How Breast Cancer Treatment Has Evolved Since the 1950s

By ACSH Staff — June 1, 2016

Treating breast cancer with a very high dose of chemotherapy doesn't improve survival any more than if using a standard dose. A recent Cochrane review [2] has put the final nail in the coffin of decades of research debunking the antiquated idea that, if only we could give a high enough dose of chemotherapy, we could cure breast cancer.

Cochrane investigators evaluated 14 randomized controlled trials showing treatment outcomes for women given very high-dose chemotherapy, compared with those given a standard dose. The studies involved 5,600 women with early but poor prognosis breast cancer, some of whom were followed for up to 12 years.

The definitive review found that not only are side-effects greater with higher doses, some women actually died from high-dose treatments; the worst kind of lose-lose situation.

High-dose chemotherapy aggressively attacks cancer cells as well as damaging normal blood cells. It is only technically feasible when used together with bone-marrow transplants that restore healthy blood cells to the body. The transplantation procedure is in itself a very traumatic and expensive experience.

Our new understanding that more isn’t better when it comes to chemotherapy is familiar, mirroring the evolution of surgery approaches to breast cancer that, a few decades ago, were far more radical than now.
We compared 14 studies involving over 5,000 women.

From then to now

In the 1980s, there was a lot of excitement about the possibilities of chemotherapy. After several clinical trials, the consensus was clear: giving chemotherapy to women after surgery for breast cancer reduced the risk of the cancer recurring, as well as the risk of those women dying of breast cancer.

Today, we realize breast cancer is not a one-size-fits-all disease. Some fast-growing breast cancers respond well to chemotherapy, while some slow-growing cancers are more sensitive to oestrogen. The latter will respond better to hormone-blocking treatments, while other types may need no further treatment beyond surgery and radiotherapy.

The vogue in the 1950s and 1960s was the idea that “if it comes back then it means you didn’t do a big enough operation.” In that era, increasingly radical surgery was carried out, involving removing not only the breast but also all the underlying chest muscles and lymph nodes under the arm. Known as a radical mastectomy, this was a very deforming procedure.

As evidence emerged, individual surgeons became more conservative with their operations. But it wasn’t until properly conducted randomized trials were collated in the 1990s, that the consensus was reached that long-term survival was identical in women who had a radical mastectomy and
those who had a lumpectomy followed by radiotherapy.

A lumpectomy, also known as wide local incision, involves taking just the breast lump out. It is now done in about 60 percent of all breast cancer cases [6]. The other 40 percent of more advanced cases are treated with a modified or simple mastectomy, with no muscle removed, which makes reconstruction easier.

The fact that a smaller operation led to similar survival meant the true cause of recurrence was not failed surgery but microscopic spread that developed early in the disease process, even before the surgeon has done her work.

Hence the concept of drug therapies: either intravenous chemotherapy or hormone-blocking treatments (mainly tablets) to mop up those stray cells after surgery. Trials started in the 1970s and 1980s and matured by 1990, when many of these treatments became standard therapy.

Death rates from breast cancer in Australia and the rest of the developed world rose until the 1990s. In Australia, they peaked in 1990 [7] at 31.6 deaths per 100,000 people and started to fall, reaching 20.4 per 100,000 by 2013. At the same time, breast cancer incidence had actually increased, from 94.9 in 1990 to 118.3 per 100,000 in 2012.

Since 2000, combined efforts of researchers in both the lab and clinic have led to further refinements in treatment. On the surgical side, randomized trials have proved the safety [8] of smaller operations to deal with lymph glands in the armpit, where breast cancer cells tend to spread initially.

It used to be the case that all the glands were taken out, but surgeons can now identify the critical one or two glands that might first be affected by cancer, known as sentinel nodes, and remove them. If they are clear, no further surgery is needed. This results in much less shoulder problems and arm swelling than before.

**Personalized treatment**

Drug therapies have also improved, with new ways of delivering better chemotherapy drugs with less nausea and vomiting. New drugs that target particular parts unique to the cancer cell are more effective and less toxic.

![HER2 breast cancers used to be the most feared diagnosis.](from shutterstock.com)

A practical example of this is the use of new antibodies [9] with barely pronounceable names to target a particular subset of breast cancers called “HER2 positive” cancers. These cancers have too much of a protein called HER2 on their cell surfaces, which is the target for the drug. Just like
the antibodies we make to kill bacteria, we design drug antibodies to kill cancer cells with lots of HER2 protein on them.

HER2 positivity used to be the most feared breast cancer diagnosis, but women with these cancers can now achieve very low recurrence rates with a combination of post-operative chemotherapy and the antibody trastuzumab. Randomized trials [10] across the world, including Australia, showed that while giving chemotherapy in this situation halved the risk of recurrence, adding trastuzumab halved the risk again.

Trastuzumab (brand name Herceptin) was listed in 2006 on the Pharmaceutical Benefits Scheme [11] and is now available to all Australian women with HER2-positive breast cancer. Another antibody, pertuzumab, was more recently added to the PBS [12] and is also used to control cancers that have spread beyond the breast.

Breast cancer still affects a lot of women (and a small number of men), but it kills fewer. While much has been achieved, much more is still to be learned. The key to success is high-quality clinical trials that test the results of laboratory findings.

The latest findings speak to the constant need to test new treatments carefully and reliably, preferably with large, international randomized controlled trials.

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