No need to hunt for micrometastases in women with early breast cancer

Routine examination of sentinel lymph nodes can miss isolated occult metastases in women with early breast cancer. Should pathologists look harder, using more sophisticated immunological tests? A cohort study from the US suggests it would make little difference to overall survival. Using immunochemical techniques, pathologists found occult metastases in 10.5% of 3326 women whose sentinel lymph nodes looked free of cancer on routine tests. These women were no more likely to die during the next five years than women with no occult metastases (95.1% v 95.7% survival; adjusted hazard ratio 0.88, 95% CI 0.65 to 1.71). Immunochemical test results did not inform treatment, and most women had both radiotherapy and adjuvant chemotherapy after their lumpectomy (2498/3247; 76.9%).

Pathologists also looked for occult metastases in bone marrow aspirates from 3413 women in the same cohort. Just 104 (3.0%) aspirates were positive, and while crude analyses hinted at reduced survival for these women, the association disappeared when researchers adjusted for tumour type, and the presence or absence of oestrogen receptors (1.83, 0.79 to 4.26).

All participants had early breast cancer—mostly stage 1 (83.3%) invasive ductal carcinomas (80.1%) that were oestrogen receptor positive (81.2%). Hunting for micrometastases in either sentinel lymph nodes or bone marrow isn’t justified for these women, say the researchers.

\[ \text{JAMA 2011;306:385-93} \]

Cranberry capsules or antibiotics for women with recurrent urinary infections?

Cranberries have a reputation for preventing recurrent urinary tract infections, thanks to at least two successful placebo controlled trials. Cranberries looked less successful in a recent head to head trial against standard prophylaxis with trimethoprim-sulfamethoxazole: women taking the “natural” treatment for a year developed significantly more urinary tract infections, significantly faster than controls (4 v 1.8 infections, P=0.02; 4 v 8 months to first infection, P=0.03).

Antibiotics clearly worked better for this selection of 221 young women, who reported six infections on average during the year before recruitment. But the authors and a linked comment (p 1279) agree that women shouldn’t give up on cranberries just yet. Prophylaxis with trimethoprim-sulfamethoxazole caused resistance to develop quickly in isolates of Escherichia coli grown from samples of both faeces and urine. After a month of antibiotics, 86.3% of faecal isolates and 90.5% of urinary isolates were resistant to this antibiotic. Resistance rates were 23.7% and 28.1% after a month of cranberry capsules. Women should still be given a choice, say the authors.

Future head to head trials should consider using bigger doses of cranberries or cranberry extract, says the comment. The bioavailability of the active ingredient (type A proanthocyanidins) is notoriously poor, and the doses of cranberry used in this trial were probably no match for an antibiotic with a bioavailability of 90%.

\[ \text{Arch Intern Med 2011;171:1244-50, 1251-7} \]

Rural isolation is linked to higher mortality from COPD

In a cohort of 26591 men admitted to US hospitals with an exacerbation of chronic obstructive pulmonary disease (COPD), those living in isolated rural areas were significantly more likely to die than those living in more urban areas (5.0% v 3.8%; adjusted odds ratio 1.42, 95% CI 1.07 to 1.89).

All were admitted to hospitals managed by the Veterans Affairs Administration, which provides patient care to veterans and their dependents, between 2006 and 2008. The link between living in an isolated small town and mortality from COPD was independent of case mix and some hospital characteristics, including volume of patients with COPD managed during the study. Distance between home and hospital didn’t explain the findings either. In fact, those who travelled further for treatment had lower mortality in this study.

The authors found no significant increase in mortality for men living in country towns that were not isolated.

\[ \text{BMJ 2011;306:385-93} \]
We don’t yet know why living in an isolated small town might disadvantage men with COPD, because the authors could explore only those factors that are routinely recorded and stored by Veterans Affairs hospitals. They suggest that future studies should take a closer look at specialist services that might be hard to access from isolated small towns, including specialist pulmonary physicians.

Risks and benefits are easier to understand as percentages

Patients need accurate information about risks and benefits before they make important decisions about drug treatments. They also need to understand that information, and researchers recently compared five different ways of presenting it, in a randomised trial.

US adults seemed to understand percentages best. Participants given numerical information in this format were more likely to pass a comprehension test than those given the same information as frequencies (so many events out of a hundred or a thousand). The difference was small, but consistent. Combining percentages with frequencies did not improve test scores any further.

Researchers drafted tables giving the absolute benefits and harms associated with a drug and risks of side effects than the placebo. Percentages are simpler than frequencies and better.

Internal carotid measurements improve prediction of cardiovascular disease

Abnormal thickening of the carotid wall is a risk factor for cardiovascular events, although experts disagree about whether it adds anything useful to prediction based on clinical factors such as age, sex, smoking, and cholesterol concentrations. Researchers from the US recently reported that ultrasound measurements of the carotid wall can improve prediction, compared with the Framingham score alone, but that measuring the wall of the internal carotid artery adds more than measuring the wall of the common carotid. Looking for plaque in the internal carotid also added predictive power, although both improvements were fairly modest.

The researchers used data from the well established cohort of Framingham offspring—nearly 3000 US adults questioned and examined during the late 1990s when they were all free of cardiovascular disease. There were 296 cardiovascular events during just over seven years of follow-up.

As expected, all measures of carotid wall thickness helped predict events. But only the maximum thickness of the intima media layer of the internal carotid added clinically useful power to the Framingham risk score, correctly reclassifying 7.6% of adults as high, low, or intermediate risk. The presence of plaque (intima media thickness >1.5 mm) correctly reclassified 7.3% of participants, also a significant improvement.

US guidance currently emphasises measurement of the common carotid, say the researchers. That may have to change.

Antidepressants don’t work for older people with depression and dementia

Doctors should think carefully before prescribing antidepressants to depressed adults with Alzheimer’s disease, say researchers from the UK, after a landmark trial reported that the two most widely prescribed agents worked no better than placebo. Sertraline and mirtazapine did not reduce depression scores for older people referred to psychiatric services with dementia and depression, and they had no lasting impact on more than a dozen secondary outcome measures, including quality of life for patients or carers. Both drugs caused significantly more side effects than the placebo.

All three groups of patients improved during the first 13 weeks of the trial. The researchers are confident that improvements had little to do with either drug treatment but more to do with the usual care given to all participants by specialist psychiatric services for older people. Usual care depended on local protocols, but it would have included a variety of supportive and problem solving strategies in the first instance.

The 326 participants had a mean age of 80, moderately severe Alzheimer’s disease, and clinically important depression, often for more than six months. The researchers and a linked comment (doi:10.1016/S0140-6736(11)60830-1) agree that an antidepressant now looks like the wrong first line choice for the many patients with similar profiles. Adults at risk of suicide were excluded from the placebo controlled trial.

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“Has it ever struck you that although eczema and psoriasis are very common, you hardly ever see them both together in the same person? Or indeed that eczema frequently gets infected while psoriasis does not?”

Read Richard Lehman’s journal blog at bmj.com/blogs