98. HORMONAL INFLUENCES IN HEREDITARY BREAST CANCER

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Approximately 5 to 10% of all breast cancer (BC) cases are hereditary. Germline mutations in the tumour suppressor genes, BRCA1 and BRCA2, account for up to 40% of hereditary cases. Carrying a mutation in either of these genes confers a high lifetime risk for female BC. Hormonal factors may modify BC risk in BRCA1 and BRCA2 carriers. Recent studies of BRCA1 and BRCA2 carriers show that (premenopausal) prophylactic oophorectomy decreases BC risk by about 50%. Conversely, use of the oral contraceptive pill (particularly for greater than 5 years or if started before age 30) may be associated with a significantly increased risk for BC in BRCA1 carriers. Also, BRCA1 or BRCA2 mutation carriers who have had a full term pregnancy may be more likely to develop BC by age 40 than nulliparous carriers. Unfortunately, data on the role of the anti-oestrogen Tamoxifen for BC prevention in mutation carriers is limited and conflicting. Importantly, the results of most studies to date of BC risk modifiers (including hormonal factors) in BRCA1 and BRCA2 carriers must be interpreted with caution. Most have been retrospective prevalent case-control studies using living cases of BC drawn from families with multiple cases of the disease. Data collection has thus usually been restricted to survivors and their living relatives, and data on exposures to potential risk modifiers have been based on recall of life events many decades earlier. These have been opportunistic, rather than designed, research studies and thus there is a high likelihood of systematic biases. Randomised controlled trials of most potential modifiers (e.g. prophylactic surgery, use of the oral contraceptive pill, parity) are not feasible. Thus it is recognized that long-term prospective, systematic follow-up of large BC family cohorts, will provide better information. Such a study is currently underway in Australasia as part of the Kathleen Cuningham Foundation for Research into Familial Breast Cancer (kConFab). Such studies are essential in order to optimise the clinical risk management strategies of individuals attending Family Cancer Centres, and hence reduce the morbidity and mortality of hereditary BC.

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