

## BEHIND THE HEADLINES

Behind the Headlines reproduces selected clinical articles which have been published online in *The Bulletin* in the preceding quarter, in order to disseminate this topical clinical information to a wider audience (including those Fellows and Members without Internet access).

The reproduced articles aim to educate and inform the wider general medical College membership about specialist items that have been reported in the international medical and mainstream media: to the non-specialist it may not always be clear how accurately such stories – whether reporting results of scientific studies or issues of concern to health professionals – have been reported. In order to clarify such situations, expert clinical comments are commissioned on matters that are recurring in the international media, or about which different reports have caused conflicting messages for those practising in other specialties.

In time, it is hoped that this section will become an invaluable source of independent and authoritative advice for Fellows and Members interested in updating their knowledge of new developments in other specialties.

### IN THIS ISSUE

- 'Full-body CT scans: are they worth the cost and the radiation exposure?';
- a twin exploration of breast cancer – 'Screening for breast cancer' and 'The surgical management of breast cancer'; and
- 'West Nile Virus'.

## FULL-BODY CT SCANS: ARE THEY WORTH THE COST AND THE RADIATION EXPOSURE?

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There has been an increasing trend in some countries, such as the US and Australia, for imaging centres to offer the general public 'full-body' computerised tomography (CT) scans to screen for possible disease. The individual undergoes scanning of the head and neck, thorax, abdomen and pelvis; the images are then reviewed and a report is produced within a matter of days. These scans are sold on the premise that a negative/normal result will reassure a concerned person; whereas a positive result might allow potentially serious disease to be diagnosed at an early stage, allowing a better chance of effecting a cure. However, this procedure is not based on any meaningful evidence that it provides any worthwhile benefit for the individual. Indeed, apart from having to pay anything up to \$1,000 for the scan (in Australia), there are other disadvantages and risks to be considered. These include: the radiation dose received by the patient; the cost of any further investigations arising from the result of the scan (especially if these are to exclude disease suggested but not confirmed on the original scan (false positive outcome)); and a possible false sense of security instilled in those with negative/normal reports (false negative outcome). This practice has served to highlight concerns rising from the increasing use of CT scanning, the complexity of some of the new scanning techniques and the subsequent increase in the radiation dose to both the individual and the general population.

### BACKGROUND

This comment was commissioned following:

- a media report in the US in October 2002, regarding the development of clinical guidelines aimed at reducing the increasing number of CT scans carried out on children who have experienced minor head injuries. 'Curbs urged for CT scans on kids', MSNBC News, 28 October 2002; and
- a media report in Australia in which the Royal Australian College of Radiologists (RACR) had welcomed a decision by the New South Wales Government to launch an inquiry into the possible health risks associated with full-body CT scans, which have increasingly been offered to the public, at significant financial cost, as a general screening tool for a variety of diseases. 'Radiation concerns prompt body scan rules', Australian Broadcasting Corporation News Online, 12 November 2002.

Computerised tomography technology has advanced dramatically in the last ten years. In particular, the latest

generation of multi-slice scanners can image the whole body in less than 30 seconds. With the production of impressive three-dimensional (3D) reconstructions and other sophisticated techniques, it is easy to forget that relatively high doses of radiation are used in the production of these images. A chest X-ray typically delivers an effective dose of 0.02 mSv (millisieverts), equivalent to about three days' exposure in the UK to natural sources of radiation in the environment. However, a CT scan of the abdomen or pelvis delivers an effective dose of about 10 mSv to the patient, which is equivalent to 500 chest X-rays, or 4.5 years' exposure to background radiation.<sup>1</sup> The estimated risk of inducing fatal cancer is one in 2,000 at this level of dose.

In the last ten to 15 years, developments in general X-ray technology have driven examination doses down by as much as 50% for some procedures. Paradoxically, developments in CT technology have pushed doses up. Improvements in scanning speed and the ability to perform extensive scan sequences (up to 1,200 slices for a single examination, compared with 40–50 on older scanners) increases the diagnostic potential but also increases the dose. Even if like-for-like scan sequences are performed on a modern multi-slice scanner, the dose may increase by 20–40% compared with a conventional single slice machine.<sup>2</sup> In 1989, CT scans accounted for 2% of all X-ray examinations but contributed 20% of the collective dose to the general population from diagnostic imaging.<sup>3</sup> By 1998, these figures had risen to 4% of examinations and 40% of the collective dose.<sup>4</sup> It is likely that the contribution from CT will continue to rise for a variety of reasons:

1. Increased numbers of scans are being requested as more scanners become available, the applications of CT scanning increase and because scans are used as a substitute for careful history taking, clinical examination and the application of clinical acumen and experience.
2. New scanners can perform various reconstructions from the data, introducing new, exciting examination techniques such as virtual colonoscopy or bronchoscopy and CT angiography. But these require large numbers of thin section slices for the reconstructions.
3. In addition, the ability to make multiple short scans through particular areas allows multiple vascular phase examinations (arterial, capillary, venous, parenchymal, etc.), or 'real-time' CT fluoroscopy for interventional procedures.

Coming back to 'full-body' CT scans for asymptomatic people, the Food and Drug Administration (FDA) in the US is of the view that 'the harms [arising from these scans] currently appear to be far more likely and in some cases may not be insignificant'.<sup>5</sup> So their advice would seem to be to keep your money in your pocket if you are in general good health.

Walk-in CT screening units will not be introduced in the UK (or elsewhere in Europe), since our legislation requires individual medical exposures to be justified in terms of potential benefit against radiation risk.<sup>6</sup> However, it is important that all of us in the clinical community, both clinicians and radiologists, are aware of the doses involved in these 'exciting' new techniques. We should consider alternative imaging techniques such as ultrasound and magnetic resonance imaging (MRI), which, while not providing colour-coded 3D constructions of the mediastinum or abdominal structures, can still provide the diagnostic information necessary for patient management without the significant exposure to ionising radiation. If a CT scan is required then every care should be taken to minimise the dose, particularly in paediatric cases, so that the necessary diagnostic information is obtained with the minimum patient exposure. Anyone requiring further information on this subject should read a recent review by Golding and Shrimpton, this provides an excellent summary of the issues involved.<sup>7</sup>

#### EDITORIAL NOTE

Shortly following the submission of this commissioned comment to *The Journal* it was reported that the New South Wales Government, in the form of the Environmental Protection Authority, had announced stringent new regulations for full-body CT scans.

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## SCREENING FOR BREAST CANCER

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In 1986, the Forrest Report recommended that breast screening should be introduced for all women between the ages of 50 and 64 in the UK.<sup>1</sup> Whilst women over the age of 64 were also to be eligible for screening, it was decided that these women should initiate their own invitations for screening due to poor compliance in Swedish studies of women in this age group.<sup>2</sup> The method of screening to be used was to be a single oblique mammogram at an interval of three years. Subsequent research has shown that 2-view mammography at the time of first screen can improve sensitivity, i.e. number of cancers detected (24%), and reduce the number of benign recalls by 15%.<sup>3</sup>

There is now a battlefield of literature debating the value of breast screening. Review of currently published data on the effect of breast screening, including the large randomised trials (Swedish Two Counties and the Health Insurance Plan (HIP) project) suggests that a reduction in breast cancer deaths in the order of 21–35% at five years should be expected for women over the age of 50.<sup>2,4–8</sup> The robustness of the evidence confirming the value of breast screening in reducing breast cancer deaths was confirmed by the International Agency for Research on Cancer (IARC), who convened an international panel of 24 experts from 11 countries to report on this matter. The working group concluded that the reduction in mortality from breast screening in women who participate in screening programmes is around 35%. The working group also found that many of the earlier criticisms were unsubstantiated and recognised that whilst there were some deficiencies in the published evidence these did not invalidate the trials' findings.

In a UK context, this means that two women in every 1,000 screened would be saved over the next ten years. It is for the individual woman to decide whether screening is worthwhile. In women under the age of 50 a significant benefit is less clear.<sup>2,6,9</sup> In the high-risk younger population, cancer detection rates are similar to the National Health Service Breast Screening Programme (NHSBSP), but there is no information on mortality reduction. Specific studies addressing this question are now being carried out.

In the UK, under the NHSBSP, women are invited for breast screening on a rotational basis to either static units in urban areas or mobile units in rural areas. In Scotland, mammograms are read independently by two experienced radiologists, increasing sensitivity by a further 10%.<sup>10</sup> Around 5–7% of women are recalled for further evaluation, including clinical examination, further mammographic views and/or ultrasound. Approximately 1% of all women screened require multidisciplinary review, including surgical, radiological and pathological input. These women require a cytological/histological diagnosis before any definitive surgery; as about 60–80% of lesions are impalpable, fine needle aspiration (FNA) or core biopsy requires image guidance. This multidisciplinary approach is vital to optimise results in order to ensure that a high quality of programme-specific quality assurance (QA) guidelines for each stage of the screening procedure have been instituted (Table 1).<sup>11</sup>

There is continual improvement in performance in relation to cancer detection ratios, standardised detection ratios (SDR) and the proportion of small cancers diagnosed. Cancers now detected by breast screening account for one-third of the workload of new cancers detected in breast units. The proportion of self-referral in women aged 65

### BACKGROUND

The following two clinical comments were commissioned in order to clarify our understanding of two separate, but related, aspects of breast cancer (screening and surgical management) following:

- the publication of two 20-year follow-up studies comparing breast conserving surgery with mastectomy for the treatment of breast cancer, in the *New England Journal of Medicine*, which demonstrated similar results between methods of surgery and led to debate regarding whether or not mastectomies are still required (see references at foot of comment);
- widespread international reporting of the publication of the above studies in the mainstream media, including 'Mastectomies often unnecessary', BBC News, 17 October 2002 and 'Studies back breast-sparing surgery', NBC News, 16 October 2002; and
- mainstream media reporting of two studies (published in the *Journal of the National Cancer Institute* and by the University of Toronto, Canada, respectively), which showed that breast self-examination does not reduce mortality and that women may over-estimate the risk of breast cancer (leading to unnecessary mastectomies) – 'Breast self-examinations don't save lives: study suggests teaching the method may be a waste of time', NBC, 1 October 2002 and 'Women over-estimate breast cancer risk', 16 October 2002.

continues to increase. Recent studies in the UK show a higher compliance than originally shown from Swedish studies. Older women have a higher breast cancer risk (7/1,000 women screened), and extension of the age range of invitation in the screening programme to include women up to the age of 70 will be implemented in Scotland from April 2003.

The benefits of screening include the detection of cancers at an earlier stage in their life history, allowing improved survival and less radical treatment with more breast conservation. The radiation dose involved in mammography is very low (a rough estimate is that one excess cancer per two million screened may be caused after a lag phase of ten years), and even with cumulative doses the number of cancers detected far outweighs those induced by several orders of magnitude. The debate about the over diagnosis of special type cancers and ductal carcinoma *in situ* (DCIS) continues, and is based on our incomplete knowledge of their natural history and appropriate treatment.

Breast screening has significant financial implications, but, provided the QA is high, it remains cost-effective.

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**TABLE 1**  
**UK Breast Screening Programme 2000–01:**  
**actual vs quality assurance (QA) guidelines.**

	Actual	QA guidelines
Invited	1,815,610	
Accepted	75%	>70%
Recalled	5.3%*	5% prevalent 3% incident
% Benign biopsied	0.29%	
Standardised detection ratio (SDR)	1.38	
Total number of cancers detected	9,866	
Cancer detection/1,000	6.6*	5.55 prevalent 4.0 incident
%=15 mm	52.6%	>50%

\*actual figures are a mixture of prevalent and incident screening figures

## THE SURGICAL MANAGEMENT OF BREAST CANCER

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The surgical management of breast cancer has undergone considerable change over the last 40 years. The gold standard was formerly the Halsted radical mastectomy, in which the whole of the breast was removed with the pectoralis muscles and axillary contents. The need for this mutilating surgery has been challenged. McWhirter, in Edinburgh, showed that a simple mastectomy plus radiotherapy was as effective as a radical mastectomy.<sup>1</sup> In the 1970s, three groups in Europe and the US set up randomised clinical trials to test the efficacy of breast-conserving surgery (removing the tumour combined with radiotherapy) compared with a radical mastectomy. The long-term results from two of these studies have been published recently in the *New England Journal of Medicine (NEJM)*.<sup>2,3</sup> Both of these studies show that, after 20 years of follow-up, breast-conserving procedures gave results equivalent to radical mastectomy in terms of death from breast cancer and overall survival.

Does this mean that there is no place for mastectomy in the treatment of breast cancer? Unfortunately not. In both trials patients were selected for entry by the size of the tumour, clinical node status and site of the tumour. In addition, patients who were initially treated by breast conservation and on histological examination were shown to have a tumour that went to the margin of excision were subsequently treated by mastectomy. Thus, breast-conserving surgery is appropriate for single tumours that are small enough in relation to the size of the breast so as to enable removal with an adequate margin and without causing marked distortion. Confirmation that the margins of excision are clear of tumour is important. However, patients with larger tumours, multifocal tumours or a single invasive tumour with extensive ductal carcinoma *in situ* are still best treated by a mastectomy.

The management of the axilla remains controversial. In both of the studies published recently in the *NEJM* the axilla was treated by a radical surgical approach in which the axilla was cleared of its contents up to at least the medial border of pectoralis minor (level II clearance). A more selective approach to the axilla would be logical. Two randomised studies comparing a four node axillary sampling procedure (with radiotherapy to the axilla only if the nodes are positive) to a surgical clearance have shown that this approach is effective and associated with less morbidity.<sup>4,5</sup> The sentinel node biopsy technique, which identifies the first node that drains the tumour-bearing region of the breast, has been shown to be over 90% accurate in determining node status of the axilla, and should allow a selective approach.

Thus, using procedures based on present evidence, many patients with breast cancer need not lose their breast or suffer the consequences of radical axillary dissection if correctly selected for less mutilating procedures.

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## WEST NILE VIRUS

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### INTRODUCTION

The West Nile Virus is a ribonucleic acid (RNA) virus belonging to the Flavivirus group. It is classified in the Japanese encephalitis virus serocomplex. The virus was first isolated and identified in 1937 in the West Nile district of Uganda. It was first linked with encephalitis in 1957 during an outbreak in Israel. Since the mid 1990s the frequency and apparent clinical severity of West Nile Virus outbreaks have increased. Outbreaks have occurred recently in Romania, Russia and the US. As of 23 September 2002, 1,963 cases had been reported in the US during that year with 94 (4.8%) deaths. For 2002, Illinois and Louisiana had the highest number of cases. The first cases in the US occurred in the north-east in 1999, but how or why the virus appeared in the US remains unknown. It has been postulated that travel and commerce may have played a role.

### BACKGROUND

In August and September 2001, a large number of reports and articles were printed in the mainstream media regarding the spread of West Nile Virus in the US. A number of these reports have now been collated into special sections on media websites, of which one of the most informative sources of information is the 'Washington Post West Nile Virus Special Report' (<http://www.washingtonpost.com/wp-dyn/health/specials/westnile/>).

### TRANSMISSION

The virus can infect humans, birds and various mammals. However, large birds appear to be the principal hosts, as they are able to survive long-term viremia. Dead crows have become harbingers of human cases, giving new meaning to the phrase, 'as the crow flies' (or falls). The mosquito most commonly implicated in transmission belongs to the genus *Culex*. The mosquito and the virus are able to survive through the winter months.

Humans are infected following a bite by an infected mosquito. The virus is located in the mosquito's salivary glands. There is no evidence of person-to-person spread, although there has been recent concern about potential spread through blood transfusion and organ donation (see below).

### CLINICAL MANIFESTATIONS

The majority of infected individuals remain asymptomatic. The incubation period is probably in the range of three to 14 days. Serosurveys conducted during the 1999 New York epidemic indicated that approximately 20% of infected individuals developed a febrile illness (West Nile fever). These patients complained of fever, headache and arthralgias. In earlier outbreaks, rash and lymph adenopathy had been noted as part of this febrile illness.

Approximately one in 150 infections result in neurologic sequelae, most frequently encephalitis. Increasing age is the most significant risk factor for severe neurologic disease. The risk markedly increases in individuals aged over 50 years (the incidence is ten times higher than in those aged 0–19 years).

The clues to implicating West Nile Virus as a cause of encephalitis include epidemiologic factors (this is a disease of late summer and early autumn), and the presence of severe muscle weakness. Complete flaccid paralysis has been described, and there is debate as to whether this represents Guillain-Barré Syndrome or anterior horn involvement.

Encephalitis typically presents with confusion, coma, cranial nerve abnormalities, etc. Aseptic meningitis is the second most frequent presentation, typically with headache, fever and neck stiffness. Specific diagnosis rests on either isolation of the virus or serology. The cerebrospinal fluid (CSF) findings are non-specific (CSF pleocytosis, elevated protein and normal glucose). Magnetic resonance imaging studies have shown enhancement of the leptomeninges and periventricular areas in about one-third of patients.

### LABORATORY DIAGNOSIS

The diagnosis is best made by detection of IgM antibodies in the serum or CSF. Since IgM antibodies do not cross the blood–brain barrier, their detection in the CSF strongly suggests central nervous system infection. The diagnosis can also be made by isolation of the virus or demonstration of specific viral antigen (or genomic-sequences) in tissue, CSF or blood.

## TREATMENT

Treatment is supportive. Ribavirin and interferon alpha-2B have *in vitro* activity against the virus, but there are no controlled clinical studies of the value of this treatment.

## PREVENTION

This involves the usual personal protective measures of avoiding mosquito bites. Local authorities have intensified mosquito control measures in response to outbreaks. A vaccine is in development; it has not yet been studied clinically.

## TRANSMISSION BY BLOOD TRANSFUSION AND ORGAN TRANSPLANTATION

This concern stems from a report in August 2002 from Georgia and Florida of evidence of confirmed transmission of West Nile Virus from a single organ donor to four organ recipients. The organ donor had received numerous transfusions of blood products prior to death, but the source of the organ donor's infection remains unknown. Furthermore, the organ recipients resided in areas of epidemic West Nile Virus activity, and accordingly the link between blood transfusion remains unclear. The Center for Disease Control is currently recommending that patients with West Nile Virus infection who have received blood transfusions or organs in the four weeks preceding symptom onset be reported. Tests for screening of routine blood donors for West Nile Virus is not currently recommended.

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Readers interested in accessing the full range of expert commissioned clinical comments, as they are published, are encouraged to access these online in the 'Breaking News Extra' section of *The Bulletin* at [www.rcpe.ac.uk/fellows/Bulletin](http://www.rcpe.ac.uk/fellows/Bulletin). Please note that *The Bulletin* is located on the secure ('Members Only') section of the College website and, as such, users will be required to enter a user name and a password in order to gain access to this material. If you do not know these access details please e-mail [webmaster@rcpe.ac.uk](mailto:webmaster@rcpe.ac.uk).