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Prevention
Tto preventive

Genetic predisposition to breast cancer

In Western society there are many women who think that they may be at increased risk of developing breast cancer because of a family history; they ask for advice. There often follows referral to a breast clinic where those at increased risk can be identified. Many of the fears that these women have are groundless but it is important that a specialized breast service can identify those at risk and counsel them accordingly. As this is a rapidly developing field, with an increasing understanding of genetic aspects, it may be difficult to provide the advice that is needed. It is therefore important that breast specialists develop a common strategy and collect information about incidence and outcome.

Any management strategy must be provisional because there is so much that is unknown, but without an identified way of defining high or moderate risk, and without a uniform management plan, there will be no progress. Women should be warned that there are no clear answers. This presents psychological dilemmas as patients prefer clear information presented with confidence and security. Whatever management strategy is proposed may be incorrect; this creates an ethical dilemma, but so does doing nothing. It is therefore vital to record strategy, treatment and outcomes.

What are the risks?

Information from the Cancer and Steroid Hormone Case–Control Study[1] and the Breast Cancer Detection Demonstration Project[2] allows an estimate of risk to be made. For example, a woman aged 50 years who has a sister with breast cancer has an estimated lifetime risk of 3·6 (95 per cent confidence interval (c.i.) 2·1–6·1), but a woman aged 50 years with both a mother affected premenopausally and a sister affected has an estimated lifetime risk of 17·1 (95 per cent c.i. 9·4–31·3). Gail *et al.*[3] have constructed a projected probabilities table which may be used to estimate individual risk. The risks can be categorized as follows: (a) high risk – women in families with four or more relatives affected with either breast or ovarian cancer in three generations and one living affected individual; and (b) moderate risk – three first- or second-degree relatives with breast or ovarian cancer on the same side of the family, or two first- or second-degree relatives with breast cancer diagnosed under the age of 60 years, or one first-degree female relative with breast cancer diagnosed under the age of 40 years, or one or more first-degree relatives with bilateral breast cancer.

What can be offered to women at risk?

It might be argued that there is very little that can meaningfully be offered. If a woman has a high risk, bilateral mastectomy might be considered, with or without reconstruction. This does not guarantee the removal of all breast epithelium and, although the risk might be lowered[4], it is not abolished. Women at high or moderate risk might be offered tamoxifen chemoprevention, but the benefit of this is unproven. When the International Breast Intervention Study and similar trials are completed, more information will be available but results and conclusions will not be ready for 5 years. Annual clinical examination and mammography can be offered but evidence suggests that such screening is not effective in younger women; nevertheless it might be effective in a group at high or moderate risk. The predictive value of genetic testing for mutations of the *BRCA1* and *BRCA2* genes is not clear. Women with breast cancer with such mutations have a 65 per cent risk of contralateral malignant breast disease[5], but the chance that a woman from a breast cancer family carries a mutation[6] is only seven in 100. It is unlikely that genetic testing, in the present state of knowledge, would alter management.

Management strategy

Despite these problems, breast surgeons should develop a common management strategy and collect data that emerges from it. Such a strategy should be capable of

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adjustment as and when new information becomes available. A possible plan might be as follows:

1 All women at high risk
   - Annual mammography
   - Teaching of breast self-awareness
   - Tamoxifen chemoprevention trial
   - Consultation with medical geneticist and discussion of bilateral mastectomy
   - (Gene testing not indicated[7])

2 Women aged 30–35 years at moderate risk
   - Annual mammography from 5 years below the age of the youngest relative with breast cancer (if the patient is over 30 years old)
   - Teaching of breast self-awareness

3 Women aged 35–50 years at moderate risk
   - Annual mammography
   - Teaching of breast self-awareness
   - Tamoxifen chemoprevention trial

4 Women aged over 50 years at moderate risk
   - Mammography every 3 years in the National Health Service breast screening programme
   - Teaching of breast self-awareness
   - Tamoxifen chemoprevention trial

Such a programme may be hypothetical and empirical but no apology is tendered. National organization and planning is needed to replace the current variability and uncertainty, and to measure the effectiveness of this strategy.

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