Introduction

Familial breast cancer screening: ethical and social implications

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The identification of BRCA1 in 1993 after years of suspecting the presence of a gene implicated in familial breast and ovarian cancers accelerated the pace of research into risk factors associated with these two feared cancers of women. This supplement presents a cross-section of how this research is being integrated into the formulation of preventive measures, screening and medical care across geographical and socioeconomic boundaries in Europe and North America. Many questions are being raised which will hopefully prove useful to oncologists, laboratory scientists and government agencies that are involved in the development of strategies for dealing with these new biomedical frontiers. Most importantly, these issues will be responsive to the needs of women at familial high risk of cancer, as well as to those with uncertain risk who reach an age where routine screening may prove useful. The following areas are highlighted in the manuscripts included in this supplement:

(i) Genetics and impact of genetic testing. Our knowledge of genetic alterations in hereditary breast cancer is summarized by Cipollini et al. [1]. In particular, they stress the importance of expanding our current knowledge of BRCA1 and -2 mutations to various demographic populations. In addition, further investigations are needed on the pathways, perhaps environmentally mediated, that lead to molecular events responsible for the development of a malignancy in women harboring mutations. It is commendable that a consortium has been initiated in Italy to collect information on these mutations, and several founder mutations have been identified among 1758 families studied. European collaboration under sponsorship of the EMQN has worked further, not only in collecting data from a number of countries, but in establishing quality control procedures for confirming information from individual laboratories, as reported by Mueller et al. [2]. These efforts should accelerate the availability of accurate genetic testing information to women across geographical boundaries. However, as with any newly introduced health care procedure, its impact is initially uncertain. Hughes [3] reviews several aspects of genetic testing, including the rates of genetic test acceptance, the psychological impact of such testing and the extent of family communication. Although some aspects are intuitively obvious (that positive results generate more anxiety than negative), others, such as the low utilization (<50%) of screening procedures by mutation carriers within 1 year following genetic testing, are somewhat surprising. Bruno et al. [4], in the Puglia region of Italy, obtained data from 677 healthy women through a questionnaire prior to implementing molecular screening programs. The interest in genetic testing was high, but there was an unrealistic appreciation of what information genetic testing would provide, and interest was primarily driven by concern about their children and altruistic considerations rather than by possible personal clinical benefit in modifying screening and diagnostic approaches. These manuscripts, as a whole, emphasize the need for gathering more information of the genetic risks for women in terms of breast and gynecological cancers, and enhancing the dissemination of this information.

(ii) Diagnostic interventions for women at risk. While screening procedures for the detection of ovarian cancer have not proceeded to widespread application, mammography has been widely applied, but is embroiled in controversy (concerning age of onset and occasionally also its overall contribution to improved outcome) as to its usefulness when applied to the general population. Smith and Andreopoulou [5] review the development of more sensitive means for the detection of breast cancer in women at high risk of breast cancer. Magnetic resonance imaging (MRI) may be particularly useful in this high-risk population: it can detect multifocal disease and also increases the limit of detection. Some technical improvements must be introduced in order to enhance its specificity and also to permit imaging-guided biopsies. However, there is already convincing evidence that MRI may play a role in the identification and follow-up of women who are BRCA1 and BRCA2 mutation carriers. Such specialized screening programs, some of them of considerable size (as presented by investigators from Germany and The Netherlands in the 2002 plenary session of ASCO) [6], may have a psychological impact on the women who undergo these procedures. The study by Warner [7] fulfills the need to assess such procedures, not only in terms of efficacy of preventing the development of cancer, but also in terms of the accompanying psychosocial issues and adjustment. Such information is needed before the widespread use of these screening techniques in these women.

(iii) Therapeutic (chemopreventive) measures. An overview of interventions is provided by Marchetti et al. [8]. Although prophylactic mastectomy probably represents the ‘goldstandard’ for breast cancer prevention among women at the highest risk, it is imperative to seek alternatives. Prevention trials

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utilizing tamoxifen have provided evidence of an effect in large studies, but a preventive effect in women who are mutation carriers is not clear at present. Moreover, there are issues concerning cardiovascular risks and risks of uterine cancer that encourage the search for other agents with similar or improved efficacy. Trials with other selective estrogen receptor modulators or with aromatase inhibitors are underway, and should prove very informative in the years to come. Hughes [3] has also reviewed some of the psychosocial issues around chemoprevention trials.

(iv) Advocacy, cost-effectiveness and ethical implications. Surbone [9] introduces the subject of science and morality, and while two more manuscripts deal with various social and ethical aspects of screening programs and of genetic testing [10, 11]. Mosconi and Leccese [10] describe the role of advocacy in ensuring widespread application of programs that deal with all aspects of breast cancer, including early diagnosis. On the other hand, governmental entities have been concerned with cost/benefit issues, and Møller [11] gives a detailed description of these as they apply to the diagnosis of inherited breast cancer. Finally, it is obvious that such issues will differ between socioeconomic groups.

The importance of developing an integrative approach towards achieving the goal of primary prevention of breast and ovarian cancers and the problems that may be encountered cannot be overemphasized. This supplement provides a glimpse at research in this area, and issues that have been raised by investigators covering this topic from a wide variety of perspectives.

References