, i.e. early fifties. In fact, it is the older women in the randomised trials that failed to show benefit, whereas there was evidence of benefit in the younger ones. A meta-analysis of 23 randomised trials including over 39,000 women showed a significant reduction in events in those women initiating HRT below age 60 years. Follow-up of the WHI estrogen-alone arm also showed a significant CHD benefit in those women initiating HRT below age 60 years. Thus, the age at initiation of HRT seems to be important for cardiovascular benefit and risk. This gives rise to the concept of a “window of opportunity” for HRT to help prevent CHD around the menopause, and the Danish Osteoporosis Prevention Study findings support this. This was a prospective clinical trial of 1000 women in the early postmenopause who were randomised to either HRT or no treatment, studied for 10 years and followed up for a further 6 years. HRT produced a significant reduction in a composite end-point of myocardial infarction, death or heart failure. Thus the totality of current evidence suggests that HRT is effective for the primary prevention of CHD in women when given appropriately. This could be an important option, as agents that are effective for the primary prevention...
of CHD in men do not appear as effective in women.