

Sir James Young Simpson Memorial Lecture 1995 Breast cancer prevention: a pathologist's approach

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Few would argue that there is not substantial room for an improvement in breast cancer practice. It has to be borne in mind that the United Kingdom experience in the 1980s was a 50:50 survival to death ratio in the 10 years after diagnosis. Preliminary analysis of the effects of mammographic screening suggests that there will be a real but small fall in overall mortality. Existing practice involves three stages: first, the 'earliest' detection of a lump by palpation or imaging; second, diagnosis by histopathology; and third, treatment by surgery, etc. Evidence is given that the limited success of existing practice could be due, in part, to a failure to recognize the precancerous state of the mammary tissue as a whole in cancer cases; and a failure to exploit this state for earlier diagnosis. In support of these contentions, comparative data from the microscopy of cancer-associated breasts and age-matched normal breasts are given. There is a gross excess of focal hyperplasia in premenopausal cancer-associated breast tissue. Further, epidemiological data are consistent in that the tissue is subject to a sixfold increase in the risk of further primary carcinogenesis. A method is presented for detecting the cancer-associated breast. It exploits the breast menstrual cycle, a subject which is reviewed *in extenso*. Physiologically the premenopausal mammary tissue goes into a monthly pregnancy rehearsal with glandular proliferation and increased blood supply. The latter effects a luteal heat cycle, which can be measured readily by an electronic thermometric bra as increased breast surface temperature (1°C). Data are presented in terms of 50 normal breasts and 41 cancer-associated breasts studied daily (with progesterone assays) for one menstrual cycle. The cancer-associated breasts exhibit an absent or altered response to endogenous progesterone during the luteal phase of the menstrual cycle. The abnormality in the luteal heat cycle is maximal during the few days just after ovulation. Our data indicate that a 1-h clinical test at this time achieves a sensitivity of 71% and a specificity of 80% for 'clinically normal' yet cancer-associated breast tissue. Such patients would be candidates for increased surveillance and chemoprevention.

Keywords: breast cancer, chronobra, mammary menstrual cycle.

HISTORICAL FAILURE TO CONTROL THE DISEASE

In 1827 at Edinburgh Royal Infirmary a Highland woman was undergoing the amputation of a cancerous breast. The operator was Robert Liston, one of the fastest surgeons of the day. This was the pre-anesthetic era when strong men were required to hold the patient down, mechanical restraints were necessary so that the surgeon could move quickly, and copious sawdust on the floor to catch the blood. As was usual, many medical students came to watch. Among them, James Young Simpson. He was appalled at what he saw. He rushed out of the theatre and ran to Parliament Square where he tried to enrol as a law student.¹

These events occurred 168 years ago. What improvements have taken place during that time? Anesthetics certainly, but today's women are clamouring for 'something to be done', and the reason is not hard to identify.

With the prevailing practice of the 1980s the overall survival:death ratio at 10 years is 50:50 in the West of Scotland population of 1.5 m.² Another statistic is that each year in the UK there are 24 000 new cases and 15 000 deaths from the disease.³ This implies a death rate of 63%. Considering the excellent prog-

nosis of treated squamous carcinoma of the skin, the skin-gland nature of the breast, the breast's superficiality and its non-vital function, could we not have expected better results by 1995?

It may well be that our biological perceptions of breast cancer are flawed and that this has led to defects in our methodology employed to control the disease. These methods can be briefly reviewed as follows. Diagnosis starts with the detection of a lump. It is considered that if this could be removed before the cancer cells have spread, the patient would be cured. Palpation is the time-honoured method to detect the lump and surgical discussion centres on the extent of the surgery, whether or not it should be complemented by radiotherapy, chemotherapy, etc. Recently X-ray imaging has supplemented palpation, and smaller lumps can now be detected in the post-menopausal breast; but is there a fall in mortality due to breast cancer? An authoritative review in July 1995 in *The Lancet*⁴ concluded that case-control comparisons in Malmö (1988), Edinburgh (1990), Stockholm (1991) and Canada (1992) had failed, thus far, to show a statistically significant fall in the death rate in the screened versus the non-screened population. The most likely outcome of the mammography initiatives is that a small reduction in mortality reported will, over a longer span, achieve statistical significance but the effect will be modest and therefore 'very expensive' in Public Health terms.⁴ Also, the age group on which mammography will be effective will be small. If the original age guidelines for UK screening³ are applied to the Glasgow Royal

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