Editorial

The emperor's new clothes – can chemotherapy survive?

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Keywords: antineoplastics, cancer.

(Aust Prescr 2006;29:2–3)

'An Australian study suggests that the benefits of chemotherapy have been oversold … Why has it been oversold? Are you suggesting that medical oncologists in Australia are just sort of marketing shysters or what?' These were some of the questions posed by Dr Norman Swan when he presented the Health Report on ABC Radio National on 18 April 2005.[1] Dr Swan was quizzing Associate Professor Graeme Morgan, the lead author of a controversial article entitled 'The contribution of cytotoxic chemotherapy to 5-year survival in adult malignancies'.[2]This article reported that chemotherapy has improved survival by less than 3% in adults with cancer.

These provocative figures were derived from a literature search of all randomised clinical trials reporting a five-year survival benefit attributable solely to cytotoxic chemotherapy in 22 major adult malignancies. The common malignancies of bowel, lung, breast and prostate were included. The total number of newly diagnosed cancer patients for each malignancy in 1998 was determined from cancer registry data in Australia and the USA. The absolute number to benefit was the product of the total number of patients with that malignancy, the proportion or sub-group(s) with that malignancy showing a benefit, and the percentage increase in five-year survival due solely to cytotoxic chemotherapy. The overall contribution was the sum total of the absolute numbers of patients showing a five-year survival benefit expressed as a percentage of the total number for the 22 malignancies.

Overall cancer survival, following all kinds of treatment, is approximately 63%. Based on the calculations in the study the contribution of chemotherapy to adult survival from cancer was estimated to be 2.3% in Australia and 2.1% in the USA. The authors, two of whom are radiation oncologists, but one of whom is a practicing professor of medical oncology, concluded that 'chemotherapy only makes a minor contribution to cancer survival' and 'to justify the continued funding and availability of drugs used in cytotoxic chemotherapy, a rigorous evaluation of the cost-effectiveness and impact on quality of life is urgently required'.

The paper attracted much attention. In the medical oncology community, there was much outrage and indignation at this 'misleading and unhelpful' paper. Associate Professor Michael Boyer, head of medical oncology at Royal Prince Alfred Hospital, Sydney, commented, 'The fact is that from a patient's perspective they are not really interested in how much chemotherapy contributes to the cure of all patients, what they are interested in is how much it will contribute to their particular disease and their stage of their disease … I don't think this paper helps from a patient's perspective. Similarly from a public funding, or public policy point of view, lumping everything together is not a terribly helpful way …'.[1]

Associate Professor Boyer raised concern about the study methodology and the fact that 'if you start … saying how much does chemotherapy add in the people that you might actually use it [in], the numbers start creeping up … to 5% or 6% …'.[1] It is true that the paper used definitions of convenience and excluded certain cancers with high cure rates from chemotherapy, such as leukaemias, childhood cancers and other curable rare cancers. In addition, the study did not account for the contribution of chemotherapy in increasing the efficacy of other modalities, for example in 'downstaging' before surgery or when used concurrently with radiation. The data set, from

In this issue…

Chemotherapy is an accepted treatment for cancer, but how many patients are aware of its very limited effect on survival? Eva Segelov questions whether our current approach to therapy is sustainable. Perhaps there will be a greater role for angiogenesis inhibitors in oncology, but as Stephen Clarke, Rohini Sharma and Paul Mainwaring point out, much more research is needed.

The breaches of the Medicines Australia advertising code make interesting reading. None of the drugs found in breach made it into the top ten most commonly prescribed drugs by population.

Drug utilisation can be improved by stopping medicines that are no longer needed. Rob Smith advises on how to withdraw antiepileptic drugs from children who are seizure-free.

1998, does not reflect recent advances with more modern chemotherapy drugs, although again their impact on survival is modest.

The article did not aim to address quality of life or other benefits from chemotherapy, or any parameters relating to palliation, which after all is the aim of the great majority of chemotherapy. It also does not discuss the curative benefit of other drugs in the medical oncology armamentarium, such as hormone therapy or 'targeted' drugs, such as bevacizumab or trastuzumab. One should not throw the baby out with the bath water, so to infer that medical oncology has no role in the management of cancer patients would be mischievous. Similarly, the article discusses issues to be considered in the formation of public policy, rather than making any statements on the management of individual patients.

Individual patients are concerned about their own chance of survival. Many patients will accept chemotherapy despite the small absolute benefit in survival.[3] A useful tool for adjuvant therapy for breast and bowel cancer, which uses a mathematical model for working out the benefit of chemotherapy, is Adjuvant! (www.AdjuvantOnline.com). Although such a model may show the small benefit, the patients and their families are often seeking a cure if at all possible. Their concerns are individual and immediate. They want to know the 'worth' of chemotherapy, but it is unlikely that the cost of the treatment is ever raised as a factor in an individual patient decision. Cost only becomes a significant issue if the treatment is not subsidised and the patient has to pay.

We are still left with the finding that the overall contribution of cytotoxic chemotherapy to survival in the 22 cancers reviewed in the study is less than 3%. Is this apparent heresy merely sour grapes from our radiation colleagues (who have previously shown a 16% survival benefit for radiation therapy[4]), or could it actually represent something close to the truth? At 2% or 6%, surely the message is the same. Modern Western society, with its obsession with cure at all costs and the focus on the outcome for an individual, has a track record of subverting community welfare on issues relating to 'big picture' sustainability.

Failure to come to terms with rationalisation of high cost medicine and the inability to convince multinational pharmaceutical corporations to provide drugs at a sustainable price will mean that our treatments are likely to have less, not more impact in the future, as only a portion of society will be able to afford them. Let us rise to the challenge rather than shrink from the spotlight. We have to hope that in the decades to come the contribution of chemotherapy to survival and well-being is significantly increased. However, we must realise that until we as prescribers, and the community as consumers, recognise our limitations and rationalise our resource utilisation, we may never achieve this goal.

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Conflict of interest: none declared

Letters

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Assessment of thyroid function in pregnancy

Editor, – Some further points on testing thyroid function need to be added to the useful information in Associate Professor Tran's review, 'Biochemical tests in pregnancy' (Aust Prescr 2005;28:98–101). First, a small but significant decrease in the concentration of serum free T4, most marked in the third trimester, has been clearly documented.[1,2] In addition, albumin-dependent methods of free T4 estimation show marked negative bias, relative to the non-pregnant reference interval; in the late third trimester, such methods may give subnormal free T4 estimates in up to 50% of samples.[3] These methods are unsuitable for assessing thyroid status during pregnancy[4], unless results are evaluated in relation to reference intervals that reflect method-specific bias at various stages of pregnancy. Clinical chemists need to be aware of this issue when choosing an appropriate free T4 method for obstetric practice and by indicating appropriate reference intervals.

Professor Tran's counsel that 'Graves' disease needs to be rigorously controlled' in pregnancy goes beyond interpretation of test results. This advice must be tempered by the fact that any degree of maternal hypothyroidism in