Multicentricity and recurrence of breast cancer

Sir—In response to Sacchini’s Nov 9 commentary on multicentricity and breast cancer recurrence, we feel that it is essential that some factual errors with respect to Vaidya and colleagues’ study are corrected, and, more importantly, that the biological and therapeutic implications of this study are emphasised.

Both Holland and colleagues1 and Vaidya’s studies used the same Egan’s correlated pathological-radiological method, and the overall frequency (63%) as well as the distribution of multicentric foci (MCF) in terms of their distances from the primary tumour were similar in the two investigations. However, Vaidya and co-workers did further two-dimension and three-dimension analyses and took the size of each breast into account. They showed that the distributions of primary tumours and MCF in the four breast quadrants differed significantly (p=0·04). The primary tumour was more common in the upper outer quadrant whereas MCF were widely distributed in all four quadrants. MCF were present beyond the index quadrant (25% of breast volume including the tumour) in as many as 79% of breasts that harboured MCF, and in half the cases when all breasts were considered. Thus, even if a quadrant were excised, 50% of patients would still have MCF left behind, which is in variance with the suggestion in Holland’s earlier study1 that MCF are contained within the index quadrant in 90% of cases.

The biological significance of Vaidya and colleagues’ study is in a way, paradoxical. In large studies of breast conservative therapy that were reviewed, greater than 90% of early breast recurrences occurred in the index quadrant; this is true whether or not radiotherapy is given.4 In view of the new findings, if MCF were giving rise to these recurrences then half would have occurred in other quadrants, and, therefore, MCF probably do not give rise to early breast recurrence. MCF in the index breast probably behave in a fashion similar to putative MCF present in the contralateral breast, since recurrence rate in the remaining quadrants of the index breast is even less than that in the contralateral breast.5 We also know that local recurrence occurs in the index quadrant irrespective of clear margins, which suggests that it does not arise from overlooked tumour. We therefore propose that the recurrence arises (a) from circulating metastatic cancer cells lodging in the highly vascular surgical bed (local relapse does harbinger a poorer prognosis), or (b) from local transfection of surrounding breast epithelium by nuclear material released from the original malignant clone resulting in artefactual mutagenesis. Thus although the margins of excision are morphologically clear they may be genetically unstable. The logical sequel to this study is a clinical trial to test whether radiotherapy to the index quadrant alone can achieve good local control. We have begun pilot studies.

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Sir—In reply to Baas and colleagues, I clearly stated in my commentary that the discrepancy in the finding of multicentricity of breast cancer in Vaidya’s and Holland’s papers may have been due to the fact that “Holland et al carried out one-dimensional analysis instead of two-dimensional analyses, and they did not take size of the breast into account”. I also emphasised a possible biological difference: “moreover, multicentricity foci may differ from residual tumour in biological potential and hence clinical progression.”

In stating that “MCF in the index breast probably behave in a fashion similar to putative MCF present in the contralateral breast, since recurrence rate in the remaining quadrants of the index breast is even less than that in the contralateral breast,”6 we also know that local recurrence occurs in the index quadrant irrespective of clear margins” is not wholly true. Many workers have shown an increased risk of local recurrences in both invasive and in-situ breast cancer when the resection margin is involved, emphasising the origin or recurrences from the residual primary disease. The implant of circulating metastatic cells in the higher vascular bed of the excised tumour may be another, less frequent, mechanism of local recurrences. This mechanism may be common in local relapses after demolitive surgery, in which local relapses themselves represent a poor prognostic factor. In conservative surgery of the breast, local recurrences and distant metastases are partly independent events that occur at different times, and several predicting factors also differ.7 The biological hypothesis stated by Vaidya is undoubtedly of interest, and could be the basis of further studies.

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Author’s reply

Sir—Sacchini1 suggests that the emerging technique of magnetic resonance imaging (MRI) might be able to detect multiple foci of breast cancer in vivo. There is already evidence to this effect with the various forms of MRI mammography proving consistently better than traditional radiographic mammography in this respect.2,3

In our initial series of 45 patients with invasive breast cancer, dynamic MRI mammography detected multicentric disease that had not been previously identified by clinical examination or radiographic mammography in 14 (31%) women.4 We have also used dynamic M R I mammography to screen a separate group of 105 women for residual tumour or local recurrence 1–2 years after breast-conserving surgery and radiotherapy and found clinically significant lesions in only nine (8·5%). Clinical and mammographic follow-up is continuing for these patients, and at a median of 341 (IQR 168–451) days after M R I mammography no further lesions have been identified. We therefore propose that the recurrence arises (a) from circulating metastatic cancer cells lodging in the highly vascular surgical bed (local relapse does harbinger a poorer prognosis), or (b) from local...
those discovered at follow-up implies that the radiotherapy and hormonal treatment given after breast conserving surgery without radiotherapy is generally accepted to be greater than 30%. The true rate of multicentric disease is probably even higher than that detected by MRI mammography because, at the resolution achieved with this technique, lesions less than a few millimetres in diameter can be missed. Even accepting this potential inaccuracy, we have found that only about 29% of those multicentric lesions identified by MRI are visible on X-ray mammography.

The use of MRI mammography to evaluate women with primary breast cancers would undoubtedly increase the number of mastectomies done for multicentric disease that would previously have remained undetected. It is therefore important that, before MRI mammography becomes a clinically established technique, a prospective trial is done to compare the outcome of women assessed with traditional imaging techniques and those evaluated with MRI mammography. Such an investigation would establish whether any clinical benefit is accrued from the increased detection of multicentric disease.

Acknowledgements P J Drew, L W Turnbull, M J Kerin, P J Carleton, J N Fox
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2 Cross MJ, Harms SE, Cheek H, et al. New investigation would establish whether any clinical benefit is accrued from the increased detection of multicentric disease.

Helicobacter pylori infection in children

Sir—In her Nov 9 news item, Fricker (p 1301)1 reviews Staat and colleagues’2 report of the prevalence of H pylori infection among American children and adolescents. It is now accepted that H pylori is an infection that almost always arises in childhood.2 It is not, however, known

Abdominal aortic screening programme

Sir—We started a screening programme for aortic aneurysms in general practice, similar to that described by Jones and colleagues (Nov 9, p 1320),1 in 1991 in the East Glamorgan area, coordinated by a hospital consultant. Patients were first requested to attend hospital for ultrasound screening by a consultant radiologist. We achieved an attendance rate of only 25%. By 1994 we realised the benefit of screening patients at the general practices; from May, 1994, to save money, the screening was done by a specially trained nurse, rather than radiologist, and only hypertensive patients were screened because of the finding3 that the incidence of aortic aneurysms in those with hypertension is about double that of the normal population. 25 of the local general practices have been requested to submit lists of their male (aged 60-80) and female (aged 65-80) hypertensive patients (Jones et al looked at men only).

Aortas are thought to be aneurysmal when their diameters exceed 3 cm. Small aneurysms (3-4 cm) are re-screened after 12 months and moderate aneurysms (4-5 cm) after 6 months. Surgery is advised for aneurysms greater than 5 cm. This protocol is identical to that of Jones and colleagues.

1659 men and 1474 women have so far been screened (73% attendance rate). Normal aortas have been found in 99% of women and 95% of men. 21 men and four women had had aneurysms greater than 5 cm requiring surgery; one died, and no other major complications have been reported. The inexpensive screening programme has been highly effective.

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