The Efficacy of Chemotherapy for Cancer

By Don Benjamin

In my previous article (Natural Health, December 1995/January 1996) I focused mainly on the efficacy of surgery. In this article I try to answer several questions related to chemotherapy:

1. What is the rationale for the use of chemotherapy?
2. What is the scientific evidence for its efficacy?
3. How much harm does it do?
4. What are the opinions of practicing oncologists about its efficacy?

1. Chemotherapy - a rationale

Chemotherapy acts differently from surgery and radiotherapy. It is designed to kill off fast-growing cells. But it also kills many fast-growing healthy cells. In addition it damages the immune system (see below) and is toxic. Also unlike surgery and radiotherapy, chemotherapy is a systemic therapy (as is hormone therapy). If cancer is a systemic disease, as claimed by most alternative practitioners, chemotherapy is the most likely of the orthodox therapies to be effective if only its toxicity could be reduced.

2. What is the scientific evidence for its efficacy?

Proof of efficacy of a cancer treatment such as chemotherapy requires a randomised trial in which it has been shown that the group treated with chemotherapy experienced a significantly increased survival when compared with that of an untreated group. This has never been done. Unfortunately most claims for the efficacy of chemotherapy come from trials showing shrinkage of tumours; or from comparison of survival rates of unmatched groups over time.

Tumour response trials assume a particular paradigm, eg the tumour is the disease. If this paradigm is wrong and the tumour is only a symptom of a systemic disease, the symptom can be removed, destroyed or shrunk without affecting the course of the disease. Unless tumour shrinkage is accompanied by evidence of increased survival the treatment cannot be claimed to be effective. Tumour response trials rarely produce such evidence of increased survival1. Tumour shrinkage can however reduce pain.

Comparison of unmatched groups over time can be valid if a very large increase in survival is observed and this cannot be attributed to other factors. For example when used to treat acute lymphocytic leukemia (ALL) in children, chemotherapy using different types of drugs has been shown to increase 10 year survival from less than 10% in the 1950s to about 60% in the 1980s2. Part of this increase is only apparent because it is due to earlier diagnosis extending the survival starting time and the increasing incidence of less-fatal forms. However it is unlikely that more than a third of this improvement is due to these factors. The percentage survival has continued to increase steadily over this thirty-year period whereas improvements in diagnostic methods and an increase in less-fatal forms are unlikely to have developed in this way.

For other forms of leukemia the evidence is questionable. An analysis of 3-year survival rates between the 1950s and 1960s showed increased percentage 3-year survival over this period for all forms of leukemia, yet for all forms combined the survival remained unchanged3. Unlike the case of ALL above, all of this increase can be attributed to the effects of earlier diagnosis extending the survival starting time and the changing proportion of the more fatal forms in the total cases.

A less dramatic improvement in survival has been observed for some lymphomas1. However much of this increase can again be attributed to poor methodology.

According to a leading epidemiologist, "for most cancers in adults, and particularly for epithelial cancers, there has been so little progress that it is difficult to distinguish any real improvement in survival rates from artifacts due to improvements in diagnosis and cancer registration4"..(survival is also slightly prolonged using tamoxifen for breast cancer; oestrogens for prostatic cancer; cytotoxic chemotherapy for small cell lung cancer and ovarian cancer; adjuvant therapy for resected breast cancer and possibly colorectal cancer.)

"The efficacy of most other treatments is not established, however, and a small proportion of patients are certainly killed by the short or long-term effects of cytotoxic treatment4."

"There have been considerable advances in avoiding disfigurement by radical surgery, limiting tissue damage by radiotherapy and controlling chemotherapeutic toxicity, but for the majority of adult epithelial cancers it is not clear whether the withdrawal of all cytotoxic therapy would measurably alter the annual number of cancer deaths."....

"....In the many situations where it is still not known whether treatment will prolong remission or survival, the oncologist is therefore in the invidious position of having to weigh the cost, inconvenience and toxicity of treatment against its unknown clinical benefit. Not surprisingly, many clinicians respond by developing a set of firmly held but unsupported beliefs in the merits of particular regimens. The primary treatment of advanced non-metastatic laryngeal cancer, for example, will usually be by surgery at certain treatment centres and by radiotherapy at others. Whether chemotherapy is given as well and, if so, what form it will take, are also determined more by the idiosyncrasies and outpatient arrangements of the particular treatment centre than by objective evidence of long-term efficacy. Similar examples could be taken from most areas of cancer therapy4."

Similarly claims that chemotherapy have produced increased percentage 5-year survival for other cancers, such as cancer of the large bowel1, could be attributed to poor methodology because none of these cancers exhibited a divergence between incidence and mortality rate curves over time5.

Ulrich Abel reviewed the evidence for the efficacy of chemotherapy for invasive epithelial cancer6, the types of cancer for which chemotherapy is most commonly used. He concluded that there was some evidence from randomised trials that chemotherapy increased survival only for small-cell lung cancer. Yet even here the gain in survival was measured in weeks or months.

Adjuvant chemotherapy for breast cancer

It is widely claimed that adjuvant chemotherapy extends survival with late-stage breast cancer. For example, in a letter in the Sydney Morning Herald of 22 November 1996 Professor Allan Langlands claimed that the results of a meta-analysis of more than 100 trials of adjuvant systemic therapy in many thousands of women with breast cancer have confirmed a reduced risk of death by more than 20% over the next 10 years. Presumably he was referring to the results of 133 randomised trials involving 75,000 women published in the Lancet in 1992.

There were 11,041 women in these trials who were randomised to long-term polychemotherapy vs. no chemotherapy. This was the chemotherapy with the best results. Looked at ten years after their participation in a randomised controlled trial, these women seemed to show a 6.3% survival advantage (51.3 % vs. 45.0%). For node-negative women the advantage was just 4% (67.2% vs.

63.2%). For node-positive women it was less than 7% (46.6% vs. 39.8%). This small difference led two researchers from Manitoba to write in the Lancet that "no overall survival advantage has been seen so far".

Before these figures can be relied on the original trials need to be analysed to see if they were methodologically sound. It is likely that they contain results from many trials that have since been found to be flawed. The history of randomised trials of adjuvant therapy for breast cancer is dotted with examples of fraud and poor methodology.

In Italy, where the first positive survival effect was seen using the combination chemotherapy of cyclophosphamide + metho-trexate + fluorouracil (CMF), later analyses revealed that many patients had been excluded because they could not complete the rather arduous treatment. So randomised comparisons were of the healthier treated women against all controls, rendering the trial results invalid.

In the United States randomised trials of chemotherapy were begun in earnest in 1957 under the auspices of the National Institutes of Health (NIH). This program eventually became the National Surgical Adjuvant Project for Breast and Bowel Cancer (NSABP), headed by Bernard Fisher. In 1994 Fisher was sacked from the program because he had failed to notify the National Cancer Institute (NCI) of enrolment of inappropriate patients, a fact that had been known for three years. Further irregularities were then discovered in data from 12 other treatment centres. Some of the earlier NSABP trials had also involved exclusions that would have affected results, as in the Italian trial.

The results referred to by Professor Langlands include the results of both the Italian and NSABP Trials.

Adjuvant treatment of breast cancer with cytotoxic drugs is one of the lynch pins of chemotherapy and the NSABP was the key element within that program for more than 40 years. According to Irwin D. Bross, writing in the New England Journal of Medicine in 1994 "..the statistical quality control was grossly inadequate in the NSABP studies. Hence, whether or not some fraudulent cases are eliminated post hoc, any findings lack scientific validity"7.

Ulrich Abel makes the following points about claims of efficacy in adjuvant breast cancer therapy6:

1. Good and consistent evidence of beneficial effects of adjuvant systemic chemotherapy on survival exists only for breast cancer, and more specifically, for patients with at most three positive nodes;

2. So far no positive results seem to have been published for definitely postmenopausal patients;

3. The restriction of beneficial effects to this small group appears somewhat strange;

4. It is probable therefore that the effect is not due to the direct cytotoxic effects on the tumour but rather to treatment-related suppression of the ovarian function.

Chemotherapy for invasive cervical cancer

Recent claims have been made that chemotherapy helps with invasive cervical cancer. In fact the US National Cancer Institute is claiming a breakthrough in the treatment of late stage invasive cervical cancer according to a news item in the Sydney Morning Herald of 24 February 1999. They claim this is the first breakthrough in the treatment of this type of cancer in more than 40 years.

(Many years ago it was being claimed that surgery was effective. This claim has now been abandoned.) However this new evidence warrants closer consideration because, unlike the claims made for surgery, this new one is based on the results of randomised trials. The evidence found from 5 randomised trials is that adding chemotherapy in the form of cisplatin at the same time as radiotherapy, following hysterectomy, increased the percentage 3-year survival by about 10-12%.

Thus for women with Stage IIB, III and IVA cancer survival increased from 63% to 75%. For women with earlier invasive cancer, Stage IA2, IB and IIA, survival increased from 77% TO 87%. It suggests that chemotherapy and radiotherapy have a synergistic effect when used together and possibly that chemotherapy stops cancer cells from repairing the damage caused by radiation.

Unfortunately trials comparing these types of treatment with no treatment have never be carried out so it is also possible that percentage survival is increasing towards what it would be without treatment. Radiotherapy has been found to increase deaths in many types of cancer so it is possible that the same result could have been achieved simply by eliminating the radiotherapy.

After considering these developments there is no reason for changing my original estimate that fewer than 6% of cancer cases would benefit from chemotherapy.

Chemotherapy for neuroblastomas in children.

A recent case involving a court requiring chemotherapy against the parents wishes for a child with a neuroblastoma raises the question: is chemotherapy effective against this type of tumour? Neuroblastomas are tumours that can occur anywhere in the sympathetic nervous system, as well as the adrenal gland, the chest or pelvis. The response rate is said to be 59% with cyclophosphamide and combinations involving high-dose cisplatin, vincristine and other drugs1. For high-risk patients the survival rate is said to be 15% "despite several therapeutic apporaches"1. This contrast between response rate and survival rate is a good example of the invalidity of most claims for efficacy with chemotherapy. This low percentage survival figure is confounded by the fact that neuroblastomas sometimes regress spontaneously

3. How much harm does chemotherapy do?

There are three main areas of harm:

- Weakening the body's natural defences
- increasing mortality
- decreasing the quality of life

Weakening the immune system

Chemotherapy has been found to reduce the activity of natural killer cells by 96%8. So if there are tumours growing elsewhere in the body and the immune system helps to control tumour growth, then chemotherapy could make things worse by allowing more rapid growth of other tumours present. However there is little hard evidence from orthodox immunotherapy that the immune system is a major controlling factor. In fact a recent editorial reporting on an immunotherapy conference in Canberra in September 1998 suggests it might be a major factor only in cancers of viral origin9.

On the other hand Immuno-Augmentative Therapy as practised at the IAT Clinic in the Bahamas

appears to produce between 15 and 18% 5-year survival with late stage cancer patients10. Similarly the Issels Wholebody Therapy produced 16.6% 5-year survival among late-stage cancer patients11. (Expected 5-year survival for late-stage cancer patients using orthodox therapies is less than 2%.) As these two therapies are based on boosting the immune system using natural methods, it appears that that orthodox immunotherapy and alternative immune-boosting techniques must be completely different.

Increasing mortality

By analysing non-cancer deaths among cancer patients it is clear that orthodox therapies often do more harm than good, a phenomenon that helps explain certain claims of apparently effective treatments. (For example cancer treatment can damage the heart and cause deaths from heart failure. This means fewer deaths from cancer.) As there is little evidence that surgery actually causes harm other than temporarily suppressing the immune system8, it would appear that most of the harm is done by radiotherapy and chemotherapy.

Analysis of the results of records of 1.2 million cancer cases in the US SEER (Surveillance Evaluation & End Results) database showed that non-cancer deaths accounted for 21% of all deaths. These deaths were in excess of the rate expected for such patients. This excess was observed in all types of cancer with an overall figure of 37%. The excess ranged from 9% for breast cancer to 173% for lung cancer12. During the year following diagnosis this excess was about 5 times higher, so it ranged from about 50% for breast cancer to about 800% for lung cancer. The authors attributed this effect to the damage caused by cancer treatment (presumably mainly radiotherapy and chemotherapy).

Decreasing the quality of life

There is no shortage of evidence that chemotherapy usually causes a serious reduction in the quality of life. The only question is whether or not the worsening in the quality of life is justified in view of the very limited claimed increased survival.

What are the opinions of practising oncologists about the efficacy of chemotherapy?

The following are extracts from the Home Page of the Burzynski Research Institute on the World Wide Web13:

"…In an article entitled "Chemotherapy: Snake-Oil Remedy?" that appeared in the Los Angeles Times of 1/9/87, Dr. Martin F. Shapiro explained that while "some oncologists inform their patients of the lack of evidence that treatments work...others may well be misled by scientific papers that express unwarranted optimism about chemotherapy. Still others respond to an economic incentive. Physicians can earn much more money running active chemotherapy practices than they can providing solace and relief.. to dying patients and their families."

"Dr. Shapiro is hardly alone. Alan C. Nixon, PhD, Past President of the American Chemical Society wrote that 'As a chemist trained to interpret data, it is incomprehensible to me that physicians can ignore the clear evidence that chemotherapy does much, much more harm than good'."

In 1986, McGill Cancer Center scientists sent a questionnaire to 118 doctors who treated non-small-cell lung cancer. More than 3/4 of them recruited patients and carried out trials of toxic drugs for lung cancer. They were asked to imagine that they themselves had cancer, and were asked which of six current trials they themselves would choose. 64 of the 79 respondents would not consent to be in a trial containing cisplatin, a common chemotherapy drug. Fifty eight found all the trials

unacceptable. Their reason? The ineffectiveness of chemotherapy and its unacceptable degree of toxicity14. "

The more familiar these doctors were with the treatment the less likely they were to accept it for themselves.

Similar findings came from two other studies published in 198715,16.

A study of how expert physicians would wish to be treated for genito-urinary cancer found a similar situation in 198817.

In relation to the treatment of 252 advanced breast cancer patients one author observed that the "risk" of being treated by cytotoxic therapy was three times as high in the terminal stage as in the remainder of the patients18. As Abel points out, this does not point to the use of a therapy that is particularly geared to patients' wellbeing6.

In March 1989 German biostatistician Dr Ulrich Abel himself investigated physicians' choices in cancer treatment. He received 150 replies to a questionnaire sent to oncologists and research units around the word, trying to gauge these doctors' feelings about the use of chemotherapy in advanced carcinoma. He reported that "the personal views of many oncologists seem to be in striking contrast to communications intended for the public"1,6.

4. And some other opinions:

"…The failure of chemotherapy to control cancer has become apparent even to the oncology establishment. Scientific American featured a recent cover story entitled: "The War on Cancer -- It's Being Lost." In it, eminent epidemiologist John C. Bailar III, MD, PhD, Chairman of the Department of Epidemiology and Biostatistics at McGill University cited the relentless increase in cancer deaths in the face of growing use of toxic chemotherapy". He concluded that scientists must look in new directions if they are ever to make progress against this unremitting killer. "13

In a 1997 reassessment of the situation Bailar's view had not changed19.

John Cairns, professor of microbiology at Harvard University, published a devastating 1985 critique in Scientific American. "Aside from certain rare cancers, it is not possible to detect any sudden changes in the death rates for any of the major cancers that could be credited to chemotherapy. Whether any of the common cancers can be cured by chemotherapy has yet to be established.13

Why so much use of chemotherapy if it does so little good? Well for one thing, drug companies provide huge economic incentives. In 1990, $3.53 billion was spent on chemotherapy. By 1994 that figure had more than doubled to $7.51 billion. This relentless increase in chemo use was accompanied by a relentless increase in cancer deaths.13

Oncologist Albert Braverman MD wrote in 1991 that "no disseminated neoplasm (cancer) incurable in 1975 is curable today...Many medical oncologists recommend chemotherapy for virtually any tumor, with a hopefulness undiscouraged by almost invariable failure."13

The main problem with chemotherapy is that the general public is generally unaware that in most cases chemotherapy does more harm than good; most doctors knowledgeable in the area know this and will admit it in private. When an oncologist is asked what he or she can do for a patient's cancer it is hard to say - Chemotherapy is unlikely to help you!

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