The Epidemiology and Aetiology of Female Breast Cancer

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This issue of BREAST CARE focuses on the epidemiology and aetiology of female breast cancer. Katalinic et al. [1] provide an interesting update of the incidence and mortality patterns of breast cancer in Germany. Based on their analyses, they are able to corroborate the recent association between decrease of hormone therapy (HT) among postmenopausal women and breast cancer incidence, as has been seen in many other countries. After more than 30 years of breast cancer incidence increase, this is good news. Even nowadays, East Germany shows considerably lower incidences of breast cancer than West Germany. Katalinic et al. give some interesting insights into the explanations for these findings.

In their narrative review, Kluttig and Schmidt-Pokrzywniak [2] give an overview of the established risk factors of breast cancer. Their review summarises results of meta-analyses and literature reviews. It helps to condense the huge amount of available literature on the risk factors of breast cancer. They conclude that preventive action against the risk factors of breast cancer could also have a beneficial effect on other diseases, including type 2 diabetes and cardiovascular diseases.

Schreer [3] gives an update on the increasing evidence that dense breast tissue is an independent risk factor for breast cancer. Besides age and mutations in the high-risk genes BRCA1 or BRCA2, dense breast tissue constitutes one of the highest risk factors. Although the association is well established, there is a lack of standardised methods to quantitatively measure breast density as a prerequisite for the offer of intensified surveillance. Also, reliable and prospective clinical data are missing that would provide clear evidence for the effectiveness of intensified surveillance strategies such as shorter mammographic intervals or the added value of ultrasound. The explicit illustration of the current dissatisfactory situation provides a rationale for the initiation of prospective studies.

Meindl [4] summarises the current search for new susceptibility genes. Given the fact that no further high-pen-

etrance gene was found by linkage analysis of large cohorts of BRCA1- and BRCA2-negative high-risk families within the last decade, the hypothesis emerged that low-susceptibility genes inherited in a complex genetic trait may be the underlying cause for the remaining unexplained familial risk. This hypothesis was further supported by twin studies. A proof of principle was provided last year by the identification of low-susceptibility alleles in several genome-wide association studies. Now the challenge is to identify the underlying genes, their function, the interaction, and the cumulated risks conferred by these alleles. Besides a complex genetic trait, an alternative explanation would be the existence of many more very rare genes with high penetrance transmitted by a dominant trait, thus allocating a distinct gene to only a few families. Candidate gene approaches have already identified a few of such genes providing the rationale for high throughput sequencing studies for the identification of such novel genes.

Another much discussed topic in breast cancer epidemiology is the amount of breast cancer overdiagnosis and spontaneous regression of invasive breast cancer in mammography screening programmes. Recently, Zahl et al. [5] published a provoking analysis of data from Norwegian counties before and after the initiation of mammography screening that triggered much debate. Zahl and his colleagues considered the possibility of spontaneous regression in screen-detected invasive breast cancer. To address this issue, they compared the 6-year cumulative incidence of breast cancer in a cohort of women aged 50–64 years at the start of the programme with that of an age-matched cohort from 4 years earlier. If spontaneous regression did not occur, i.e. if all screen-detected breast cancers were to progress or even remain the same size, the cumulative incidence in the 2 cohorts would therefore be expected to be equal. As expected, invitation to the first screening round was associated with a dramatic rise in invasive breast cancer relative to the age-matched control

cohort. As time passed and cancer in the control group had the opportunity to become clinically evident, the difference narrowed. However, even after prevalence screening in the control cohort, the cumulative incidence of invasive breast cancer remained 22% higher in the screened cohort (6-year cumulative incidence: 1,909 vs. 1,564 per 100,000 women, relative risk 1.22, 95% confidence interval 1.16–1.30). Zahl et al. conclude that some invasive breast cancers detected by repeated mammography would not persist to be detectable by a single screening at the end of the 6 years. In other words, the natural course for some screen-detected breast cancers may be to spontaneously regress. Interestingly, a Canadian trial of women aged 40–49 years that had a truly unscreened control group also found an excess incidence of 22% in the screened group [6]. Although the study of Zahl et al. was not based on a randomised trial, it has several strengths. It was a population-based study with high participation rates, and outcomes were assessed by a virtually complete registration via the nationwide cancer registry in Norway. The provoking findings of Zahl et al. reveal that little is known about the spontaneous regression of invasive breast cancer and that further studies are needed to address this question.

References

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