synergistic effect with *cis*-diamminedichloroplatinum, but not doxorubicin, *in vitro*. Presently, one of his antibodies is in phase 1 clinical trials to assess lack of toxicity in humans and localisation to tumours. N. Hynes has used rDNA technology to produce an immunotoxin. The heavy and light variable domains of one antibody were cloned and a fusion gene coding for a single chain antibody molecule was produced by linking the two domains by a short nucleotide sequence. This fragment was then coupled to a sequence encoding a modified exotoxin A and the whole was expressed in *E. coli*. The immunotoxin thus produced specifically bound to *erb*B-2 protein, inhibited protein synthesis in *erb*B-2 expressing cells and tumour growth in nude mice in a dose-dependent fashion and was considered to have therapeutic potential.

PREVENTION

In view of the real but limited success of existing treatments and the time required for new treatment strategies to get off the ground and enter phase III clinical trials, it is eminently sensible to look at prevention methods that could exploit available medications. Aside dietary fat restriction, several types of drug are reputed to possess a preventive action: tamoxifen, retinoids, oral contraceptives and the progestin gestodene. A retrospective analysis of 10 000 patients included in various tamoxifen trials has shown that there was a one-third reduction in the development of contralateral tumours in the tamoxifen-treated compared to control groups. Such observations and others have led to the setting up of three large-scale trials designed to evaluate the benefits of tamoxifen in prevention. In the trial coordinated by the U.K. and presented by J. Cuzick (London), 15 000–25 000 women will be randomised to receive 20 mg/day for 5 years. Inclusion criteria will be based on the following risk factors: family history (relatedness, age at onset, bilaterality, multiple affected relatives), abnormal pathology (biopsy-proven breast disease except for fibro-adenoma, lobular cancer *in situ*, atypical hyperplasia), nulliparity and mammographic dysplasia.

The use of this type of anti-oestrogen as a preventive measure raised some anxieties. First of all, there have been reports of iatrogenic endometrial cancer but as pointed out by M. Namer (Nice) the estimated benefit afforded by tamoxifen should be weighed against the expected low incidence of endometrial cancer. Fears were also voiced by F. Kuttenn and P. Mauvais-Jarvis (Paris) that, in healthy women, the administration of tamoxifen would lead to polycystic ovaries and high production of oestrogens thus overwhelming the action of the drug. A proposed solution to this problem was a gel formulation of *trans*4-hydroxy-tamoxifen for local administration to the breast.Cell-culture experiments implied that this tactic might be effective and that isomerisation to the *cis*-hydroxy compound would not be a problem.

Concluding remark

As stressed at this symposium on 'Hormones and Breast Cancer—From Biology to the Clinic', the gap between laboratory research and the clinical availability of new treatments is still wide in spite of sustained efforts to improve upon existing drugs, to find new applications for them, to design biologicals on the basis of state-of-the-art knowledge of cellular mechanisms of action, and also in spite of efforts to identify modalities for the prevention of disease in high-risk populations.

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Letters

Follow-up of Breast Cancer patients Stage I–II

Stefano Ciatto

IN THEIR paper Hannisdal *et al.* (992–997) provide further evidence of the lack of efficacy of instrumental tests (chest X-ray, bone X-ray, bone scan) in improving prognosis when used in the periodic follow-up of breast cancer patients. This finding is consistent with other reports comparing the prognosis of asymptomatic and symptomatic recurrent patients and challenges the common and expensive practice of instrumental periodic follow-up.

On the contrary, I do not understand their enthusiam for the use of blood tests as a convenient alternative. According to their results a panel of three tests (alkaline phosphatase, erythrocyte sedimentation rate and glutamyltransferase) had a sensitivity of only 31%. Increasing the sensitivity to 56% would cause the specificity to drop to 91%. Blood tests do not seem to be superior to instrumental tests and the authors provide no evidence that early detection by blood tests may have any favourable impact on prognosis. They also provide no evidence to support the statement that blood tests may be important "to avoid unnecessary morbidity" in recurrent cases. Even admitting such a benefit, someone might argue that the morbidity of earlier treatment of asymptomatic metastases would minimise the final effect on the quality of life.

It seems to me that the paper provides convincing evidence that following up breast cancer patients with blood tests, as well as with instrumental tests, has probably no favourable impact on prognosis. Periodic follow-up should be based on history/physical examination/mammography and diagnostic assessment with blood and instrumental tests should be limited to symptomatic/suspected cases.

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