

# TESTING TREATMENTS

## Chapter 3, 3.1.2 TESTING TREATMENTS

professionals effectively challenged the surgical excesses of the past almost everywhere. Incredibly, however, there are still some reports of unnecessary and mutilating breast surgery being done – for example, in 2003, over 150 radical breast operations were carried out in Japan.<sup>5</sup>

By 1985, the sheer volume of breast cancer trials on all aspects of treatment made it very difficult for people to keep sufficiently up to date with the results. To address this problem, Richard Peto and his colleagues in Oxford drew together all the trial findings in the first of a series of systematic reviews (see Chapter 8) of all the information about all of the women who had participated in the many studies.<sup>6</sup> Systematic reviews of treatments for breast cancer are now updated and published regularly.<sup>7, 8</sup>

### Bone marrow transplantation

However, the demise of mutilating surgery did not spell the end of the ‘more is better’ mindset – far from it. During the last two decades of the 20th century, a new treatment approach, involving high-dose chemotherapy followed by bone marrow transplantation or ‘stem cell rescue’, was introduced. A report in the *New York Times* in 1999 summed up the reasoning behind this approach:

‘Doctors remove some bone marrow or red blood cells from the patient, then load her with huge amounts of toxic drugs, quantities that destroy the bone marrow. The hope is that the high doses will eliminate the cancer and that the saved bone marrow, when returned to the body, will grow back quickly enough so that the patient does not die from infection. A version of the procedure, using donations of bone marrow, had long been established as effective for blood cancer, but solely because the cancer was in the marrow that was being replaced. The use of the treatment for breast cancer involved a completely different – and untested – reasoning.’<sup>9</sup>

In the USA especially, thousands of desperate women pressed for this very unpleasant treatment from doctors and hospitals, even though as many as five out of 100 patients died from the

treatment. Many thousands of dollars were spent, including some from the patients' own pockets. Eventually, some patients were reimbursed by their health insurance companies, who caved in to pressure to do so, despite the lack of evidence that the treatment was useful. Many hospitals and clinics became rich on the proceeds. In 1998, one hospital corporation made \$128 million, largely from its cancer centres providing bone marrow transplants. For US doctors it was a lucrative source of income and prestige and it provided a rich field for producing publications. Insistent patient demand fuelled the market. Competition from private US hospitals to provide the treatments was intense, with cut-price offers advertised. In the 1990s, even US academic medical centres trying to recruit patients for clinical trials were offering this treatment. These questionable programmes had become a 'cash cow' for the cancer services.

Unrestricted access to such unproven treatments had another serious downside: there were not enough patients available to

#### **THE STRUGGLE FOR UNBIASED EVIDENCE**

Researchers expected it would take about three years to enrol about 1,000 women in the two studies. Instead it took seven years . . . That is not so surprising . . . Patients in the clinical trials must sign a consent form spelling out their grim prognosis and stating that there is no evidence that bone marrow transplants are any better than standard therapies. To enter the trial, you have to face these realities, which is never easy. But if the patient has a transplant outside a trial with a control group of patients, known as a randomized trial, enthusiastic doctors may tell her that a transplant could save her life. Although patients have a right to the truth, they understandably are not going to go to doctors who take away hope.

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*New York Times Special Report*, 2 October 1999.

take part in trials comparing these treatments with standard therapies. As a result it took far longer than anticipated to get reliable answers.

But despite the difficulties of obtaining unbiased evidence in the face of such pressures, some clinical trials were carried out and other evidence reviewed critically. And by 2004, a systematic review of the accumulated results of conventional chemotherapy compared with high-dose chemotherapy followed by bone marrow transplantation, as a general treatment for breast cancer, failed to reveal any convincing evidence that it was useful.<sup>10, 11</sup>

### DARE TO THINK ABOUT DOING LESS

So, more is not always better – and this message remains important. Today, in women with metastatic (widespread) breast cancer, there is considerable enthusiasm for treatments such as Herceptin (see above and Chapter 1). Yet, at best, Herceptin offers these patients a small chance of a longer life – measured sometimes only in days or weeks – at the expense of serious side-effects, or sometimes even death from the treatment itself.<sup>12, 13</sup> This tendency to over-treat is also evident at the other end of the breast cancer spectrum. For example, excessive and often unnecessary treatments have been used in women with pre-cancerous conditions such as ductal carcinoma in situ (DCIS) detected by breast screening (see Chapter 4), when DCIS might never go on to cause a woman a problem in her lifetime if left untreated. Meanwhile, the need for routine surgery to remove lymph nodes in the armpit, which risks unpleasant complications affecting the arm such as lymphoedema (see Chapter 5), is being increasingly challenged, since its addition to other treatments does not seem to improve survival.<sup>14</sup>

#### KEY POINT

- More intensive treatment is not necessarily beneficial, and can sometimes do more harm than good