



Heart disease, cancer and hormone replacement therapy

The use of hormone replacement therapy (HRT) has been highly controversial in recent months. HRT was initially introduced to treat post menopausal symptoms in those women who suffered from flushes, vaginal dryness, mood changes, irritability, depression, fatigue or malaise accompanying or following menopause. HRT with oestrogen and progestin replaces the natural fall in the female hormones which accompanies the menopause. HRT was gradually taken up by many women for use on a long term basis, in an attempt to maintain some assumed aspects of femininity and youth. In the USA oestrogen alone tended to be preferred; in Australia a combination of oestrogen and progestin was commonly used. Hormone replacement could be from manufactured chemicals or refined from mare's urine.

A very large study in the USA (The Nurses' Study) showed that those who took long term HRT developed less heart attacks and suffered fewer deaths, although this was partly offset by a few extra uterine or breast cancers. This last was again somewhat offset by there being less colon cancers amongst those using HRT.

Thus it appeared that we had evidence to suggest that HRT could be taken by women after the menopause as a treatment to prevent heart disease and to delay death. It was recognised that those who took HRT were more likely to be those who

visited their doctor frequently, who were more health conscious and maybe more physically active and less overweight. There was some evidence that HRT may lower cholesterol levels and blood pressure. It was suggested that these effects on cholesterol and blood pressure could explain the possible mechanism of assumed benefit. However, there was also some evidence that HRT could lead to greater likelihood of developing venous blood clots (particularly deep vein thrombosis or DVT) – in a similar way to sitting for hours in an airplane could cause DVT. It was known that HRT reduced the incidence of hip fractures, arising because of osteoporosis (bone softening which accompanies ageing in some post-menopausal women).

Large studies were mounted to compare HRT with a placebo (an inactive tablet) in post menopausal women, with follow up over many years. The thoughts were:

- women who took HRT seemed to have fewer heart attacks
- women who took HRT long term were likely to be healthier on other grounds
- women who took HRT long term were likely to develop a few more cancers of the breast or cervix and a few less cancers of the colon.

Research questions were:

- Is it the HRT or the lifestyle factors which cause an apparent prevention of heart attacks?
- Would the possible benefits of HRT outweigh the potential hazards

One large study, published in 1998, reported on the outcome amongst women with known heart disease taking HRT (combined oestrogen and progestin) compared with women taking placebo tablets. These women were all at risk of episodes of heart disease

as they were already known to have heart disease. It appeared that HRT did not reduce the chances of having heart attacks. The other major study was of healthy women taking combined HRT to see if, compared with placebo, HRT prevented the development of heart disease. The HRT was found not to reduce heart attacks and other conditions caused by blood clotting: it increased them after the women had been taking combined HRT for five or more years. This, together with the tiny increase in cancers, led to the trial being terminated. There was no increase in the number of deaths amongst those taking HRT compared with deaths amongst those women taking placebos. The report was published in July this year.

The report was followed by a gross exaggeration of risks in the media. That publicity led to consequent attacks on the marketing practices of pharmaceutical companies and the attitudes of medical practitioners. It also frightened many people because of the possibility of developing cancer, particularly breast cancer.

There were over 16,000 women in the study. The chances of developing any cancer while taking HRT per year were 1.14% on HRT compared with 1.11% on placebo. That is an increased chance of 2.7%. That does not mean that 2.7% will develop cancer each year because of taking HRT; it still means that the increase is only 0.03% per year, ie three more cancers (14 in all) in 10,000 women each year, compared with 11 in all amongst 10,000 women taking placebo – a tiny increase but enough to stop the trial, which was now already showing that HRT increased rather than decreased heart disease.

Thus, the search for truth means that we are now back where we were 20 years ago. Combined HRT can be used to suppress menopausal symptoms, but it should not be used to suppress possible heart attacks. Hence it should not be taken on a long term basis (over several years).

That means that other methods should be used to reduce post menopausal osteoporosis. We must also look elsewhere to reduce the incidence of heart disease in older women.

It is of interest that another large study of HRT continues with oestrogen alone, compared with placebo. It has not yet been shown to be dangerous. It has not yet been shown to be beneficial. Maybe oestrogen alone is safe and effective; maybe not.

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