

Breast cancer over the past 100 years

As we approach the end of the 20th century, it is salutary to appreciate that 100 years has passed since William Stewart Halsted designed on anatomical principles, an operation which, in modified form, many surgeons still regard as the best treatment for cancer of the female breast.¹ There is now clear evidence from a meta-analysis of nine randomised trials including more than 4800 women that local excision of the tumour combined with radical radiotherapy gives equal survival. For six studies (involving 3107 women) there were fewer recurrences with mastectomy, but this difference was not significant.² This observation is not new. In 1920, Geoffrey Keynes was exploring the use of radium implants for the treatment of breast cancer in St. Bartholomew's Hospital, London. After observing "astonishingly good results" in patients with inoperable disease, he extended this treatment in combination with local excision of the tumour, to early cases. In 1936, he reported that the results equalled those of the Halsted procedure.³ It has taken 60 years to provide proof. Not all patients are suitable for such breast-preserving treatment, and physical, radiological, and pathological considerations must be taken into account when advising patients. This makes demands on the time of the surgeon, who may prefer the simpler approach of mastectomy. If this is the case, the surgeon must make the patient aware that reconstruction of the breast can be carried out as a primary or delayed procedure.

Halsted's initial objective was to improve the unacceptably high local recurrence rates seen following mastectomy in European centres, where many patients then presented with locally advanced disease. He concluded that "if three years had passed without detecting either local recurrence or symptoms of internal disease, one could feel sure that a cure had been achieved." This view agreed with the accepted dogma of the time that breast cancer was primarily a loco-regional disease, spreading by a wave-like permeation along the lymphatics to the regional nodes, where initially it was contained, only later spreading systemi-

cally to distant sites.⁴ Fifty years passed before the results of long term follow up studies of patients treated by radical local surgery (such as that of Brinkley and Haybittle) revealed the fallacy of this belief by demonstrating that an excess mortality from metastatic disease persisted for more than 30 years.⁵ Invasive breast cancer is now recognised as being a chronically progressive disease which gives rise to systemic micrometastases early in its natural history. Because of its heterogeneous biology, the time lapse before these metastases become clinically evident varies greatly. The management of primary breast cancer must now include not only local control but also the eradication of micrometastatic disease. This requires systemic treatment.

One hundred years have also passed since George Beatson first demonstrated that the behaviour of recurrent breast cancer could be influenced by removal of the ovaries. This was subsequently shown to be due to the deprivation of oestrogen.⁶ Recognition that this effect was limited to premenopausal women, led to the use of crude pharmacological antagonists of oestrogen in older women and later, to procedures such as adrenalectomy and hypophysectomy.⁷ These have now been superseded by the anti-oestrogen product, tamoxifen, which is the preferred first-line treatment for advanced disease.⁸ Cytotoxic chemotherapy has generally been used as a second-line treatment.

Sporadic reports of the use of ovarian ablation as an adjuvant to the local treatment of early breast cancer began to appear during the middle of this century. In 1953, Ralston Paterson in Manchester tested this in a randomised trial, the first ever in the management of breast cancer.⁹ Later trials of adjuvant systemic therapy have concentrated on tamoxifen and cytotoxic chemotherapy, and there is now unequivocal evidence that all three approaches reduce mortality. The meta-analysis of 133 randomised trials involving 31 000 recurrences and 24 000 deaths among 75 000 women reported by the Early Breast Cancer Trialists' Collabo-

rative Group has shown that the annual odds of recurrence or death are reduced by 25% following ovarian ablation in young women and by tamoxifen and polychemotherapy at any age.¹⁰ Although this effect may appear to be modest, it represents a reduction in mortality at 10 years which approximates 10% in node-positive and 5% in node-negative patients. In worldwide terms this amounts to a reduction or delay of 100 000 deaths for every 1 million women with breast cancer.

Adjuvant systemic therapy must now be considered part of the initial treatment of all women presenting with primary breast cancer. The choice depends on a number of factors, including the extent and aggressiveness of the tumour, its oestrogen receptor status, and the availability, cost and risks of treatment. Only in those with minimal disease of good prognostic type can the need to treat micrometastases be disregarded.

The genetic changes which lead to the development of invasive and metastasising characteristics in cancer cells are time-dependent. The detection of breast cancer during its pre-clinical phase is a desirable objective and this can be achieved by using screening mammography. The results of eight randomised trials including more than 500 000 invited women, now indicate a reduction in breast cancer mortality in women older than 50 years of age by 25%, with this effect persisting for at least 10 years.¹¹⁻¹³ It is now 100 years since Roentgen first discovered X-rays, and 85 years since the German pathologist Salomon recognised their potential value in detecting occult cancers in mastectomy specimens.¹⁴ However, it was only in the 1960s that the coordinated effort required for the development of modern high-quality mammography occurred and the first randomised trial of population screening was initiated.^{15,16}

A screening mammogram is not a diagnostic test, only identifying women in whom an abnormality requires further investigation. If unnecessary biopsies for benign conditions are to be kept to a minimum, these further tests (e.g. sophisticated imaging, stereotactic localisation procedures, fine-needle aspiration cytology [FNAC]) must be of high quality. This demands expertise and experience. In the United Kingdom, multidisciplinary assessment teams, which include radiologists, cytologists, histopathologists and surgeons, are part of the national screening programme. These teams aim to reach a pre-operative diagnosis wherever possible. Surgical biopsy rates are low (re-

ported figures for the more than 1.2 million women screened in 1993-1994 are 0.76%) and malignant to benign ratios are high (13:1).¹⁷ For women with clinically palpable disease, whether detected by screening or through self-discovery of the lump, mammography and FNAC now allow an immediate and confident diagnosis in nearly all patients.

Although progress in the management of breast cancer during this century may appear to have been slow, it is now substantial. Mortality due to the disease in the West is decreasing.¹⁸ However, for a woman to benefit, she must be aware of the available options, and recognise that these can be best delivered by multidisciplinary breast-care teams, the development of which is being recommended by professional bodies in the United Kingdom.^{19,20} As participation in the decision-making process is complex, professionally trained counsellors, armed with the basic knowledge and understanding to enable them to recognise a patient's needs, have become essential members of these teams.

Breast cancer is on the increase in Hong Kong. The seminar on breast cancer published in this issue of the *Journal*, which indicates that the required expertise is available to Hong Kong women, is therefore timely.

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