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New anti-cancer drugs: out of the black hole and coming to a clinic near you

Overview

F Boyle

Royal North Shore Hospital
St Leonards, NSW

It is almost 30 years since US President Nixon declared "War on Cancer". Cynics would say it was a ploy to distract attention from the Vietnam War, then grinding to a close. A National Cancer Act led to the identification of funding for Comprehensive Cancer Centres, and a massive increase in resources for basic cell biology research with the hope of uncovering the magic bullet that would be "a" cure for cancer that wouldn't cause collateral damage for normal cells. Until recently, the billions were pouring into the black-hole and there was little change in the types of therapy the average cancer patient received, although outcomes improved inch by inch with better application of conventional therapy in a multidisciplinary setting.

For the past five years however there has been a new sense of excitement at international research meetings, followed by ripples in the clinical world, and the first agents based on our new understandings of molecular pathways controlling cancer formation have at last emerged into the clinic. Understanding the genes controlling cellular growth, which are overactive in cancer cells, has allowed development of targeted molecules to interrupt these pathways. Some agents target cell surface receptors (Trastuzumab, Cetuximab), others the signalling pathways connecting receptor to nucleus (Imatinib, Iressa), and others nuclear structures directly (Oxaliplatin). In order to improve the therapeutic index, drugs which are preferentially activated by enzymes within malignant cells deliver a high dose to cancer cells and spare normal tissues (Capecitabine). Agents which target the normal cells that are recruited into assisting in metastasis formation (bisphosphonates) aim to render the environment hostile to cancer cell growth. Each of these agents is described in more detail in the articles in this series, and all are based on fundamental insights into cancer cell biology that have emerged within the past 30 years. Each targets better the malignant cell, and has fewer side effects than conventional chemotherapy. Antiangiogenic agents are also promising, but as yet have not entered clinical practice and are not reviewed here.

Yet it turns out that curing cancer does not require a single bullet – more a steady stream of machine-gun fire. Each of these agents is given continuously – this has become possible as their toxicity is more manageable. We anticipate that they will work even better when combined with one another, or with conventional chemotherapy and radiotherapy. Perhaps we will be maintaining control or remission, rather than "curing"? Cancer treatment may become like treatment of blood pressure or diabetes or asthma – rarely are these cured, and combination oral therapy is the norm. Nixon presumably did not envisage we would be "sleeping with the enemy".

What is clear is that these agents challenge our paradigms – oral administration allows patients coveted freedoms, yet the potential for toxicity requires that supervision be maintained, perhaps in different ways. Prospective pharmacoeconomic evaluation will be critical as overall costs of these agents are high – they are harder to produce and have been tooled up out of expensive basic research, the markets are small for individual agents, chronic use and combinations will add to the overall outlay. For these reasons the developmental emphasis should shift to the incorporation of these agents into definitive treatment and adjuvant treatment strategies. Meanwhile improved survival and quality of life for patients with advanced cancer will be the immediate outcome of their availability in Australia, assuming we can find a mechanism to pay for the peace.

Antagonists of the epidermal growth factor receptor

Dr W Liauw

St George Hospital
Kogarah, NSW

Background

The human receptor protein-tyrosine kinases (RPTK) constitute a large family of membrane spanning receptors that govern diverse cell regulatory signal-transduction pathways[1]. There are currently over 90 recognized protein tyrosine kinases of which 58 are associated with receptors. These form 20 distinct subfamilies that are sufficiently different in the structure of their extra-cellular domains, tyrosine kinase domains and downstream functions to represent distinct targets for pharmacological intervention. Dysregulation of these (RPTK) by mutation or over-expression is potentially oncogenic. Examples of receptors important in oncogenesis are the epidermal growth factor receptor (EGFR), insulin receptor, platelet-derived growth factor receptor, vascular endothelial growth factor receptor and fibroblast growth factor receptor.

The epidermal growth factor receptor is one of the first proto-oncogenes recognized. Avian viral erb-B produces a constitutively activated protein that induces avian erythroblastosis. In humans there are four members of the erbB (or HER) family. Ligands are recognized for types one (EGF and TGFa), three and four but the erbB2 receptor (or HER2/neu) receptor currently has no recognized target. An important feature of these receptors is that ligand binding leads to homodimerisation (the associated of two like receptors) and heterodimerisation (the association of two different receptors). This increases the chances for cross-talk between different signal transduction pathways.

In the normal mammalian cell EGFR is important in the control of cellular growth and differentiation. EGFR knockout in mice is essentially a lethal mutation. In the malignant cell EGFR and its downstream effects have been shown to control cell cycle control, apoptosis, angiogenesis, invasion and metastasis[2]. EGFR is not just a proliferative signal but one of many components of the apparatus that a normal or malignant cell uses to decide whether to survive (or undergo apoptosis / cell death). Perturbation of EGFR leads to a strong survival signal whereas blockade of EGFR should decrease the impetus to survive in the face of cell damage induced by insults such as chemotherapy and radiation.

It has been demonstrated that EGFR or TGFa expression is observed on many epithelial tumours including (squamous) non-small cell lung cancer, epithelial ovarian cancer, colorectal carcinoma, gastric and oesophageal carcinoma, breast carcinoma, bladder carcinoma, renal carcinoma, prostate carcinoma and glioblastoma multiforme[2,3]. For many of these tumours there is evidence from small series that EGFR or ligand over-expression is an adverse prognostic factor for tumour metastasis, recurrence and overall survival.

Given the ubiquity of EGFR, its diverse cellular functions and apparent prognostic importance it is an obvious target for the development of anti-cancer agents. Several strategies could be employed or are possible[3]. Humanized monoclonal antibodies to the extra-cellular domain of EGFR have been developed (C225). Small molecules that bind the ATP-binding domain of the tyrosine kinase have been identified. Toxins have been linked with either ligand or antibody to target the receptor but these efforts have largely been superceded by the former two strategies.

Cetuximab (C225)

C225 (Cetuximab, Imclone Systems Inc., New York, NY) is a human-chimeric monoclonal antibody of the immunoglobulin G1 subtype. It binds the extra-cellular domain of EGFR to inhibit binding of the ligands EGF and TGFa. In vitro C225 has been associated with cell cycle arrest (at G1 to S transition) and enhanced apoptosis. In vivo studies with human xenografts have demonstrated reduced angiogenesis secondary to decreased VEGF and bFGF production by tumour cells. Matrix metalloproteinase-9 is reduced, possibly leading to a decrease in metastases. Synergy and additive cytotoxicity have been demonstrated with radiation and cytotoxics including platinoids, gemcitabine, taxanes and camptothecins.

C225 has progressed into clinical trials and has reached phase III registration studies where it is being targeted for head and neck cancer. The recommended dose is 400mg/m^2 intravenous loading dose followed by 200mg/m^2 weekly. Typical adverse events included the allergic reactions seen with other monoclonal antibody therapies such as Mabthera® and Herceptin®. An acneiform rash commonly occurs on the face and trunk and tends to resolve with repeated administration.

Encouraging evidence for the activity of C225 has included the addition of C225 to therapy in patients who have failed chemotherapy. C225 has been shown to re-sensitize tumour to chemotherapy in patients with squamous cell carcinoma (SCC) of the head and neck receiving cisplatin and in colorectal cancer patients receiving irinotecan[4,5]. C225 is being combined with radiation and/or cisplatin in phase II and III trials for head and neck SCC.

Tyrosine kinase inhibitors

The second class of agents that target EGFR do so by inhibiting the tyrosine kinase activity or the receptor. These agents agent structural mimics of ATP and so bind at the tyrosine kinase ATP binding site. There are two main biochemical classes being investigated, the anilinoquinazolines and the pyrazolo-pyrrolo-pyridopyrimidines[6]. The first group of agents tend to be selective for EGFR whilst the latter appear to have a broader spectrum of activity blocking some of the other EGF receptors including the type two receptor (HER2/neu). These agents are being developed for oral administration.

Iressa®(ZD 1839)

ZD1839 (Iressa; AstraZeneca, Wilmington, DE) is the most advanced in development having reached what are expected to be pivotal phase III trials[7]. In phase I trials of continuous and intermittent oral dosing ZD1839 has demonstrated good tolerability with a similar acneiform rash to that of C225 and a dose-limiting toxicity of diarrhoea which was not seen with C225, suggesting the importance of the mode of inhibition of EGFR. Importantly, and unlike classical cytotoxic agents, biologically relevant drug concentrations and tumour responses were seen at doses substantially lower than the maximal tolerated dose (MTD). Biopsies of skin have demonstrated molecular changes consistent with EGFR inhibition. This has allowed subsequent trials to use recommended doses below MTD and allowed the design of phase III trials in non-small cell lung cancer that combine either carboplatin and taxol or gemcitabine and cisplatin with placebo or ZD1839 at 250mg or 500mg per day. If a benefit of ZD1839 is demonstrated then it may also be possible to define a dose response relationship and a minimally effective dose.

The EGFR antagonists appear to have enormous potential in the clinic but obviously the final results of phase III studies are awaited with interest to see whether the encouraging response data translate into survival advantages. There are a significant number of issues that will need to be resolved with these agents. Given the synergy of these agents with radiation and cytoxics it is logical to develop them as a combination therapy, as is illustrated by the phase III studies in progress. It is probably helpful, however, to know their activity as single agents prior to registration and to facilitate the planning of trials of maintenance therapy and chemoprevention.

Prior to the demonstration of anti-tumour activity these agents had conceptually been thought of as cytostatic agents. In some senses this concept this is still relevant as maintenance therapy may be an option, particularly in the case of easily administered oral agents. Trials to confirm this will have to focus on time to progression and survival as the major efficacy variables. It may also be necessary to intermittently use chemotherapy or use modified chemotherapy schedules to optimise the effect of these agents.

The potential impact of EGFR inhibition is comparable to the effects of hormonal therapies for breast and prostate carcinoma and Herceptin for HER2/neu positive tumours. They promise improved efficacy with a relatively manageable toxicity profile. The results of phase III studies are awaited with interest but it should be remembered that as a new era of targeted therapies emerges it is going to be years before it is understood how to most effectively and economically exploit their activity.

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Trastuzumab (Herceptin®)

F Boyle

Royal North Shore Hospital
St Leonards, NSW

Our understanding of cancer has progressed dramatically in the past two decades, following the discovery that changes in important growth-regulating genes within cells can alter their behaviour and lead to cancer. One such gene, HER2/neu, is amplified in some cases of breast cancer, including about 25-30% of women with advanced breast cancer. Extra copies of the gene lead to the production of extra copies of a receptor on the surface of the cell. Growth factors bind to the receptors, and stimulate tyrosine kinases, leading to unrestrained multiplication of the cell. Breast cancers with excess receptors may behave more aggressively[1]. Trastuzumab (Herceptin®) is now commercially available in most of the Western world, including Australia, for the treatment of women with advanced breast cancer who overexpress HER2 receptors.

Biological activity

Trastuzumab (Herceptin®) is a recombinant humanised mouse monoclonal antibody that has been developed to bind to the HER2 receptor. It induces immune attack on the cell, blocks receptor function and growth factor binding, and promotes the degradation of the receptor. It also appears to enhance chemotherapy cytotoxicity.

Pharmacology

Trastuzumab is administered intravenously over 30-90 minutes, weekly, either alone or together with cytotoxic chemotherapy. An initial loading dose of 4mg/kg is followed by maintainance of 2mg/kg[2,3]. Third weekly schedules are currently under investigation as the half life is long.

To determine suitability for treatment, over expression of HER2 needs to be determined. HER2 expression is measured on breast cancer cells, usually from a sample stored after initial surgery. There are a number of different methods. Immunohistochemistry (IHC) and fluorescence in situ hybridisation (FISH) are currently the best methods of measurement. By IHC, HER2 expression is characterised as 0, 1+, 2+, and 3+. Overexpression is defined as moderate (2+) or high (3+) staining. FISH is more sensitive, less observer-dependent, but technically more difficult and less widely available at present. Reference laboratories have been developed to perform FISH when the IHC is equivocal (2+ or patchy). These tests are expensive and do not currently attract a rebate. Data presented at the annual meeting of the American Society of Clinical Oncology in 2001 suggests that FISH positivity is a better predictor of response and survival[4].

Toxicity

Side effects of trastuzumab include chills or fever during infusion (40% of patients), usually occurring during the first infusion[2,3]. These can be managed with paracetamol and antihistamines.

In combination studies neutropaenia is more common with coadministration of trastuzumab[3]. Cardiac dysfunction, of unknown aetiology, occurs in about 4% of patients treated with trastuzumab alone[2], up to 10% of patients treated with trastuzumab + paclitaxel, and up to 28% of patients treated with trastuzumab + anthracyclines (doxorubicin or epirubicin)[3]. Patients with poor baseline cardiac function and advanced age have a higher risk of cardiac dysfunction when treated with combination therapy[6]. Cardiac monitoring is recommended

prior to commencement of therapy, particularly in patients pretreated with anthracyclines, and at regular intervals. Cardiac dysfunction appears to remit and to respond to ACE inhibitor therapy, and reintroduction of trastuzumab may be possible[6]. Patients with extensive pulmonary involvement with metastatic breast cancer may experience acute deterioration in respiratory function, presumably due to an acute inflammatory response. Caution is advised in this setting.

Trastuzumab in advanced breast cancer

In highly HER2 over-expressing patients with advanced breast cancer who had received prior chemotherapy, trastuzumab used alone induced major responses in about 15% of patients, and minor responses or stable disease in a further 10%. The median duration of response was nine months and in all patients treated, the median survival 13 months[2]. Monotherapy was well tolerated, with only 1% of patients discontinuing because of treatment related adverse events. In studies of trastuzumab alone responses are usually seen within two to three months of starting treatment. First line monotherapy studies are currently underway.

First line controlled studies of trastuzumab plus chemotherapy (paclitaxel or doxorubicin) compared to the same chemotherapy alone have shown that the addition of trastuzumab significantly improves response rate (52% vs 45%), time to progression (7.6 vs 4.6 months), one year survival (78% vs 67%) and overall survival (25 vs 20 months). Survival benefits are probably underestimated as two-thirds of patients receiving initial chemotherapy crossed over to trastuzumab when they progressed. Significantly larger proportions of patients in the combination arms experienced an improvement in quality of life[5]. Benefits were greater in the HER2 highly over-expressing group but also occurred in the HER2 moderately over-expressing group[3]. Older patients (>60 year old) had worse overall outcomes but still benefited from the addition of trastuzumab. Patients responding after combination therapy for six months were continued on trastuzumab until progression. Because of the high risk of cardiotoxicity in the anthracycline arm, combinations of anthracyclines and trastuzumab are not recommended.

Current trials are exploring other combinations of trastuzumab and chemotherapy. Combination with Vinorelbine yielded a response rate of 75% in a phase II study in pretreated women[7], and preliminary data with docetaxel and cisplatin also appearing promising. Preclinical data suggests that synergy with these agents will occur, rather than the additive benefit with paclitaxel and anthracyclines.

A number of international adjuvant studies are either underway or in final planning stages. Cardiotoxicity will be of greater concern in the adjuvant setting and close monitoring is planned.

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Imatinib mesylate (STI571, Glivec®)

Y Antill

Royal North Shore Hosptital
St Leonards, NSW

Biological action

Tyrosine kinase (TK) receptors are receptors that cross the entire cell membrane. The intracellular portion of the receptor switches on a communication cascade within the cell. This enables activation and coordination of biochemical changes within the cell that allows the cell to undergo changes such as growth, proliferation and prevention of cell death depending on which pathway is activated. Normally, the process of activation is regulated by substances within the cell, that is, they stop the receptor from continuing to initiate the signalling pathway. In some disease states, the TK receptor becomes permanently switched on so that the end products of the pathway, such as proliferation, go on unimpeded. If the receptor is mutated or activated by an abnormal substance that doesn't respond to the normal regulatory substances, the cell may continue to signal for growth and proliferation. Chronic myeloid leukaemia (CML) and gastrointestinal stromal cell tumours (GIST) are two examples of diseases with TK receptor abnormalities.

Administration

Imatinib is a novel small molecule that functions as a tyrosine kinase inhibitor. Specifically it inhibits the tyrosine kinase receptor for BCR-ABL, c-kit, stem cell factor (SCF) and platelet derived growth factor (PDGF)[1]. The drug is taken orally, presented as 100mg capsules. It has a peak plasma concentration within two to three hours of administration and is metabolised by the liver. The major cytochrome pathway of metabolism is with CYP3A4[2]. The disadvantage of this is that it is susceptible to induction or inhibition of metabolism with other drugs also metabolised by the same route. Elimination is largely faecal. Carcinogenicity studies have not been completed, however it is teratogenic in rat models and should be avoided by pregnant and lactating women[2]. To avoid GI upset, it is recommended that the drug is taken with a full glass of water and that it be taken at meal times with food.

Toxicity

Generally the drug is well tolerated with minimal side effects. The most commonly reported adverse effects are fluid retention and oedema (the probability of this increases with both increasing age and dose), nausea, diarrhea and dyspepsia, neutropenia and thrombocytopenia (grade three and four in blast and accelerated phase CML), rash and myalgias[2]. For patients with severe neutropenia and thrombocytopenia, dose reductions or interruption of treatment are recommended. For other nonhaematological toxicities, the drug should be ceased until the event has resolved or been appropriately treated. For patient safety, monitoring for adverse effects and toxicities is vital while the patient remains on the drug. In solid tumours (eg GIST) haemorrhage into the tumour may reflect rapid response to therapy.

Clinical application

Chronic myeloid leukaemia

CML is a disorder in which one line of myeloid cells undergoes massive expansion. There are three phases of the disease: the chronic phase, the accelerated phase and the blast crisis. BCR-ABL is a constitutively activated TK receptor in CML. It is the product of the Philadelphia chromosome, the genetic abnormality that causes CML. Both invitro and invivo studies have shown that activation of this receptor alone results in an increase in cell cycling, proliferation, cell viability through a reduction in apoptosis and genetic instability[3]. Because of this single mutation, ideal treatments should be aimed at disabling this receptor. Imatinib binds to the ABL portion of the receptor thereby blocking its ability to be activated. Three phase II, open label studies have been reported, investigating the use of this drug in the three different phases of the disease, and recent approval for marketing in Australia is based on these results. Comparative studies with standard therapy (Interferon/ cytarabine) are underway to evaluate cost-benefit ratios and use in earlier phase CML. Whether it will replace transplantation as curative therapy is unknown at present.

a) Chronic Phase CML

Five hundred and thirty-two patients who had previously failed interferon treatment were entered in the trial. The median time from diagnosis was 32 months. The median time of treatment with interferon was 14 months[4]. All patients received 400mg of Imatinib. In patients who had previous haematologic resistance, 28% had a complete response with a further 26% having a partial response. In patients who had cytogenetic resistance 53% had a complete response and 36% had a partial response. Patients who had discontinued interferon treatment due to intolerable side effects rather than resistance had the best responses with 69% complete response and 38% partial response.

b) Accelerated Phase CML

Two hundred and thirty-three patients were treated with either 400mg or 600mg daily[5]. The criteria for accelerated phase was well defined. Ninety-one percent of patients achieved a haematological response; 44% complete haematological response (CHR) with recovery of peripheral blood counts; 19% CHR without peripheral blood count recovery and 28% improved blood counts only. The 12 month durable response rate was 64% with 75% 12 month survival.

c) Blastic Phase CML

Sixty patients were evaluable following treatment with 400mg or 600mg of Imatinib[6]. In previously untreated patients the response was 48% at four weeks and 47% at eight weeks. In previously treated patients, the response rate was 38% at four weeks and 33% at eight weeks.

Gastrointestinal stromal cell tumour

GIST is a rare soft tissue sarcoma arising usually from the stomach. This tumour expresses a trans membrane TK receptor for stem cell factor known as KIT (CD117). Normally this receptor is activated when stem cell factor is bound to it. In GIST, mutations in the c-kit gene lead to automatic activation of the receptor, bypassing the need for stem cell factor binding[7]. Preclinical research has demonstrated that constant signalling from the mutated receptor results in an increase in cellular proliferation and a reduction in cell death. While the incidence of this tumour is small, it has been notoriously resistant to all forms of treatment apart from surgery. To date, overall response rates to standard chemotherapy and radiotherapy have been less than 5%. For patients with advanced, unresectable or metastatic disease the outlook has been very grim with overall survival less than two years. This year has seen the first reports of promising data using Imatinib for patients with unresectable or metastatic GIST.

A single case report from Finland prompted the rapid development of two trials looking at effective dosages and response to this drug for stromal cell tumours[7]. Imatinib binds to several different types of the c-kit receptor, with the same "switching off" of downstream signalling pathways that had previously been seen in CML patients. The preliminary results from an ongoing international study looking at two different doses of Imatinib in advanced or metastatic GIST, were presented at the annual meeting of the American Society of Clinical Oncology earlier in the year, reporting 145 evaluable patients. Most of the patients had received prior therapy with a less than 1% response rate at the time of entry into the study. Overall response rates to Imatinib were impressive with 59% achieving a partial response and 26% having stable disease. The drug was generally well tolerated with 21% having serious adverse toxicites, including gastrointestinal bleeding[8]. PET scans demonstrate a rapid reduction in metabolic activity of the tumour after commencing Imatinib, with shrinkage on CT following more slowly. Receptor mutations were correlated with response. While these results are very promising the investigators stressed that it was very early days and the medium and long term outcomes are still unknown. A current European Organisation for Research and Treatment of Cancer trial comparing 400mg and 800mg per day has included Australian patients through the Australian Gastro Intestinal Trials Group. GIST is not yet an approved indication for use in Australia.

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Addendum

Clinical studies in chronic myeloid leukemia demonstrate that many patients with advanced stage disease respond initially but then relapse. Through biochemical and molecular analysis of clinical material, it has recently been demonstrated that drug resistance is associated with the reactivation of BCR-ABL signal transduction. This may occur as a result of single amino acid substitution in the ABL kinase domain known to form a critical hydrogen bond with the drug, or progressive BCR-ABL gene amplification. These studies provide evidence that genetically complex cancers retain dependence on an initial oncogenic event and suggest a strategy for identifying inhibitors of STI-571 resistance.

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Oxaliplatin (ELOXATIN®)

S Baron-Hay

Royal North Shore Hospital
St Leonards, NSW

Oxaliplatin is a diaminocyclohexane analogue of platinum with a wide spectrum of both in vitro cytotoxicity and in vivo activity in a variety of tumour model systems. Its mechanism of action is not completely elucidated but is believed to be related to the formation of DNA adducts, similar to those formed with cisplatin, however with increased ability to inhibit DNA synthesis[1]. Unlike the standard platinums, the adducts formed with oxaliplatin are not repaired by proteins of the mismatch repair system (hMLH1 and hMSH2), explaining its activity in tumours known to be resistant to cisplatin and carboplatin[2]. The drug has been commercially available in France since 1996 and in other European countries since 1999. It is currently under development for the treatment of advanced colorectal cancer in combination with other chemotherapy in Australia.

Oxaliplatin has predominantly been studied in the treatment of metastatic colorectal cancer. Most of the studies have examined the drug's activity in combination with standard fluorouracil-leucovorin. Its activity has also been evaluated in patients with advanced ovarian cancer and preliminary trials are examining its potential efficacy in a number of other tumour types including non-small cell lung cancer, non-Hodgkin's lymphoma, mesothelioma and breast cancer.

Metastatic colorectal cancer

Following initial promising in vitro data in human colorectal cancer cell lines oxaliplatin was investigated clinically as a monotherapy and in combination with other agents. The highest responses have been observed when it is used in combination with fluorouracil/folinic acid, typically ≥ 50% in the first line setting and 13% to 45% as a second-line treatment. Two preliminary small multicentric Phase II studies (EFC2960 and EFC2963) examined the activity of oxaliplatin as monotherapy in previously untreated patients with advanced colorectal cancer and confirmed a response rate of 18%[3,4], similar to the response rate achieved with 5-Fluorouracil alone. However when oxaliplatin was added to first-line 5-Fluorouracil/folinic acid therapy the objective response rate was significantly increased.

Two large randomized trials have measured the objective response rate of standard fluorouracil/folinic acid with or without oxaliplatin (FOLFOX trials)[5,6]. The objective response rates were 53% vs 16% ($p<0.001$) and 50.7% vs 22.3% ($p<0.001$) in patients receiving fluorouracil/folinic acid with or without oxaliplatin respectively. The median progression-free survival was significantly longer for patients receiving oxaliplatin in both trials (nine vs six months). There was no difference in overall survival, which was probably due to crossover and second line therapies with either oxaliplatin or irinotecan. These trials also demonstrated that the early introduction of oxaliplatin in the management of advanced colorectal cancer enabled a substantial reduction in the number of early deaths related to bulky or rapidly progressive disease.

EFC2964, an open label multicentric study, examined the addition of oxaliplatin in patients whose disease had progressed on 5-Fluorouracil/folinic acid. The patients were continued on the same 5FU regimen with the addition of oxaliplatin. Objective response rates were in the vicinity of 18% to 25% with the triple therapy. Median progression-free survival was in the order of five months and median overall survival nine to 13 months.

The triplet oxaliplatin/fluorouracil/folinic acid has also been shown to be effective in rendering previously unresectable liver metastases amenable to surgery with potential curative intent. In two separate studies (n=330 and 151) surgery with curative intent was performed in 16% and 51% of patients with initially unresectable liver metastases following oxaliplatin/ fluorouracil/ folinic acid therapy (complete resection was achieved in 87% and 75% of these patients)[7,8]. The five-year survival rates were 40% and 50%.

Although there is no universally accepted fluorouracil/folinic acid regimen, two-weekly high dose continuous infusion schedules have proved superior to bolus schedules in terms of response rate and progression-free survival[9].

Oxaliplatin has also shown promise in combination with irinotecan and ralitrexed for second-line treatment of metastatic colorectal cancer. Initial studies examining the combination of oxaliplatin and irinotecan produced response rates of 28% to 44%[10]. The addition of fluorouracil to oxaliplatin and irinotecan produced response rates of 16%[11] and 58%[12]. These combination trials have not yet reached their primary and secondary goals. Studies examining sequential oxaliplatin/ fluorouracil and irinotecan/fluorouracil (FOLFOX/ FOLFIRI) are also underway with initial response rates looking promising.

Advanced ovarian cancer

Oxaliplatin has been trialled as both monotherapy and in combination with either cyclophosphamide, cisplatin and/or paclitaxel in women with advanced ovarian cancer. Misset et al compared the combination of Oxaliplatin/Cyclophosphamide to Carboplatin/Cyclophosphamide in a multicentre phase II/II trial as first-line therapy in women with advanced ovarian cancer[13]. There was no significant difference between the two arms for objective response rate (33% vs 42%), median progression-free survival (13 months) and median overall survival (36 vs 25 months). Oxaliplatin appears to have comparable efficacy to cisplatin as first-line treatment for women with advanced ovarian cancer.

Oxaliplatin has also been investigated as second-line therapy in platinum pre-treated advanced ovarian cancer and demonstrated similar efficacy to paclitaxel (objective response rates 16% and 17% respectively)[14]. There was also no significant difference in median progression-free survival (12 weeks for the oxaliplatin arm and 14 weeks for the paclitaxel arm) and median overall survival (42 and 37 weeks).

Other cancers

Oxaliplatin has also been studied as monotherapy and in combination with other agents for the treatment of a number of different cancers including prostate, non-Hodgkin's lymphoma, breast cancer, squamous cell carcinoma of the head and neck, non-small cell lung cancer, mesothelioma, malignant melanoma, glioblastoma, and pancreatic cancer. The current data is from small patient studies in these tumours measuring response rate, with limited survival and progression time results reported. Additional large patient number studies are required to evaluate its effect in these tumour types. The largest studies to date have been reported in breast cancer (n=53)[15] and mesothelioma (n=58)[16] examining oxaliplatin in combination with either fluoruracil or ralitrexed with response rates of 25% and 26% respectively.

Pharmacokinetics

Oxaliplatin is given as a two to six hour infusion; 85mg/m^2 every two and 130mg/m^2 every three weeks. No intravenous hydration is required. After two hours only 15% of the platinum is present in the circulation with the remainder being distributed to the tissues. The drug binds irreversibly to red blood cells. Elimination is via the kidneys into the urine. Elimination is slowed in patients with renal impairment, although this does not appear to be associated with increased toxicity.

Tolerability

The side effects of oxaliplatin are similar to the other platinums with nausea, vomiting, diarrhoea, anaemia and altered liver function tests being common. However unlike the other platinums there is little to no nephrotoxicity, audiotoxicity or haematological dose-limiting toxicity at the recommended dose.

Phase I and II trials indicate that peripheral sensory neuropathy is the major dose limiting toxicity, associated with cold intolerance[17]. This neuropathy is cumulative and dose-dependent, but reversible on treatment cessation. The symptoms are occasionally associated with pain and cramps. After an accumulative dose of 800mg/m the risk of developing impairment is in the order of 10% to 15%. Oxaliplatin alters the voltage-gated Na(+) channel kinetics on sensory neurons. Therefore carbamazepine, which is a Na(+) channel blocker has been investigated as a potential neuroprotectant, and preliminary studies have confirmed this protective role in patients who develop WHO grade I or greater neurotoxicities[18]. A sporadic laryngopharyngeal dysaesthesia has been observed in 1-2% patients characterized by a subjective sensation of dysphagia and dyspnoea without any objective evidence of respiratory distress. These symptoms usually regress within hours of treatment cessation.

The above trials have all reported acceptable toxicity for the combination of oxaliplatin and other chemotherapeutic agents including irinotecan, paclitaxel, fluorouracil, ralitrexed, cisplatin and cyclophosphamide, however a number of these studies have been in small patient populations and data is limited.

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Capecitabine (Xeloda®)

J Vardy

Royal Prince Alfred Hospital
Camperdown, NSW

Capecitabine (Xeloda®) is an oral fluoropyrimidine, which inhibits thymidylate synthetase (TS), after activation by thymidine phosphorylase (TP). It is currently approved in Australia for use in metastatic breast cancer after failure of standard therapy, and for advanced or metastatic colorectal cancer (CRC). Trials are underway examining the efficacy of capecitabine in all the other malignancies currently treated with 5-Fluorouracil (5-FU), and in combination with other agents.

Biological activity

Thymidine phosphorylase is a tumour-associated angiogenic growth factor that induces neovascularisation and decreases apoptosis. As tumour cells have higher doses of TP than normal cells, capecitabine is preferentially activated to 5-Fluorouracil in tumour cells. This has the advantage of tumour selectivity with increased tumour drug concentrations but lower systemic 5-FU levels[1]. Tumour selectivity was confirmed in a colorectal cancer trial, which demonstrated that after capecitabine administration the concentration of 5-FU in the tumour was 3.2 times greater than in adjacent tissue and 21 times higher in the tumour than in plasma[2]. Preclinical studies suggest that there is a correlation between increased tumour biochemical markers (TP, DPD) and sensitivity to capecitabine[3]. If this proves to be correct this may allow for individualisation of treatment. Further to this, at the annual meeting of the American Society of Clinical Oncology 2001 Park et al presented a paper reporting that patients who are homozygous for double repeats of the 28 base-pair sequence in the TS gene (S/S) respond much better to capecitabine with 80% responding compared to 10% with S/L and 14% with L/L variants. They conclude that genotyping of patients may be helpful to select patients likely to benefit from capecitabine[4].

Pharmacology

Capecitabine taken daily or twice daily has been shown to provide a steady plasma or tissue level to mimic continuous 5-Fluorouracil (5FU) without the inconvenience of requiring central venous access. It is a prodrug that is metabolized via a three-step enzymatic process to the active agent fluorouracil. The capecitabine is rapidly and extensively absorbed through the wall of the intestine and is then hydrolysed in the liver by carboxylesterase to 5′-deoxy-5-flourocytidine (5′-DFCR). It is then converted by cytidine deaminase to 5′-deoxy-5-fluorouridine (5′-DFUR) in the liver and/or tumour cells. The 5′-DFUR is then activated by thymidine phopshorylase (TP) within tumour cells to 5-FU where it is subsequently converted to false nucleotides leading to inhibition of the enzyme thymidylate synthase (TS) and RNA & DNA disruption[5,6].

Phase II and III trials have confirmed that Capecitabine at 1250mg/m^2 twice daily after food, for two weeks followed by a one-week rest period appears to be the most beneficial dosing schedule[7,8,9]. The tablets are available in 150mg and 500mg doses. Mild to moderate hepatic impairment does not significantly alter the pharmacokinetics of capecitabine and therefore dose modification is not necessary[6]. Capecitabine is contraindicated in severe renal impairment and moderate impairment is likely to require dose modification.

Capecitabine can interact with both warfarin and phenytoin making careful monitoring essential. Altered coagulation parameters and serious bleeding have been reported with capecitabine and concomitant warfarin. Capecitabine should not be used in pregnancy[5].

Capecitabine in advanced breast cancer

Phase II trials in patients with metastatic breast cancer have shown that capecitabine is efficacious following taxane therapy[5]. Blum et al conducted a trial of capecitabine in 163 women with metastatic breast cancer who had progressed with paclitaxel. Ninety percent of the patients had previously received anthracyclines and 82% had been treated with 5-FU. They demonstrated a 20% objective tumour response with capecitabine including three complete responses and achieved stable disease in a further 43% of patients. Progressive disease was reported in 31% of patients. The median duration of response was 7.9 months, median time to progression three months, and median survival 12 months. A Clinical Benefit Response assessing pain, analgesic consumption and Karnofsky Performance Status was applicable to 147 patients with 20% reporting an improvement in each parameter and 31% of patients remaining stable[10].

Blum et al reported that generally the drug was well tolerated; however grade three to four toxicities included diarrhoea (14%), hand-foot syndrome (10%), fatigue (7%), stomatitis (7%), nausea (4%) and vomiting (4%). Neutropenia occurred in only three percent of patients and no alopecia was reported. Grade four toxicity occurred in 3.7% of patients. Seven percent of patients ceased capecitabine due to adverse effects and 55% required dose reductions[10].

Hand-foot syndrome (HFS) or palmar plantar erythrodysaestheia is a cutaneous reaction that has been reported after use with capecitabine as well as with 5-FU, doxorubicin, vinorelbine and cytarabine. Parasthesiae of the hands and feet is classified as grade one toxicity. This progresses to oedema and erythema of the palms and soles in grade two toxicity and involves desquamation of the hands and feet with ulceration in grade three toxicity. This condition can be extremely painful, impairing walking and limiting hand function. Treatment should primarily target prevention of serious toxicity with early detection of the syndrome. This highlights the importance of patient education prior to commencing treatment so that the patient, and the health professionals involved, recognises the early signs and symptoms of capecitabine toxicities and is able to implement timely management of toxicities. Mild cases generally only require an emollient although pyridoxine and steroids can also be used to treat more advanced HFS. Grade two toxicity requires interruption of treatment until the HFS has fully resolved with dose reduction if the toxicity reappears.

A phase II trial of 95 women aged 55 or older who had had no prior cytotoxic treatment for their metastatic breast cancer were randomised to either capecitabine or CMF. The capecitabine arm had an objective response rate of 30% (CI 14-37%) compared with 16% (CI 15-33%) in the CMF arm. There were five complete responses in the capecitabine group. Median survival was 21.6 vs 17.2 months and median time to progression was 4.1 compared with 3.0[5,6]. A study to confirm these findings of first line activity in elderly patients is planned by the Australia and New Zealand Breast Cancer Trials Group.

Encouraging single agent activity with modest toxicity has encouraged the exploration of capecitabine in combination therapy. Initial reports of a phase III study compare the combination of capecitabine and docetaxel vs docetaxel alone in women with metastatic breast cancer who had previously failed anthracycline treatment. The trial reports increased survival with a 22.5% reduced risk of death (p=0.013), an increased median survival of three months over docetaxel alone (median survival 14.5 vs 11.5 months) and increased median time to progression (6.1 vs 4.2 months, p=0.001). Tumour response rate was 32% vs 22% (p=0.009). The combination treatment had more adverse events with an increase in diarrhoea, stomatitis, HFS and nausea and vomiting. The taxotere alone arm reported increased neutropenic sepsis, myalgias and arthralgias[11].

Capecitabine in advanced colorectal cancer

Two phase III trials in metastatic colorectal cancer have been conducted comparing capecitabine with intravenous 5-Fluorouracil/leucovorin (5-FU/FA) The trials used the Mayo Clinic regimen of 5-FU with bolus IV injection daily for five days in four week cycles. The trials were prospectively integrated, giving data on 1,200 patients. There was a significant improvement in response rate in the capecitabine arm (25.7% vs 16.7% in the 5-FU/FA arm (p<0.002)), however no significant difference in time to disease progression (median 4.6 vs 4.7 months respectively) or overall survival (12.9 vs 12.8 months). HFS was more common in the capecitabine arm, however only half the patients required treatment. Stomatitis, diarrhoea, nausea, stomatitis, neutropaenia and alopecia were all significantly more frequent in the 5-FU/FA arm. Vomiting and fatigue were similar in both groups. Fewer patients required dose modification or hospitalisation for treatment related toxicity in the capecitabine arm[6].

In metastatic CRC trials are currently investigating capecitabine and weekly irinotecan as first line treatment, and capecitabine and oxaliplatin. Adjuvant studies have been completed and results are awaited.

In summary the oral administration of fluoropyrimidines appear to offer at least equivalent efficacy to intravenous 5-FU but with significantly less toxicity, increased patient acceptance[12], with the advantage of a home based treatment, and possibly a reduction in the total healthcare costs associated with 5-FU sensitive tumours.

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Bisphosphonates

N Pavlakis

Royal North Shore Hospital
St Leonards, NSW

Bone metastases are a major cause of morbidity in patients with solid tumours, particularly those with breast, prostate, lung, kidney and thyroid cancers[1]. Common bone related complications include pain, pathological fractures, hypercalcaemia, spinal cord compression and reduced mobility. The pathophysiology of bone metastases is multi-factorial resulting in osteolytic metastasis (when increased bone destruction predominates), sclerotic metastases (when increased osteoblastic activity predominates) or mixed osteolytic and osteoblastic metastases[1].

Bisphosphonates are chemical compounds known to inhibit osteoclast function and bone resorption[2]. They are effective in conditions characterised by osteoclast-mediated bone resorption such as Paget’s disease and osteoporosis, and, since the 1990s they have become the treatment of choice for tumour-induced hypercalcaemia[2]. Many studies have investigated the use of bisphosphonates in reducing skeletal complications (hypercalcaemia, bone pain, fractures, need for surgery or radiotherapy) associated with bone metastases, particularly in patients with multiple myeloma (MM) and breast cancer.

Pharmacology

Bisphosphonates, analogues of naturally occurring endogenous pyrophosphate, are drugs that have a high affinity for bone mineral. This is determined by their common chemical motif (P-C-P), whilst their potency and side effects is determined by the structure of their side chains[2]. The precise mechanism(s) of bisphosphonate inhibition of bone resorption is not known

but osteoclast inhibition (through a variety of mechanisms), macrophage inhibition and possibly direct anti-tumour effects have been proposed[2].

Bisphosphonates are available in both oral and intravenous forms. Of the oral formulations approved for use in malignancy, clodronate is the oldest. Whilst there have been published studies indicating some benefit from oral pamidronate, its poor oral bioavailability, gastrointestinal toxicity and the superiority of intravenous pamidronate have kept the oral form out of the clinic[3]. In Australia there are currently two bisphosphonates commercially available: clodronate (Bonefos®, oral) and pamidronate (Aredia®, intravenous).

The recommended dose of sodium clodronate is 1,600mg p.o. daily, ½ hour before a meal or two hours after a meal, whilst that of disodium pamidronate is 90mg i.v. over one to two hours every three to four weeks. Toxicity with oral clodronate is usually mild and in the form of gastrointestinal disturbance that can be alleviated with divided dosing. Common adverse reactions with disodium pamidronate are asymptomatic hypocalcaemia, influenza-like symptoms and mild fever. These are usually mild and transient. Monitoring of electrolytes, calcium, magnesium and phosphate is nonetheless recommended.

More potent bisphosphonates under clinical evaluation or approved overseas for use in malignant states include ibandronate (1,000 times as potent than clodronate) and zolendronate (10,000 times as potent as clodronate)[4]. However the oral bioavailability of these new agents remains poor. Apart from the greater potency of these new agents, advances in the administration of the intravenous forms have permitted shorter infusion times without complications.

Bisphosphonates in multiple myeloma

Multiple myeloma is a plasma cell disorder characterised by lytic bone lesions, abnormal bone marrow plasmacytosis or paraproteinaemia. In patients with MM, skeletal complications are inevitable and hypercalcaemia is common. In fact, 95-100% of patients with MM develop lytic bone lesions during the course of their illness[1]. Randomised controlled trial evidence has shown that in MM, bisphosphonates reduce bone pain, increase quality of life, and reduce the number of skeletal events[5,6,7]. Subgroup analyses in two oral clodronate studies have suggested that oral clodronate may prolong survival in MM patients without overt skeletal disease at diagnosis[7]. This observation is now the subject of ongoing study. In Australia, pamidronate 90mg i.v. every four weeks is the most commonly used bisphosphonate strategy in multiple myeloma. Use in this setting is supported by the Pharmaceutical Benefits Scheme (Highly Specialised Drugs Programme).

Bisphosphonates in advanced breast cancer

Sixty to 75% of women with advanced breast cancer suffer from bone metastases, which are a significant cause of cancer-related morbidity in these patients[1]. Since the 1980s there have been numerous studies investigating the role of bisphosphonates in women with advanced breast cancer[4,5,6,7]. These include oral clodronate and pamidronate, as well as intravenous pamidronate, clodronate, ibandronate and recently zolendronate. Several reviews have summarised the current status of the literature and Guidelines were published in 2000 by the American Society of Clinical Oncology (ASCO)[4,5,6,7]. A Cochrane systematic review is currently in progress[8]. Interim results from this review were presented at the 2001 Annual Scientific Meeting of the Australian and New Zealand Breast Cancer Trials Group and will be referred to here.

Since 1983, there have been 16 published randomised controlled studies comparing therapy with a bisphosphonate to therapy without a bisphosphonate in women with early or advanced breast cancer. Of these, 10 studies have been in women with established bone metastases and three studies in women with advanced breast cancer but no bone metastases. Eight of these studies have been with oral bisphosphonates (six with oral clodronate and two oral pamidronate), three with i.v. pamidronate and one study with i.v. clodronate and ibandronate respectively. The largest studies in advanced breast cancer were the combined Aredia Study Group studies 18 and 19, with 751 patients included, an ibandronate study (462 patients) and two other pamidronate studies (404 and 295 patients respectively). The oral bisphosphonate studies in advanced breast cancer were all relatively small studies, with a range of 10 to 173 patients included in each.

The primary study endpoints varied across the studies but included at least one of the following outcomes: skeletal events (defined as any or all of the following: new bone metastases, pathological fractures, spinal cord compression, irradiation of or surgery to bone or the development or progression of bone pain); Quality of life (QoL); bone pain; survival. A pooled comparison of efficacy across these studies is difficult because of differences in patient selection, concomitant therapies and outcome measures. Nonetheless, one can still consider the global effect of bisphosphonates on skeletal events, where the observed clinical benefits include reduced hypercalcaemic episodes, pathological fractures, the need for surgery and bone pain. Only six studies adequately evaluated QoL.

With regards to skeletal events in women with established bone metastases the strongest evidence for benefit is seen with the use of pamidronate i.v (90mg every three to four weeks for two years) which reduced skeletal morbidity by 35% ($p<0.001$, in Aredia Study Group Studies 18 and 19). There was a significant reduction in the cumulative number of skeletal events observed with 60mg pamidronate every three to four weeks for two years ($p<0.01$), whilst a significant delay in progression of bone metastases and reduction in bone pain was observed with 45mg pamidronate i.v. every four weeks (increase median time to progression by 48%, $p = 0.02$). There was a 44% reduction in the skeletal event rate observed with the use of ibandronate 6mg i.v. monthly ($p = 0.025$). There was a trend for improved overall QoL and significantly reduced bone pain with 90mg pamidronate i.v. and significantly improved QoL and reduced bone pain with high dose ibandronate 6mg i.v monthly). No study showed an effect of therapy on survival.

The use of oral bisphosphonates is associated with a 36-60% reduction in skeletal events in women with advanced breast cancer. This evidence comes from the two largest clodronate studies (N= 133 and $p < 0.01$, and N = 173 and $p = 0.001$ respectively) and a single oral pamidronate study (N = 161, $p < 0.001$). In women with advanced breast cancer but no bony metastases, one of three studies showed that oral clodronate compared to placebo significantly reduced the incidence of bone metastases (32 vs 63, $p<0.005$) however the number of patients affected was not significantly different (15 vs 19 respectively)[6].

From this evidence the American Society of Clinical Oncology Bisphosphonates Expert Panel recommended in 2000 the use of i.v. pamidronate over one to two hours every three to four weeks in women with metastatic breast cancer and radiographic evidence of bony metastases who are concurrently receiving hormonal therapy or chemotherapy[4]. In Australia, i.v. pamidronate has been approved for several years by the Pharmaceutical Benefits Scheme (Highly Specialised Drugs Programme) for patients with lytic bone disease from breast cancer, whilst the indication for oral clodronate has recently been extended to permit its use in this setting.

The optimum timing and duration of bisphosphonate treatment for women with advanced breast cancer is not known. Safety data is available beyond three years for oral clodronate and up to six years for i.v. pamidronate and zolendronate[3,9]. This data suggests that women with advanced breast cancer could be treated indefinitely.

Bisphosphonates in early breast cancer

In the adjuvant setting three studies have been presented of results to date[4]. Two published studies compared adjuvant oral clodronate (up to three years) in addition to standard adjuvant chemotherapy or hormonal therapy with an open control in women with high-risk early breast cancer[4]. These two studies showed contradictory results[4]. The third and largest study compared the addition of oral clodronate to placebo for two years in over 1,000 women. Results from this study are only available in abstract form with final study results in preparation[4]. Interim pooled analysis of these studies shows a 37% reduction in the risk of developing bone metastases with the use of adjuvant oral clodronate (Relative risk of developing bone metastases 0.73 (95% CI 0.55-0.98), unpublished results[8]). Whilst the use of bisphosphonates as adjuvant therapy to reduce bone metastases remains open, there is some evidence indicating reduced decline in bone mineral density with the use of adjuvant oral clodronate[4]. The NSABP-34 study, a double blind randomised placebo-controlled study of oral clodronate in women with early breast cancer, has recently commenced.

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Self-image in Female Cancer Patients
Overview

P Butow

Medical Psychology Unit, Dept of Medicine
University of Sydney, NSW

This issue contains two short papers providing insight into the impact of cancer on women's bodies and self-image. The first paper is a sociological exploration of the meaning of breasts and their loss, while the second paper reports an evaluation of the Look Good…Feel Better program, a free cosmetic workshop for women undergoing chemotherapy and/or radiotherapy for cancer.

Body image is a component of self-concept and involves the perception and evaluation of one's body, appearance and functioning. Early studies indicated that mastectomy scars, prostheses and the development of lymphoedema had a devastating impact on the lives of almost one in four women with breast cancer[1], while more recent data suggest that these problems often continue for years after treatment has ceased[2]. Similar effects have been reported in other cancers, with specific issues arising as a result of the site and treatment of the cancer.

Issues associated with appearance are important for many women, at any age, when making treatment decisions and in adjusting to their cancer diagnosis and treatment. The Psychosocial Clinical Practice Guidelines produced by the National Breast Cancer Centre and endorsed by the National Health and Medical Research Council recommend that clinicians be alert to a woman's body image concerns before, during and after treatment[3]. The guidelines suggest that clinicians directly ask about body image concerns, assess their nature, severity and impact, and appropriately refer when needed.

The first paper in this issue by C Boyd, provides an historical overview of the literature on the value and meaning of breasts and their loss, with quotes from the Bible, Shakespeare and art historians. The author argues that by showing an understanding of the personal, cultural and societal value and meaning of the breast, health professionals can provide better individualised care to their patients.

The second paper reports a pre and post program evaluation of the Look Good…Feel Better program that has been offered in Australia since 1990. The evaluation showed significant improvements in body and self image three days and one month after the course, although these are hard to interpret without a control group. Nevertheless, the paper provides useful information on the range of concerns reported by women receiving chemotherapy or radiotherapy, including their facial appearance, the feel and look of their skin, the eye area and unsurprisingly, their hair. Many women reported that their body image affected their self-confidence, and that the program had provided benefits for both their body image and their self-image.

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Breast cancer: The value and meaning of breasts

C Boyd

Mater Health Services and
Australian Catholic University
Brisbane, Qld

Abstract

Understanding the value and meaning of the female breast for women with breast cancer and their partners can assist health professionals in understanding how a woman may react to breast cancer and surgery and enable appropriate interventions to be implemented. One in eleven women in Australia will develop breast cancer by the age of 75[1]. According to Spiegal[2] as many as 80% of breast cancer patients may report significant psychological distress during their initial treatment. Based on the most recent national data about 10,000 women will be diagnosed with breast cancer this year[3]. On this basis approximately 8,000 women may report significant distress. This distress can result from anxiety about recurrence, threats to sexuality and occupation[4]. A woman's health, everyday activities, self esteem, sexuality and relationships may all be affected as a result of this distress causing them to feel helpless and powerless[5,6]. Why does breast cancer have such an impact on women? It stems back to the value and meaning that the female breast has in society and culture. This article reviews the historical and contemporary perspective of the value and meaning of breasts and application to health care.

Introduction

"The chest, the house of the heart, is an important centre of a person's being. I may locate my consciousness in my head, but myself, my existence as a solid person in the world, starts from my chest, from which I feel my self rise and radiate." (Young, 1992:215)[7].

The female breast has both symbolic and functional meanings. In one sense breasts have come to symbolise motherhood, beauty, self esteem, body image and femininity[8,9]. They provide visible evidence of femininity, sexuality and desire[10,11]. Breasts also serve as a source of nourishment for the young. The female breast is one of the first signs that children use to differentiate male from female. Because female breasts have this dual meaning and value they contribute to a woman's body image and confidence on personal, social and societal levels. The loss of a breast can have devastating psychological effects on a woman, including self-consciousness, insecurity, inferiority and fear of undesirability[12].

Historical perspective

Historical research has traced the ways in which both sensuality and functionality have contributed to the meaning and value of the female breast[13]. In literature, art and religion female breasts are more commonly portrayed as objects of sensuality and desire. For example, Shakespeare and Joyce frequently mention women's breasts in their works, referring to the sensuous desire associated with them[14]. De Mondeville, a 12th Century philosopher (1260-1320), philosophises that women's breasts show the quality of virtuosity, graciousness and gentleness of a woman's image of femininity and motherhood, and a woman's integrity of purity[15].

In European art galleries and churches women's breasts are more commonly portrayed in paintings and statues as items of desire[16] than as functional organs (or glands). See, for example, the statue Venus de Milo (c.100BC), Botticelli's (1444-1510) The Birth of Venus, and Ruben's (1577-1640) War and Peace. Each of these portray the beauty of the perfect nude female body. Artemis of Ephesus is an ornate image of the goddess of nature and a symbol of fertility. She has 17 swollen breasts and, clearly, the breasts are the symbol of this fertility[17]. In the Bible, King Solomon sings to his beloved "Your two breasts are like two fawns, like twin fawns of a gazelle that browse among the lillies" [18] (Song of Solomon 4:5).

The significance of the amputation of breasts, which during the middle ages was used as a form of punishment, is also portrayed in art. This can be seen in the story of Agatha, Patron Saint of breast diseases. Agatha (who later became St Agatha) lived in the city of Catania in Sicily at the time Quintiamus was Governor. She was a very beautiful virgin woman. Quintiamus noticed her beauty and vigorously sought her favour. Agatha was committed to her beliefs and did not respond favourably to the advances of the older Roman governor. This enraged Quintiamus to the point where he threatened her with mutilation of her body. When this did not produce the expected outcome, he condemned her to be bound to a martyr stake and have both breasts "torn off". St Agatha is preserved in paintings as a martyr, enduring suffering while her breasts are being torn or cut off. She is often portrayed in paintings carrying her breasts on a platter. Her story depicts the sadness women feel with the amputation of breasts[19]. Quintiamus' assault of this woman's breasts was an attack on Agatha's fertility and femininity. A woman maimed, rendered unattractive and unable to rear young, was inferior to other women in society. This form of punishment of women continued throughout the middle ages. Women who committed certain crimes were punished by the removal of one or both breasts. Male domination of women was perpetuated through threats to this sacred part of a woman's body rendering her both dysfunctional as a mother and undesirable to men.

Contemporary meaning

Body image is developed during the first 12 years of life, according to Finn[20], Young[21] and the World Health Organisation[22]. During this time of developing body image, young girls are growing up with their cultural and societal values. It is during this time that women are influenced by fashion, magazines, advertisements, clothing designs, music and movies. The meaning and value of women's breasts in this post-modern and post-feminist era varies from woman to woman. Contemporary value and meaning of women's breasts remain to be sensuality, nurturing and femininity. Women's magazines and fashion constantly reflect these themes.

Post-feminism has enabled a diversity of meaning attributed to the value and meaning of the female breast among women. For example, it may be important for a woman who has had breast surgery to have reconstructive surgery at the time of operation to maintain the value attributed to her breast, while another woman may be very content to have both breasts removed with no need for prostheses. Contemporary meanings reflect the postmodern thinking of today's society reinforcing contemporary values and meanings attributed to the breast[23,24].

Summary

Throughout history, in literature, art, religion and in contemporary Australian society, breasts have a dual meaning. On one hand they have come to symbolise femininity and sensuality. On the other hand, they function to support life of the young. The amputation of a breast or breasts can alter the body image of the woman. A diagnosis of breast cancer and its associated treatments pose this same threat but also imposes changes in lifestyle.

Implications for practice

By showing an understanding of personal, cultural and societal values and meanings of the female breast, health carers show their interest in providing care in context with their population of patients. This principle of contextual care goes beyond breast cancer and women, to those in need of any health intervention, regardless of race, culture or gender. Caring with such empathy and understanding the "person on the mattress" perspective, may improve health outcomes and increase job satisfaction. Providing individualised treatment and care for each woman is of paramount importance. Health professionals should assess each woman's value and meaning of their breasts before treatment and offer appropriate treatment and support for each woman and their partner. Research is needed in this area.

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The Look Good…Feel Better program: A pathway to self-esteem for women with cancer

A Kirsner and Colmar Brunton Research

The Look Good…Feel Better Program
Bay Village, NSW

Abstract

The Look Good…Feel Better program offers a free cosmetic workshop to women undergoing chemotherapy and/or radiotherapy for cancer. The central aim is to improve the self-image, self-esteem and confidence of each participant, through providing women with the knowledge, techniques and encouragement to use make-up to make themselves look better. This paper documents an evaluation of the Look Good…Feel Better program carried out in 1998, and further improvements to the program since that time. The evaluation showed that the program achieved modest but statistically significant gains for participants in a number of areas relating to their self-image, sense of confidence and self-esteem. Women of all ages gained from the course, but the largest overall gains were made by younger women (under 45 years), who were initially significantly more unhappy about their overall appearance. The reaction of the participants was overwhelmingly positive, and their feedback has led to further improvements in the program.

Introduction

Look Good…Feel Better, a program that offers a free cosmetic workshop to women undergoing chemotherapy and/or radiotherapy for cancer, has been offered in Australia since 1990. The central aim of the program is to improve the self-image, self-esteem and confidence of each participant. Look Good…Feel Better, which is also offered in the United States, Canada, the United Kingdom and New Zealand, is now available in this country at over 90 hospitals and cancer centres and was attended by some 4,100 women in 2000.

The Look Good…Feel Better workshops are presented by professional beauty advisors, who volunteer their time to teach women how to apply skin care and cosmetics, paying special attention to the physical changes that have occurred as a result of treatment. About 15 women are generally enrolled in each workshop, with six to eight beauty advisors. Over the two hours of the workshop, the beauty advisors provide women with techniques to combat changes in skin texture and pigmentation, and loss of eyelashes and eyebrows, and they demonstrate how wigs, turbans, hats and other accessories can be used – often with flair – for dealing with partial or total hair loss. As each technique is demonstrated, the women are encouraged to practice it, and each woman receives her own complimentary kit of skincare and make-up products, tailored to her particular needs, to enable her to learn 'hands-on' the techniques being taught, and to take home.

The volunteer beauty advisors all receive basic training in working with women with cancer, with annual updates and opportunities to workshop the skills they learn. The training includes how to best work with women who are upset or emotional, but volunteers are encouraged to focus on the workshop techniques and positive aspects of the workshop, and discouraged from becoming involved with women's emotional issues. The beauty advisors are also encouraged to debrief with their State Look Good…Feel Better managers.

The program is sponsored and funded by the cosmetics industry, through the member companies of the Cosmetic, Toiletry and Fragrance Association. This covers the cost of running the program and all the products used in the workshops, a contribution worth over $1 million per year.

How does it measure up? Evaluating the program

In 1997-98, Colmar Brunton Research was contracted to evaluate the effectiveness of the Look Good…Feel Better program. The aims of the evaluation were to provide an understanding of:

- the program's immediate and longer term effects on women with cancer, specifically in terms of their self-esteem, body image and perception of attractiveness; and
- the key needs of these women, which of these needs the program met, which elements of the program met these needs, and where improvements could be made.

How was the evaluation done?

The evaluation provided quantitative data through three questionnaires, one before the course, the second three days after completing the course and the third one month later.

The questionnaires asked women to rate body satisfaction in relation to a range of indicators, using a mark on a linear scale. They were also asked to indicate their mood and feelings (eg attractiveness, self-esteem, anxiety, pain), and to express their degree of agreement with a number of statements relating to mood and feelings.

In addition, two focus group discussions, one three days after the course and the second a month later, provided qualitative insights into women's experiences of the course and their suggestions for improvements.

The women involved

Ninety-six women were recruited and completed the first questionnaire, 90 completed the second, and 78 the third. The two focus groups involved four and five course participants respectively.

Over half of the initial 96 women (55%) had a diagnosis of breast cancer, with others spanning a range of diagnoses. The large majority had been diagnosed within the previous six months, 44% within the past three months, and 33% within three to six months.

Three-quarters of the women (75%) had undergone surgery for their cancer at some stage, most at least two months ago. At the time of the evaluation, however, the majority (68%) were undergoing chemotherapy and 23% were receiving radiotherapy, and almost four in every five (78%) had had treatment within the last fortnight.

Almost three-quarters of the women (74%) were married. One-third (34%) were aged over 55 years, another third (33%) aged 46-55 years, and the remainder younger than this, including one under 18 years.

Results from the questionnaires

Before the course

Before attending the course, the women rated fairly low their satisfaction with their hair, the look and feel of their skin and eye area, and their body weight, as shown in table 1. They were more satisfied with their face and nails although even here the mean score was around five on a scale of one to 10.

For the most part, as shown in table 2, the participants did not feel particularly beautiful, attractive or desirable. Most, however, felt generally optimistic, with a moderately high quality of life and a sense of control over their lives. They were not generally feeling a great deal of pain or nausea, nor were they particularly anxious or emotionally upset, although some had significant problems in these areas.

Most of the women also felt they could still confidently communicate with others, and that their appearance had not had a negative impact on their interaction with others, particularly close family and friends – areas of confidence that the later questionnaires showed to be maintained (see table 3).

On completion of the course

The questionnaire completed three days after the course showed a significant improvement in the women's body satisfaction in all areas other than nails and body weight (areas that had not been addressed at any length in the course) (see table 1). The improvements were not dramatic, with mean scores in the moderate range, from 4.5 for hair to 6.3 for overall appearance (a mean of 7.0 would be considered high). These are the sorts of gains that might be expected by a course that, rather than offering a 'miracle cure', aimed to make women feel better through helping them to cope with symptoms and side-effects of treatment.

Moods and feelings also improved, with statistically significant gains in confidence and self-esteem; feeling attractive, desirable, beautiful; and the women's sense that they 'looked more normal' (see table 2). There was also a trend towards feeling more normal, though this was not statistically significant.

The general trend was that the women felt better and more confident overall, and this was reflected in the significant increase in the level of agreement with the statements 'I feel confident about myself because I know I look good' and 'I feel better about myself because of how I look', as shown in table 3.

Women found the make-up used in the course to be very useful, and most of the make-up provided was used following the course. Many of the women were using a wider variety

TABLE 1

Body satisfaction before and after the course

	Pre-course	Initially post-course	1 month post-course
Nails	5.2	5.7	5.5
Overall appearance*	5.1	6.3	6.4
Facial appearance*	5.0	6.0	6.4
Eye area*	4.6	5.8	6.2
Feel of my skin*	4.6	5.9	6.4
Look of my skin*	4.4	5.9	6.1
Body weight	4.0	4.4	4.3
Hair*	3.5	4.5	4.6

0 = very unsatisfied, 10 = very satisfied, * Significant difference, p=<0.05

TABLE 2

Mood and feelings before and after the course

	Pre-course	Initially post-course	1 month post-course
Optimistic	6.7	7.1	7.1
Quality of life	6.3	6.6	6.7
In control	6.1	6.5	6.8
Happy*	5.1	5.7	6.1
Feel normal	4.9	5.8	5.6
Look normal*	4.9	6.0	5.8
Confident*	4.8	5.9	6.2
Self esteem*	4.5	5.7	6.0
Anxiety	4.0	3.7	3.7
Emotionally upset	3.9	3.3	3.5
Beautiful*	3.9	5.0	5.1
Attractive*	3.7	5.1	4.8
Desirable*	3.4	4.7	4.4
Physical pain	2.8	2.3	2.0
Nausea	2.3	2.0	1.9

0 = low level, 10 = high level, * Significant difference, p=<0.05

of cosmetics and skin care products, and using them more often. This included products previously used, as well as eye shadow, eyebrow pencil, lip liner, face concealer, face powder and toner. There was also a slight increase in daily use of head wear, possibly reflecting some experimentation.

The overall reaction to the course was overwhelmingly positive, with participants finding it enjoyable, useful and relevant, and the course leader and volunteers helpful and friendly. In general, women felt that the course exceeded their expectations.

One month later

One month later, the positive gains of the course had been maintained. The women's level of satisfaction with their bodies remained at a similar level, with a slight but statistically non-significant further gain in most areas (see table 1). All gains in mood and feelings had also been maintained, with the largest overall gains in this area being improved confidence and self-esteem (see table 2). In addition, at this stage participants felt significantly more happy, compared to their pre-course feelings – a gain not seen initially after the course. Perhaps this reflects time taken for others to notice and comment on the changes, or for feelings of happiness to grow out of increased confidence.

Women continued to use the cosmetics provided, and continued to use more cosmetics than before the workshop. Their patterns of use remained very similar to those seen immediately after the course.

Who gained most?

The largest overall gains were made by younger women. Before the course, women aged 45 years and younger were significantly more unhappy about their overall appearance, compared to women over 45 years. They were more emotionally upset, less likely to feel normal or feel they looked normal, less confident in their day-to-day lives, and more likely to feel others had taken over their lives. After the course, the only significant difference between the two groups was that the younger age group had not gained in confidence in their day-to-day life to the same extent as the older women. Their gains in all other areas had brought them to the same levels as the women aged 45 years and over.

Patterns of improvement also varied with relationship status. Before the course, there were few differences between those who were in a married or de facto relationship, compared to those not in a relationship. Immediately after the course, however, there were many significant differences. Those not in a relationship were significantly more likely to feel lower self-esteem, more emotionally upset, believe they had worse nausea and not feel good, be more pessimistic and negative about the future, be less confident about themselves, and think they looked different from their appearance before they were ill. A month later, most of these differences had disappeared. Women not in a relationship had made significant gains across a range of areas relating to appearance, moods and feelings, and the only significant difference between the two groups was that those not in a relationship were more likely to feel unsure about themselves because of the way they looked. This same pattern was seen in those not working: the benefits of the course tended to increase over the month following the course, whereas there was little different over the month for those who were working.

The focus groups: a spur to further improvement

The two focus groups confirmed women's positive experience of Look Good…Feel Better. Typical comments were, 'it wasn't a very big course but it really works', 'I can bring back some control that I didn't have', 'it's a boost, I feel like a new person', 'I feel more confident', 'the whole thing made you feel special… I've got to like myself better', 'If it wasn't for Look Good…Feel Better saying "fix yourself up", I wouldn't have', 'somehow it made a big difference'. There was also a strong sense that the individual attention and the cosmetic gift bags for each woman made the women feel special.

The groups identified a number of things that could further enhance women's experience of the program, and their comments and recommendations have led to a number of improvements.

The American video shown at the start of the session has been replaced by a new, Australian production that is culturally more relevant to the experiences of Australian women, and an Australian patient booklet has also been prepared and is given out at the workshops. Publicity for the course has improved, with new patient brochures and posters to promote the program, a website (http://www.lgfb.org.au), and a 1800 telephone line. Publishing companies have supported, free of charge, an advertising campaign that has run through 2000 and into 2001.

These developments have fostered considerable further growth in the program. The number of centres offering Look Good… Feel Better in Australia has grown from around 55 at the start of the evaluation, in 1997, to over 90 in 2001, and the number of women attending has increased from 2,975 in 1997 to 4,100 in 2000.

Conclusion

The evaluation clearly showed that the Look Good…Feel Better program is effective in improving the self-image, self-esteem and confidence of women with cancer. It provides them with the knowledge, techniques and encouragement to use make-up to make themselves look better, and it increases women's sense of control over their situation and their confidence in life.

For further information on the Look Good…Feel Better program, contact the national office: Freecall 1800 650 960; Ph: 02 4334 6445; or visit the website, http://www.lgfb.org.au

Acknowledgment

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Abstract

Objectives: To document the views of trainees in medical and radiation oncology regarding the content of their training,

TABLE 3

Women's agreement with statements before and after the course

Statement	Pre-course	Initially post-course	1 month post-course
'I feel positive about the future'	7.0	7.4	7.3
'I feel better about myself because of my interaction with other cancer sufferers'	5.4	6.0	5.9
*'I feel unsure about myself because of how I look'	4.4	3.6	3.5
*'I feel confident about myself because I know I look good'	4.4	5.5	5.6
*'I feel better about myself because of how I look'	4.3	5.9	5.9
'The way I feel now makes me feel less confident in my day-to-day life'	4.1	3.7	3.5
'I feel that I look good but I don't feel good'	3.8	4.7	4.0
'I feel I look just the same as I did before I was ill'	3.8	4.4	4.4
'I feel that it's obvious that I have cancer by the way I look'	3.7	3.1	3.1
'I don't feel as confident in communicating with others now'	3.4	3.3	2.6
'I feel that other people have taken over control in my life'	3.1	3.2	2.7
'I feel the way I look has changed the way people in my community interact with me in a negative way'	2.6	2.4	2.3
'I feel the way I look affects the way my close family and friends interact with me in a negative way'	2.1	2.0	1.9

0 = strongly disagree, 10 = strongly agree, * Significant difference, p=<0.05

Training of medical and radiation oncologists: the views of Australian and New Zealand trainees

K Fife

Dept of Radiation Oncology, Royal Prince Alfred Hospital, Camperdown, NSW

M Tattersall

Department of Cancer Medicine, University of Sydney, NSW

and its assessment.

Design and setting: Postal questionnaire survey of medical oncology trainees in Australia, and radiation oncology trainees in Australia and New Zealand.

Main outcome measures: Experiences of and views about training.

Results: Currently, 40% of medical and 59% of radiation oncology trainees rotate to the other specialty during training. All medical oncology trainees thought it was important to train in radiation oncology (36% very important) and 97% of radiation oncology trainees thought it was important to train in medical oncology (54% very important). In addition, training in palliative care for three or more months was regarded as important by all medical and 96% of radiation oncologists (48% and 24% respectively rating it as very important). Overall 72% of trainees considered that a common modular basic science curriculum would be useful, and 48% were in favour of joint training during the first year ie a common experience for both groups of trainees. Medical oncologist trainees were not supportive of formal assessment of training, and radiation oncology trainees were supportive of the FRANZCR examinations.

Conclusions: Trainees in medical and radiation oncology favour experience in the other discipline, although the minority of medical oncology trainees have formal radiation oncology training experience. The majority of both groups also favour training in palliative medicine, for between three to six months. They support a modular core curriculum with some form of assessment. The views of trainees should be considered in postgraduate oncology training.

Introduction

Excluding non-melanocytic skin cancer, there were almost 80,000 new cancer cases diagnosed and 34,000 deaths due to cancer in Australia in 1997[1]. Cancer is the commonest cause of death in Australia, comprising a quarter of all deaths[1]. A large and increasing proportion of people with cancer will be assessed and treated by oncologists. The revolution in molecular biology of the past 30 years has vastly increased our understanding of the basic science and mechanisms of oncogenesis, and new biological treatments are now becoming a reality[2]. Likewise, advances in cancer genetics have resulted in a new subspecialty. Combined treatment programs comprising both radiotherapy and chemotherapy are increasingly used, based on evidence of enhanced effectiveness. An increased diversity amongst cancer specialists seems likely to become necessary as our knowledge base increases. The quality and appropriateness of oncology training is therefore of major importance both to the medical profession and to the wider community.

The traditional division of cancer specialists into medical and radiation oncologists is a source of professional identity and pride. In Australia and New Zealand, medical oncology trainees enter the training program with part I FRACP, and have to complete a minimum of two years clinical training in oncology and a further elective year, often spent in research. Many undertake a formal research degree. Radiation oncology trainees, after completing resident training (commonly two years), enter a four years training scheme in which they take parts I and II of the FRANZCR examination. After obtaining the FRANZCR they are eligible for consultant appointment, although many undertake a year's further training as a research fellow.

Rather than divide into modality specialists in line with the model practiced in the United States and, to a large extent, in Australia and New Zealand, opinion in the UK has generally been in favour of closer integration of the specialties, particularly during training, as much of cancer medicine is common to both specialties. Against this background, a questionnaire was conducted in 1997 by the junior radiologists forum in the UK, which sought the opinions of registrar grade medical and clinical (radiation) oncologists about training[3]. As the contexts are very different, we felt it would be interesting to survey medical and radiation oncology trainees in Australia and New Zealand using the same questionnaire and to compare responses to those of UK trainees.

TABLE 1

How would you rate the importance of training in the following departments on a scale of 1 to 5?

	Not important (Score 1)		Between (Score 2-4)		Important (Score 5)	
	MOT	ROT	MOT	ROT	MOT	ROT
Medical Oncology (for ROTs)		3		43		54
Radiation Oncology (for MOTs)	0		64		36	
Palliative Care	0	6	52	70	48	24
Haematology	0	14	72	81	28	5
General surgery eg to observe an axillary dissection	32	14	68	86	0	0
Gynaecological oncology	32	12	68	86	0	2
Radiology	20	19	76	59	4	22
Pain management	4	12	64	72	32	16
Multidisciplinary clinics	0	0	36	43	64	57

MOT: Medical Oncology Trainee ROT: Radiation Oncology Trainee

FIGURE 1

How long should a medical oncology trainee train in radiation oncology?

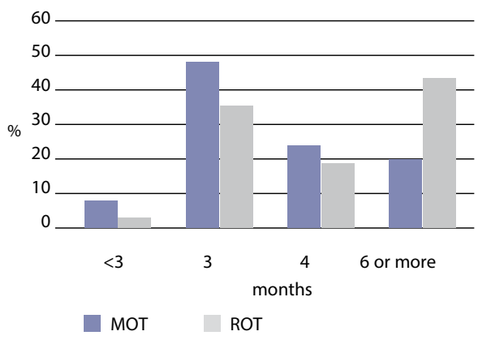
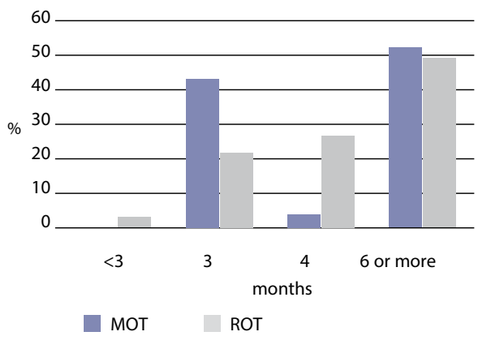


FIGURE 2

How long should a radiation oncology trainee train in medical oncology?



Methods

Permission to use the original questionnaire was given by Dr T Illidge[3,4]. In order to make valid comparisons, the questionnaire was identical to that sent to UK trainees, apart from some very minor changes relevant to the different contexts. These changes are noted below. The questionnaire was mailed to all trainees from lists obtained from the Royal Australasian College of Physicians and the Royal Australian and New Zealand College of Radiologists, and a stamped addressed envelope was enclosed to encourage replies. A covering letter was included to explain the background to the questionnaire, and that it was a comparative study. The envelopes were coded to ensure a representative sample of replies from different regions was obtained, and to enable repeat mailing of the questionnaires to non-respondents in the event of a low number of replies. Fortunately the response rate was high and repeat mailings were not thought necessary. The envelopes were then discarded before reading the replies so that complete anonymity was maintained. The replies were analysed by one author (KF) using the same methods as the UK survey, and the results were compared.

The questionnaire

The questionnaire was divided into two sections: on rotation to other specialties and units, and on a common core curriculum and assessment of training. General comments were also invited. Questionnaires sent to MOTs and ROTs were almost identical apart from specific items on rotation to other specialties.

Amendments to the questionnaire

There were three minor differences from the British questionnaire. Multidisciplinary clinics were included in the question on training in other departments (table 1), because of increasing recognition of their importance in patient management. A question on medical oncology training after completing the FRACP Part I was added because of its relevance to trainees in Australia. In the final question (figure 4), an option of 'no planned period of research' was included in the Australian questionnaire.

Results

Responses were received from 66% of trainees overall, including 68% of 56 radiation oncology trainees (ROTs) and 64% of 39 medical oncology trainees (MOTs). Replies were received from all Australian states with trainees. Medical oncology trainees in New Zealand were not surveyed.

Rotation to other oncological specialties and units

Forty percent of MOTs and 59% of ROTs said that they had rotated to the other discipline, and virtually all had found the rotation useful. For MOTs, the length of rotation was three months for 70% and four to six months for the remainder. All had attended general radiation oncology clinics, 89% had attended radiotherapy planning sessions and 78% had observed brachytherapy. Amongst ROTs, 27% had rotated to medical oncology for two to three months, 50% for four to six months and 23% for more than six months. General medical oncology clinics were attended by the majority and over half observed patients having high dose chemotherapy.

All MOTs and 95% of ROTs felt it was important to spend some time in other departments and they were asked to score the importance of training in a variety of specialties (table 1).

Most MOTs and ROTs rated supervised training as fairly or very important. Similarly, most trainees felt it was unimportant or not very important for their optimal learning to be an observer without clinical responsibility.

All trainees were asked what was the optimal time for a medical oncology trainee to rotate to radiation oncology, and vice versa. The results are shown in figures 1 and 2. They were also asked about training in palliative care and most felt this was important (figure 3). Assuming trainees spend several years in the same cancer centre, rotation to other centres was thought to be necessary by all MOTs and by the majority of ROTs. The later training years was the preferred time for this rotation by 60% of MOTs and 80% of ROTs. More than two-thirds of MOTs and more than half the ROTs felt they should rotate to work for oncology consultants based at district hospitals. Most of the ROTs felt that three months was the optimal length of time for a district hospital rotation, but for MOTs, three months was favoured by 35%, three to six months by 30%, six months by 30% and 12 months by 5%.

Common core curriculum and assessment

Trainees were asked whether they felt all oncology trainees should attend a course with a common core curriculum (during

which medical and radiation oncology trainees would have lectures together on, for example, basic radiotherapy, cancer epidemiology, etc). More than two-thirds of both MOTs and ROTs favoured this proposal. If the common course led to a Masters degree, trainee preferences for assessment were sought. Some gave more than one preference. Eight per cent of MOTs and 18% of ROTs preferred a single examination at the end of the course but more than half the MOTs and 66% of ROTs preferred short examinations at the end of each course module. No formal assessment was the preference of 32% of MOTs and 26% of ROTs.

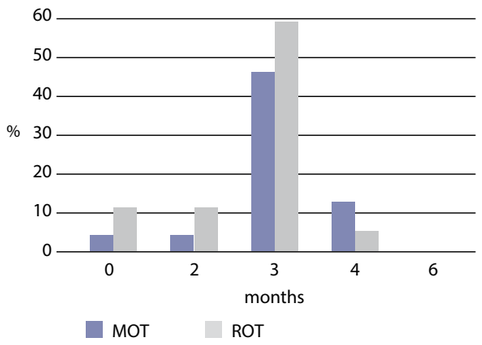
With more structured training, assessments and closer integration between radiation and medical oncology (perhaps with a Masters degree), trainees were asked what should be done with Part II FRANZCR (this examination may make the integration of radiation and medical oncology training difficult). Again, many respondents gave more than one preference. Ninety per cent of MOTs and 80% of ROTs felt that it should be kept as an examination for those wishing to give radiotherapy, but 5% of MOTs and 11% of ROTs thought it should be abolished. A replacement modular examination for medical and radiation oncology trainees was preferred by only 14% of MOTs but by 48% of ROTs. MOTs only were asked what assessment of medical oncology training after FRACP part I was preferred, and 96% thought that an exit exam should not be introduced.

Forty per cent of MOTs and 54% of ROTs thought it appropriate that new trainees should start as general oncology trainees and spend some time working in both radiation and medical oncology departments for the first year before deciding whether to train as a medical or radiation oncologist.

Trainees were asked how the current training influenced their decision to do some research. Two-thirds of the MOTs, were encouraged, none was discouraged and 20% felt it had no influence. Corresponding figures for ROTs were 45% encouraged, 24% discouraged and 30% no influence. Trainees were then asked if they wanted to do one year of research leading to a Masters degree, lengthen the training period to allow two years for an MD or three years for an PhD, or to undertake no planned period of research. The results are shown in figure 4.

FIGURE 3

How long would you like to train in palliative care?



Discussion

Rotation to other oncological specialties and units

Forty and 59% of medical and radiation oncology trainees respectively rotated to the other specialty during training. The great majority of these trainees found the experience valuable. However all medical oncologists and 97% of radiation oncologists thought training in the other discipline was of importance though only 36% of MOTs and 54% of ROTs rated training in the other specialty as 'very important'. Half of the MOTs felt that three months training in radiation oncology would be adequate, whereas more than two-thirds of ROTs thought MOTs should spend at least four months in radiation oncology. More than three-quarters of ROTs wished to spend four months or more training in medical oncology.

Training in palliative care was regarded as very important by half of the MOTs and one-quarter of the ROTs. The most popular length of palliative care training amongst all trainees was three months, although a third of MOTs felt that six months was more appropriate. Approximately half of the workload of medical oncology is palliative treatment and 30-40% of radiotherapy courses are for palliation. Experience in other specialties was generally rated as less important, although the value of multidisciplinary clinics was recognised. Rotation to other cancer centres during training was thought to be necessary by both MOTs and ROTs. Rotation to district hospitals was considered to be less important, particularly by ROTs.

Common core curriculum and assessment

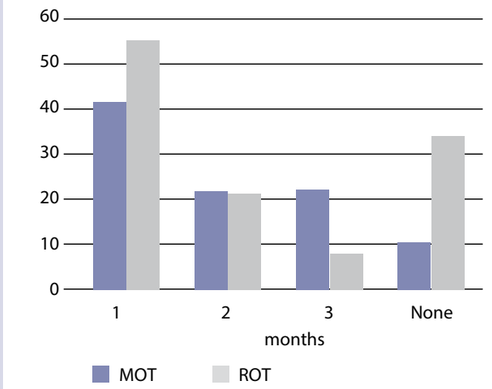
A course with a common core curriculum was popular with most MOTs (76%) and ROTs (69%), with some respondents commenting that they already attend joint lectures. If a Masters degree was the outcome of such a course, a modular examination was preferred by 52% of MOTs and 66% of ROTs. In contrast 96% of MOTs were opposed to an exit FRACP exam. The FRANZCR examination was strongly supported, with 80% of ROTs in favour of keeping its current form, although 48% felt it could be extended, as a modular exam and include MOTs. Only 14% of MOTs were interested in this possibility however. Combined training during the first year was supported by 54% of ROTs and 40% of MOTs. A research year was the most popular option for both MOTs and ROTs, although 36% of ROTs and 11% of MOTs favoured no planned period of research.

Comparison with UK trainees

In the United Kingdom, the division between non-surgical cancer specialties has traditionally been more blurred, and clinical (radiation) oncologists are trained in the use of both radiotherapy and chemotherapy with an emphasis on cancer site specialisation. Medical oncologists, whilst originally mainly academically based, are increasingly involved in chemotherapy administration at a community level, as the indications for chemotherapy widen. Medical oncologists undergo four years of clinical training following general physician's training during which MRCP Parts I and II are obtained. There are no oncology examinations, although recently more thorough assessment of training has been introduced and most trainees attend lecture courses, and undertake a formal research degree. Clinical oncology trainees also enter the training scheme after a postgraduate diploma, most commonly the MRCP. There are five years of clinical training and during the first three years the FRCR examination is taken. The final two years are advanced professional training with cancer site specialisation. Up to

FIGURE 4

What period of formal research would you prefer?



a year of this may be spent in research, and many trainees undertake a formal research degree.

Forty per cent of MOTs in Australia and 30% in the UK had experience in a radiation oncology department. Although the rotations were shorter (mostly three months in Australia rather than six months or more in the UK), the quality of training was better in Australia with most trainees observing radiotherapy planning and brachytherapy. All MOTs who rotated to radiation oncology found it useful but overall, only 36% of Australian MOTs rated radiotherapy training as 'very important' as opposed to 76% of UK MOTs. The ideal length of rotation to radiation oncology was stated as three months by 48% and four to six months by 45% of Australian MOTs; 70% of UK MOTs wished to train in clinical oncology for at least six months.

Rotation of radiation (or clinical) oncology trainees to medical oncology was also more common in Australia/NZ with 59% rotating as opposed to 43% in the UK. The experience obtained appeared to be equivalent and 50% rotated for at least six months. The vast majority of UK clinical oncology trainees and 54% of Australian/NZ ROTs rated training in medical oncology as very important. Two-thirds of UK clinical oncology trainees wanted to rotate to medical oncology for at least six months.

Training in palliative care was rated as 'very important' by 72% and 62% by MOTs and clinical oncology trainees in the UK. Both these figures are considerably higher than in the Australian/NZ counterparts. This difference may reflect different exposure to palliative medicine between the cancer training institutions in the two countries.

A course with a common core curriculum was a popular proposal amongst both Australian/NZ and UK trainees. If a Masters course was to be introduced, the majority of trainees on both sides of the world favoured assessments or short exams after each module, with no examination being preferred by 35% of Australian and 20% of UK MOTs. An introductory year as a general oncology trainee before specialisation was considered appropriate by 48% of Australian/NZ and 63% of UK trainees.

Most MOTs and 45% of ROTs felt that the current system encouraged extending their training time to do research whereas 40-50% of UK trainees were discouraged by the training system. In spite of this, more UK trainees were interested in undertaking a research degree.

In conclusion, training in the other oncology specialty and in palliative care was given more importance in the UK, and there was more interest in joint training initiatives than in Australia.

Summary

Most Australian/NZ medical and radiation oncology trainees appear to be satisfied with their training, whilst criticism of the other specialty's training was common. Medical oncology trainees felt that the general medical knowledge of ROTs was inadequate, and ROTs felt that MOTs had too little understanding of radiotherapy. There was some enthusiasm for combined courses and training programs, which could improve understanding and cooperation between the specialties. Joint training committees between the Royal College of Physicians and Radiologists could promote such cooperative training.

These findings are largely in accordance with the more rigid divisions between the specialties found in Australia/NZ and the USA[5,6] as compared to the UK. There is a large area of common ground between the two specialties, and a basic knowledge of radiotherapy by medical oncologists and of cancer therapeutics by radiation oncologists, and of palliative care by both, is surely essential for comprehensive cancer care[7]. Some of the comments in the questionnaire reflected an adversarial rather than complementary attitude between trainees. However, it could be questioned whether such a rigid division is of benefit to the patient, particularly in light of the increasing complexity of cancer treatments.

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ARTICLES

REPORTS

Australian Behavioural Research in Cancer

This is a regular feature in Cancer Forum describing behavioural applications in cancer prevention.

Australia has four behavioural research centres: the Centre for Health Promotion and Cancer Prevention Research (CHPCPR) of the University of Queensland, the Cancer Education Research Program (CERP) of The Cancer Council New South Wales, the Centre for Behavioural Research in Cancer (CBRC) at the Anti-Cancer Council of Victoria and the Centre for Behavioural Research in Cancer Control (CBRCC) at Curtin University of Technology, Perth.

This report has been edited by Cathy Swart (CHPCPR) from the reports received.

New results

n Centre for Health Promotion and Cancer Prevention Research (CHPCPR), Queensland

Prevention of regular smoking among adolescents

This qualitative study aimed to determine the processes associated with the progression from experimentation to regular smoking among adolescents. The study specifically examined factors and contexts surrounding the influences on youth to become regular smokers and the resistance by other youth who have been or are experimenters and have not become regular smokers.

Results of the study indicated that the question may need to shift from how do we prevent experimentation by youth to an equally important question of how we stop the progression from experimentation to regular smoking. The study highlighted the diversity in adolescents' progression along different smoking trajectories indicating the need to examine multiple approaches to the prevention of regular smoking by adolescents.

Specifically, participants demonstrated a broad range of themes that partly reflect those found in the literature. These themes reflect the factors and contexts surrounding continuation, to regular smoking, and resistance to regular smoking, for this group of adolescents, and include the reasons for smoking and the strong social focus given to smoking.

In addition, other unique themes emerged, including:

- Initiation and experimentation with smoking were viewed as normative behaviour.
- Although firmly bedded in the lifestyle of many regular smokers, smoking itself emerged as of little conscious importance.
- Many participants were unaware of the factors associated with progression from experimentation to regular smoking.
- Regular smoking was often simply a consequence of continued experimentation with few adolescents making conscious efforts to resist regular smoking or to become a regular smoker.
- Movement from experimentation to regular smoking was defined by a change in the status of smoking from "incidental" to "instrumental".
- Stages of change in smoking for some participants reflected markers such as being offered a cigarette, movement from puffing to deep inhalation, seeking out a cigarette, sharing cigarettes, buying cigarettes and smoking alone.
- Regular smokers clearly defined addiction, buying cigarettes and smoking alone as significant indicators of being a regular smoker.

While some participants made conscious efforts not to become addicted, those adolescents were in the minority. Those who did make conscious efforts reported restricting the number of cigarettes smoked, setting personal boundaries, changing peer groups, and keeping themselves occupied.

Participants located smoking as an integral part of their lifestyle and acknowledged the negative effects that it has on their physical fitness, their daily lives and their spending patterns.

n Cancer Education Research Program (CERP), NSW

Patterns and outcomes of care for advanced cancer in New South Wales: A feasibility study.

For most patients with advanced cancer, the focus is not on cure but on enhancing the quality of remaining life. However, there is very little information at a population-wide level on the patterns of care for patients with advanced cancer. Even less information is available on the outcomes of end-of-life care for cancer. A/Professor Afaf Girgis and Professor Bruce Armstrong received funding from the Commonwealth Department of Health and Aged Care and Janssen-Cilag pharmaceuticals to undertake a feasibility study in preparation for a state-wide study of the patterns, pathways, outcomes, costs and predictors of care for advanced cancer.

Participants were recruited to the feasibility study through notifications to the NSW Central Cancer Registry database. Information about their physical and psychosocial well-being and cancer care was obtained by telephone interview, self-administered questionnaires and a four week Cancer Care Diary. Carers also completed self-administered questionnaires to assess their psychosocial well-being. Preliminary results based on 78 patients and their carers recruited from the Hunter indicated that participants appreciated the chance to discuss their own personal cancer experiences with others and a majority were supportive of the measures used and the Cancer Care Diary. In terms of pain, one-quarter of the sample reported experiencing pain related to their cancer in the previous 24 hours, with approximately half of this sub-sample reporting limited pain relief from their prescribed medications. Three-quarters of those who reported pain also indicated high levels of interference with their sleep in the last 24 hours and with their enjoyment of life. Two thirds of the sample agreed that "people get addicted to pain medicine easily" and a further 55% reported that "complaints of pain could distract a physician from treating my underlying illness". Furthermore, patients who reported experiencing pain were more likely to report high levels of anxiety. These data suggest that further research is needed to understand the reasons for the possible under-treatment of cancer-related pain and its psychosocial impact on cancer patients.

n Centre for Behavioural Research in Cancer (CBRC), Victoria

The impact of a media campaign on cervical screening knowledge and self-efficacy

A three-phase cross-sectional face-to-face interview study has recently been completed. It investigated the impact of the PapScreen Victoria media campaign, and the extent to which a media campaign can influence women's perceived self-efficacy associated with having a Pap test . Madeline Fernbach's paper has been accepted for publication in the January 2002 edition of the Journal of Health Psychology.

In total, 1571 women aged between 25 and 69 years were interviewed about prompted and unprompted recall of media messages, intention to have a Pap test and perceived self-efficacy associated with having Pap tests, and barriers to cervical screening. Chi-square and logistic regression analyses revealed that women's awareness of Pap testing messages and priority of this health issue was greater at the first follow-up, and was maintained at the second. Multivariate analyses of variance indicated that it was perceived as more difficult to choose a practitioner and ring for results at the first follow-up, and perceived self-efficacy was lower then than at baseline. However, the screening rate increased over the campaign period. It appears that women become aware of the barriers to screening before overcoming them to have a Pap test.

Public reaction to the movie "The Insider"

A paper exploring public reaction to the movie "The Insider" by Dixon, Hill, Borland & Paxton was recently published in Tobacco Control. Results suggest the anti-tobacco content of the movie served to promote an anti-smoking message to viewers.

n Centre for Behavioural Research in Cancer Control (CBRCC), WA

The Healthway-funded 'disgust project' is into the second phase; Nadine is interviewing 14-16 year olds about what they find disgusting in general, and what they find disgusting about smoking in particular. The first phase, interviewing psychologists and other professionals working with this age group, gave us several new leads on message strategy.

After several pilot studies, we are in the data collection phase of the Healthway-funded study of people's evaluations of the multiple consequences of health behaviours, and Sandra is delighted to note that the data are supporting the hypotheses. Data collection is also in full-swing on the population survey of people's perceptions of cancer, and Sandra will be commencing the data analysis within a few weeks.

In 2001, the Cancer Foundation of WA (CFWA) conducted its seventh annual public information campaign, "Cancer Update", to raise awareness of cancer-related issues in Western Australia. Following the completion of the information campaign (in September), telephone surveys were conducted in both the metropolitan and country areas to measure awareness of the Foundation and the services it provide to the community. Analysis of the data is in progress.

Focus groups with 14-16 year olds are being conducted this week to assist in developing a new sun protection message and ad targeted at young people this summer. We tested two previous ads ("Egg" and "Home and Away stars" ads) with a total of 280 children aged 12-17 year surveyed in schools. We found that the "Egg" ad could be re-run for the younger age group as it appears to perform quite well, but if the primary target is the older age group, we recommended developing a new ad.

Rob and Geoffrey have almost completed the book chapter reporting details of the tracking survey undertaken by the National Tobacco Campaign Research and Evaluation Committee, as part of a comprehensive evaluation of the National Tobacco Campaign. Rob and Nadine are working hard on completing the textbook they're writing on Social Marketing.

Research in the pipeline

n CHPCPR

Is there a place for complementary and alternative medicine (CAM) in palliative care? The experiences of patients with advanced cancer.

The use of complementary and alternative medicine (CAM) by patients with cancer has been documented in Australia and elsewhere. However, few studies have explored advanced cancer patients' perceptions of the use of CAM and the role these therapies play in palliative care. Dr Ignacio Correa-Velez, a PhD candidate, and colleague are currently carrying out a study, founded by the Centre for Palliative Care Research and Education (Brisbane), to longitudinally explore the experiences of patients with advanced cancer who use CAM. Participants are being followed up at monthly intervals until close to death. The study focuses on patient's beliefs about CAM and their reasons for using it, the perceived risks and benefits of the modalities used, the factors affecting changes in the use of CAM over time, and patients' views regarding the possible integration between CAM and conventional medicine in palliative cancer care.

n CERP

Improving rates of sun protection in adolescents

Australia has the highest rate of malignant melanoma in the world. While there have been improvements in sun protection behaviour in the Australian population, the sun protection practices of those in their teens and early 20s have been shown to be particularly poor. Those aged 14-29 are less likely than older groups to wear clothing covering most of their body, less likely to wear hats and more likely to wear briefer clothing to get sun.

Dr Chris Paul and colleagues are undertaking qualitative research in order to explore adolescents' perceptions about sun protection and suntans. Eighteen single sex focus groups are being conducted with students aged between 12 and 17 years, recruited through public high schools in the Newcastle region. Focus groups are being conducted within each of the following age groups: years 7 or 8 (aged 12-13); years 9 or 10 (aged 14-15) and years 11 or 12 (aged 16-17) and are single sex to enable gender specific issues to be examined. Information about participants' age, hair, skin and eye colour and usual tanning and sun protection behaviour is collected before the commencement of focus group by a brief anonymous self-report questionnaire. This research will provide a better understanding of the issues critical to increasing levels of sun protection among 12 to17 year-old Australians and help guide the development of Cancer Council NSW policies and programs in this area.

n CBRC

Adolescents' appraisal of anti-smoking advertisements

Melanie Wakefield is leading a group of researchers in the US, Scotland and Australia in a cross-national comparison study to examine adolescents' appraisal of anti-smoking advertisements. The research, funded by the US National Cancer Institute, will assess main point comprehension, emotional and cognitive responses to each ad, as well as subsequent recall and cognitive processing of messages. The research aims to determine to what extent adolescents from broadly similar cultures might have similar responses to advertising messages and executional styles. A wide range of anti-smoking ads produced by state and national anti-smoking campaigns, pharmaceutical companies and tobacco companies are being tested. Among other things, the study will have implications for the extent to which anti-smoking ads might be recycled across countries, thereby making the tobacco control dollar go further.

n CBRCC

Building Stronger Families: Empowering Parents to Prevent Bullying

We have begun work on an innovative bullying prevention project, funded by the Commonwealth Family and Community Services Department over two years as part of their Stronger Families and Communities Strategy. The study takes a community-based approach, primarily using a media campaign to recommend strategies to prevent bullying. Our intention is to change social norms about bullying from seeing it as a school-based problem to seeing it as a community issue.

News

n CHPCPR

The Centre was very happy to welcome back Liane McDermott in July after she decided to defer her studies in Perth. Liane is a Senior Research Assistant and is currently working on two projects: the Australian Longitudinal Study on Women's Health (WHA) and Sun Protection in Community Settings (SPICS).

Professor John Lowe, former Centre Director, spent a couple of days at the Centre (Sept 27, 28 and Oct 1) during a recent trip to Australia. John was in Australia to attend the PHAA Conference in Sydney and talk on bioterrorism.

Dr Paul McDonald, Assistant Professor at the Department of Health Studies and Gerontology, University of Waterloo, Ontario, Canada, visited the Centre on Sept 28 to meet with like researchers. Dr McDonald gave a presentation as part of the School of Population Health Seminar Series on 'Increasing the population impact of treatment programs for smoking through improved recruitment/utilization'. This was a very interesting and well-received presentation.

The 13th Australian Health Promotion National Conference was attended by Liane McDermott and Lynette Saeck. Liane McDermott presented 'Collaborating with the Wiggles. Can "Dorothy the Dinosaur" help parents protect their young children from the sun?'

Warren Stanton attended the first national Tobacco Control Conference in Adelaide, and presented 'Predictors of adolescent smoking trajectories'.

n CERP

A/Professor Afaf Girgis and PhD student Michele Bandaranayke recently attended the 8th World Congress on Cancers of the Skin in Zurich, Switzerland. Afaf gave a presentation on community practices in relation to early detection of melanoma. Michele gave a presentation on the reasons why some non-melanocytic skin cancers reach an advanced stage before they are diagnosed.

Dr Raoul Walsh and Dr Christine Paul recently attended the First National Tobacco Control Conference in Adelaide. Raoul gave two presentations, one about public practices and attitudes in relation to environmental tobacco smoke and another on smoking cessation pregnancy. Chris gave a presentation on inappropriate use of nicotine replacement therapy in the Australian community.

Congratulations are extended to Dr Raoul Walsh on his appointment as Deputy Editor of the Drug & Alcohol Review.

n CBRC

Dr David Hill, Director of CBRC, has been awarded an AM in the recent Queen's Birthday Honours. David's award is for "service to the promotion of community health, particularly in the development of cancer awareness and prevention programs."

n CBRCC

Nadine has joined the WA Cancer Foundation Consumer Participation Project Advisory Board. Sandra and Rob will be conducting a regular review of the literature on behavioural aspects of breast cancer for the WACOG Breast Scientific Group newsletter.

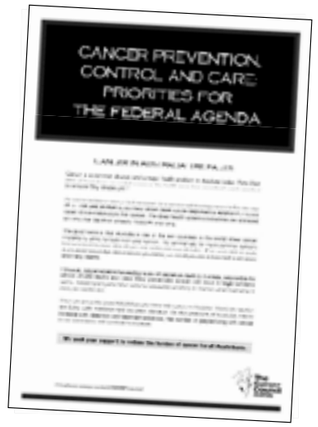
With regret, we have had to say goodbye to Liane McDermott, at least for the time being. Liane has deferred her studies and returned to Queensland but we hope to welcome her back into the CBRCC fold next year.

Meanwhile, we welcome a new PhD student, Debora Brown, who has joined us. Debora completed her Masters degree at Edith Cowan University this year on attitudes of older, 'hard-core' smokers to anti-smoking messages. She will also be working part-time for the Centre. We also welcome Natatsha Watson and Narelle Weller. Natasha is completing a Healthway-funded study of smoking in the media, and Narelle is working on a similar Commonwealth-funded study.

NEWS & ANNOUNCEMENTS

Call for bipartisan support for cancer priorities

The Cancer Council Australia has called on all major political parties to commit to action to help drive down cancer rates and reduce the impact of the disease on patients and their families.



In the lead up to the federal government election, The Cancer Council Australia wrote to the leaders and health spokespersons of the Liberal and National parties, the ALP and the Democrats seeking a commitment to national initiatives to address eight priorities:

- A comprehensive tobacco control program
- Support for clinical trials, to increase patient access and benefit
- A national skin cancer prevention program
- Enhancing palliative care, to ensure all people with cancer have access to care and support
- Improving radiation oncology services, to ensure timely access to treatment
- Increased support for cancer research, to advance prevention, detection and treatment
- Improving rural and regional services, to ensure equitable access to treatment, support services and information for all Australians with cancer
- A comprehensive colorectal cancer campaign, to reduce preventable deaths and illness caused by the most common serious cancer in Australia.

The document, Cancer prevention, control and care: Priorities for the federal agenda, includes further detail about the eight priorities and recommendations for action and funding. It also was sent to every federal election candidate, seeking their support.

The Cancer Council said any party that does not include commitments to improve cancer control in its election platforms is ignoring the concerns of a majority of voters. More than 60% of Australians nominated cancer as the health issue they considered most important in a recent Roy Morgan poll.

The president of The Cancer Council Australia, Professor Ray Lowenthal, said there were many actions governments could take, which would have a massive impact on cancer incidence and mortality.

"The next Federal Government will need the courage and commitment to apply the knowledge we now have to improve prevention, treatment and care," Professor Lowenthal said. "We hope all parties will commit to doing so."

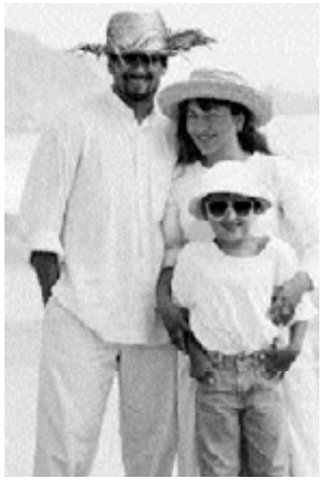
For further information or a copy of the document, please contact Lisa-Maree Herron: (02) 9380 9022 or lisa.herron@cancer.org.au

New appointment for Cancer Foundation CEO

The chief executive of the Cancer Foundation of WA, Mike Daube, has been appointed director-general of the state's Health Department.

A former acting health commissioner, Mr Daube this year chaired the government's Health Administrative Review Committee. He has a long and distinguished history in the health industry both in WA and internationally, having worked in many senior roles within Government, including Assistant Commissioner, Public Health, and chief executive of Princess Margaret Hospital.

SunSmart: Twenty years on



A summary of the development and achievements of the SunSmart program has been published as a monograph by the Anti-Cancer Council of Victoria. The monograph describes the social, political and economic contexts within which the SunSmart program developed and what, importantly, have been the key factors and lessons learned since 1980.

The monograph is an edited extract from the paper "Slip! Slop! Slap!" and SunSmart 1980 to 2000: Skin Cancer Control and 20 years of Population Based Campaigning by Meg Montague, Ron Borland and Craig Sinclair, published in Health Education and Behaviour (Vol 28 No 3 June 2001).

Copies of the monograph can be obtained from the Cancer Education Unit, Anti-Cancer Council of Victoria on

Ph: (03) 9635 5000 or email: enquiries@accv.org.au.

Herceptin decision prompts call for drug funding review

The Cancer Council Australia welcomed Federal Health Minister Michael Wooldridge's announcement on October 12 that the Government will fund Herceptin for women with advanced breast cancer.

While welcoming the Minister's decision to make the drug available, The Cancer Council urged the next government to face the issue of new drug funding in a more comprehensive way.

The Cancer Council Australia CEO Professor Alan Coates said the current Pharmaceutical Benefit Scheme approval process seems to place too much emphasis on cost rather than value.

"Australia aspires to offer a world-class health service, as part of which government has an obligation to properly consider funding for new drugs which are proven to be effective," he said.

"I expect this will mean doubling what we're currently spending on cancer drugs, because many new drugs now in the pipeline may have the capacity to extend the lives of cancer patients.

"Increasingly the focus will shift from 'cure' to improving quality of life for people who are living with cancer, particularly those in whom the disease cannot be eradicated. In many cases this will involve drugs offering long-term disease control."

UICC Translational Research Fellowships

The UICC has announced that, in addition to AstraZeneca and Novartis, Aventis Pharma Recherche-Développement (France) has agreed to sponsor a third TCRF fellowship to be awarded at the Spring 2002 selection. This fellowship will support projects that concern any aspect of the study of cell proliferation, apoptosis or angiogenesis as applied to solid tumours.

Applications for these fellowships (and the American Cancer Society UICC International Fellowships for Beginning Investigators) must be received by the UICC by 1 December 2001.

For further information, see http://fellows.uicc.org

BOOK REVIEWS

BRAIN TUMOURS – AN ENCYCLOPAEDIC APPROACH, SECOND EDITION

A Kaye and E Laws Jr (Eds)

Published by Churchill Livingstone (2001)
ISBN: 0-433-06426-1. 1,031 pages plus index.
RRP: $608.99

The text is designed to provide a comprehensive coverage or, as the editors state, "an encyclopaedic approach". In addition to the two editors there is an extensive author panel of neuro-oncologic (principally neurosurgical) authorities.

Neurosurgeons appear to be the primary target audience of the book. The relative details and selection of authors are consistent with such a strategy. Despite this emphasis, the approach is broad, albeit at times superficial. There are examples of suboptimal review of the non-surgical literature, not only with respect to detail and depth but also prioritisation.

The text is divided into two components. Section 1, Basic Principles, covers in 23 chapters a range of subjects from the historical, through recent scientific advances to particular aspects of therapy and its complications. Section 2 is divided into 10 parts which, through 26 specific chapters, cover the range of specific tumour types and locations. The second edition seeks to systematically update the content and introduce new contributions in evolving fields.

The format is reader friendly, consistent, systematic and accompanied by helpful illustrations. The content is relatively cohesive given the multiplicity of authors with some repetition and limited discord. Despite the challenge of this enormous task the text provides a useful reference resource not only for neurosurgeons but others interested in aspects of neuro-oncology.

L White
Sydney Children's Hospital
Randwick, NSW

CANCER MEDICINE – 5 REVIEW

R Bast

Published by Holland & Frei (2000)
ISBN: 1 55009 115 8.
RRP: $59.40

This small book of multiple choice questions is based on the Holland & Frei text book, Cancer Medicine (reviewed in the July issue).

The book is divided into three sections: cancer biology and epidemiology, treatment principles and specific neoplasms. The book includes answers which are given in some detail with an appropriate reference to the text book.

Advanced trainees may find this a useful aid to be used in association with the reading of the text book. It would allow a degree of self assessment. Basic trainees in internal medicine may also find the multiple question format helpful in their own exam preparation.

D Bell
Department of Medical Oncology
Royal North Shore Hospital
St Leonards, NSW

COLORECTAL CANCER: METHODS AND PROTOCOLS

S Powell (Ed)

Published by Humana (2001)
ISBN: 0-89603-767-3. 283 pages plus index.
RRP: $US119.50

This is quite interesting and a valuable volume. It aims to instruct investigators in the key genetic, cellular and molecular biological methods for analysing colorectal tumours. It's quite precise in its description of these techniques and, as the preface says, "The focused techniques and assays are described in sufficient detail to allow researchers to start an experiment on colon tumours and proceed from beginning to end as if the expert in the field who has performed these studies were guiding them at the bench".

Certainly the chapters cover a wide variety of techniques ranging from gross microdissection of specimens to molecular analyses. Included are the coverage of mutational assays, instability testing, immunohistochemical analysis, chromosome studies and gene expression analysis.

A large amount of practical information is packed into one small volume and this volume is ideal for students and fellows who wish to expand their knowledge in this area and have a ready volume for reference in developing new techniques.

The volume is also good value for those of us who don't get into the lab as it clarifies many of the techniques which are used and helps the non-involved reader to understand the terminology and techniques used in this important area of cancer research.

R Thomas
Peter MacCallum Cancer Institute
East Melbourne, Vic

THE EFFECTS OF LOW AND VERY LOW DOSES OF IONIZING RADIATION ON HUMAN HEALTH

World Council of Nuclear Workers (Ed)

Published by Elsevier (2000)
ISBN: 0-444-50513-X. 536 pages plus index.
RRP: $US183.50

This book contains the Proceedings of the First International Conference on the Effects of Low and Very Low Doses of Ionizing Radiation on Human Health, held at the University of Versailles in 1999. The Scientific Committee and contributors comprise a global "who's who" of low dose exposure radiation researchers and policy makers. The volume is representative of a growing trend in radiation research publications where many of the most relevant and informative publications are expansions of conference proceedings.

The subject is one of growing interest for those in policy and regulatory areas and is receiving increasing attention, as reflected in the extensive research program currently underway and funded by US authorities. A recent funding allocation from

that program to researchers at Flinders Medical Centre further increases the local interest in this subject.

The range of topics discussed includes natural radiation exposures, industrial exposures, Chernobyl, genomic instability after low-dose irradiation, molecular biological mechanisms, difficulties encountered in epidemiological studies at low exposures and the controversy surrounding the validity of the linear no-threshold hypothesis. Some of the highlights of this excellent book are given below.

Tubiana provides an excellent discussion of the reasons why radiation protection specialists have not formally rejected the linear no-threshold hypothesis despite evidence contradicting it, and he outlines the detrimental psychological impact of the use of the hypothesis in risk calculation after the Chernobyl accident. An alternative way to deal with the control of dose that is currently being discussed by the International Commission on Radiological Protection is the philosophy of Controllable Dose, which is outlined by Clarke. It represents a shift in emphasis from societal-oriented criteria to an individual-based philosophy, where if the risk of harm to the most exposed individual is trivial, then the total risk is regarded as trivial, irrespective of how many people are exposed.

Gustaffsson of the International Atomic Energy Agency considers the impact of the model of the dose-response relationship on the regulation of low-level exposure. The epidemiological evidence for risk estimates for radiation-induced cancer is discussed by Kellerer, including a discussion of the A-bomb survivor data and the uncertainties in the neutron data, recent developments and their implications. Mothersill and Seymour detail the implications of genomic instability for risk assessment of low-dose irradiation, including the many uncertainties involved. Trott and Rosemann outline the multistage process of carcinogenesis and models of radiation carcinogenesis and caution the reader that the linear non-threshold hypothesis should not be mistaken as a stringent scientific conclusion derived directly from the present state of knowledge of the processes involved in radiation carcinogenesis.

This book provides an excellent overview of this evolving and controversial field and would make a worthwhile addition to the libraries of researchers, policymakers and regulators.

T Utteridge
Institute of Medical and Veterinary Science
Gilles Plains, SA

For the living: coping, caring and communicating with the terminally ill.

M Golubow

Death and Meaning series
Published by Baywood Publishing Company Inc (2001)
ISBN: 0-89503-257-0 161 pages plus index.
RRP: $US39.35

This book, written by a communications expert whose father's death forced a re-evaluation of life goals, explores the experiences of 12 oncology health professionals who work with the dying. The book is divided into two sections. The first presents unedited, transcribed interviews with each of these 12 professionals (two social workers, three nurses and seven doctors). The second section interprets these narratives within the theoretical framework of symbolic interactionism, focusing on three themes: professional identity, coping with death and health-professional-patient communication.

The transcribed narratives are quite lengthy (10-12 pages), and range widely over many issues. As open accounts of the impact of working in this area are few, many health professionals may find these stories personally relevant and thought-provoking. For example, the narratives cover coping strategies used by nurses and social workers (a focus on the spiritual and philosophical aspects of dying) and those of doctors, who deal with the dissonance between their perceived role (to save lives) and the common outcome (death) by emotional distancing. One young doctor says: "You know, they say the more you give the more you receive? But that's not true. You give a little here and you give a little there and something happens, you lose something. Every day you lose a little something…" Both stress and burn-out and enormous occupational satisfaction are presented in the narratives.

The second section provides a summary of symbolic interactionism for the uninitiated. While I did not find the theory particularly useful in illuminating the data, the themes discussed pulled together a number of elements from the transcripts into a more consumable form. Overall, the book focuses on a neglected area in oncology research: the impact of cancer care on health professionals.

P Butow
Dept of Medicine, University of Sydney
Camperdown, NSW

Minimally invasive cancer management

F L Greene and B T Heniford (Eds)

Published by Springer (2001)
ISBN: 0-387-98710-X. 371 pages plus index.
RRP: $US129.00

This is an excellent text, which provides an (almost) comprehensive outline of the advances that have been made by use of what are, mostly, endoscopic techniques. A surprising omission from the text is reference to gynaecological surgery, particularly as it was in the discipline of gynaecology that laparoscopy initially held sway.

Despite this, the book is an up-to-date description of detailed general principles. These lead on to chapters divided according to anatomical area, followed by chapters on paediatric cancer management, sentinel lymph node biopsy and a very brief outline of future prospects.

At a cost of $US129, it cannot be recommended for every interested clinician's bookshelf, particularly in view of ongoing developments in this area.

An unusual, but welcome, aspect of the book is an attempt to address the issue of credentialling in areas of new technology. For example, minimum standards are set for the performance of sentinel lymph node biopsy. Questions are also asked about the effect on survival of a false negative finding when this procedure is performed for melanoma or for breast cancer. The text calls for development of clinical pathways to ensure the appropriate use of new technology and it concludes with the following quote (in a book written by enthusiasts): "We must constantly be reminded that technology moves faster than knowledge, which, in turn, moves faster than wisdom".

Finally, the book is based on the premise that surgery is "the ultimate curative endeavour, with far and way the largest proportion of patients with cancer cured by surgical means than all others combined". Non-surgical specialties may quibble with this statement. This book, whilst covering its stated objectives well, might have at some point speculated on the likely impact of advances in molecular biology on cancer prevention and treatment.

A Spigelman
Dept of Surgery, John Hunter Hospital
New Lambton, NSW

Nursing in haematological oncology

M Grundy (Ed)

Published by Balliere Tindall (2000)
ISBN: 0 7020 2323 X. 299 pages plus index.
RRP: $87.45

Despite the myriad haematology texts available today it remains difficult to confidently recommend one comprehensive and appropriate enough to meet the needs of nurses working in this area. This book goes some way towards meeting these needs. Nursing in Haematological Oncology provides an informative, well organised and easy to read overview of this subject area.

The text is cleverly pitched at a level to engage both the experienced and novice practitioner. The authors provide case studies, reflection points and discussion questions throughout which assist in bridging the gap between theory and practice by encouraging readers to apply new knowledge and reflect on their own experience.

The book is divided into three sections. The first deals with normal and pathophysiology and provides a succinct overview of management approaches in specific diseases. Section two addresses treatment modalities while section three provides useful coverage of significant patient care issues often unique to these patients and their families.

There are several things that commend this book, written largely by and for nurses. Firstly, it clearly and uncompromisingly focuses on holistic care of the haematological oncology patient. This is evident in a robust overview of approaches to management of these malignancies and the significant physical implications of various treatments. This is followed by informative and provocative chapters dealing with the psychological, social and spiritual impact for patients and families of living and dying with these diseases. Ethical decision making is covered in a very engaging manner, while the far reaching implications of curative treatments are highlighted in well researched discussions on fertility, quality of life, employment and other survivorship issues.

The limitations of this text are, in my view as a haematology nurse and tutor, related to the breadth and depth of the information provided. Most haematology nurses also care for people with non-malignant haematological conditions which, as the book title suggests, are not covered here. Childhood leukaemias and lymphomas are covered, but in a very limited fashion. While this book does provide an excellent introduction to a broad range of issues relevant to haematological nursing, some readers, particularly those pursuing post graduate study in this area may need to look beyond this text. In the book's defence, further readings are recommended throughout, some in the form of a useful minor literature review.

In conclusion this is a genuinely useful text and represents a worthwhile contribution to nursing literature in this specialty area. It provides a basic yet comprehensive overview of the unique and often complex care required by patients and families living with a haematological malignancy and the pivotal role that nurses play in delivery and coordination of that care. This book is recommended as a resource for haematology nurses, a growing number of generalist nurses involved in caring for these patients and indeed interested allied health professionals and general medical practitioners.

L Daly
Haematology Nurse , St Vincent's Hospital
Darlinghurst, NSW

Outline of oncology therapeutics

M Ratain et al (Eds)

Published by Saunders (2001)
ISBN: 0-7216-8123-9. 259 pages plus index.
RRP: $127.05

Outline of Oncology Therapeutics is one of many texts on the market that provides a summary of the agents in the therapeutic armamentarium. The American contributors include many of the clinicians and academics involved in the development of the drugs described and the overall level of information provided is high, representing a text that can be used as a reference work rather than just another pocket guide to chemotherapy doses.

The text is divided broadly into five sections describing the drugs, toxicity management, management of disease complications, drug-disease interactions and treatment administration devices. The range of drugs described include all of the commonly used cytotoxic, hormonal and biologic agents as well as several agents still in development such as the newer anti-folates and oral fluoropyrimidines. Each drug is decribed in point form on a drug per page basis. Areas described include FDA-indications and other uses, mechanism of action, dosing, pharmacokinetics, toxicity, and pharmacy, nursing and supportive care considerations. References for important reviews and therapeutic articles are provided.

Regional chemotherapy is described in more detail than most similar texts and includes intraventricular, intravesical, intraperitoneal and intra-arterial treatment. Toxicity management issues are covered in detail with individual sections devoted to drugs such as anti-emetics, colony-stimulating factors, and miscellaneous toxicity prevention agents. Similarly analgesics for cancer pain, antibiotics for neutropenic fever, and agents to treat anorexia, cachexia and hypercalcemia are discussed. There is a comprehensive section describing venous and other access devices including pumps and this reinforces the usefulness of the text for both nurses and physicians.

There are few topics that are not adequately addressed in this text. Recommendations regarding dose adjustment for patients who have experienced toxicity, who are heavily pre-treated or have organ dysfunction vary significantly from drug to drug, perhaps reflecting the uncertainty and lack of uniform guidelines in this area. The dosage guidelines for capecitabine are consistent with the company product information but do not reflect more recent evidence suggesting that lower doses can be administered to avoid hand-foot syndrome without compromising efficacy. Given increased understanding of the cytochrome P450 enzymes and other metabolic pathways it would be worthwhile to discuss in greater detail potentially meaningful and common drug interactions.

Overall this is an excellent text that can be incorporated into the daily practice of practicing oncologists, cancer nurse specialists and oncology pharmacists. It incorporates the ease of use of other ready-references but with greater detail and scope as well as providing practical rather than just theory-based information.

W Liauw
Cancer Care Centre, St George Hospital

Sydney, NSW

Principles & Practice of Oncology 6th Edition

J DeVita Jr et al (Eds)

Published by Lippincott Williams & Wilkins
ISBN: 0-7817-2229-2
RRP: $595.10

The latest version of this comprehensive standard text is organised in sections, which means that information on a given topic will be found in several places. As is it unlikely, due to its weight (5kg), that it would ever be read cover to cover, this means an excellent index and a willingness to cross reference are required.

Part 1: Oncology Science
Updates basic and applied molecular biology, signal transduction and immunology.

Part 2: Principles of Oncology
Updates cytogenetics, the cell cycle, apoptosis, invasion and metastasis, and angiogenesis. Sections on etiology and epidemiology, surgery, radiation therapy and chemotherapy and biological therapies (including detail on all classes of anticancer drugs) are excellent.

These background areas are followed by the more applied Part 3: Practice of Oncology.

This section includes: Prevention, Screening, Diagnosis, Cancers categorised by disease site (each reviewing pathology, epidemiology and management), Oncological Emergencies, Metastatic Disease by site, Supportive Care (including management of toxicity, pain, psychosocial issues, rehabilitation), Palliative care – alternative/unproven methods, Ethics and information issues and Emerging therapies.

The scope is unlike that of more portable references, and the detail is also impressive, comparable to that seen in a well-referenced review article in a major journal. This is a book for every oncologist's shelf and every clinic and hospital library to own as a reference.

This text would also be an invaluable resource for those aspiring in oncology or for those junior medical staff seeking answers on oncology wards. It would be easy to imagine getting lost among its 3,000+ pages, but there is a wonderful sense of order to this book (aided by a detailed index). Initially, well-explained and readable sections on the science behind cancer, through to comprehensive information on the current practice of oncology (including references from the year 2000), with effort made to incorporate knowledge of advancing technologies and emerging therapies. Put to the test, on questions as diverse as tumour lysis, PET scanning in cancer and genetic counselling, it seems nothing is amiss, except, of course, Australian statistics.

F Boyle and A Rutkowski
Department of Oncology
Royal North Shore Hospital
Sydney, NSW

Renal Cancer: Methods & Protocols

J Mydlo (Ed)

Published by Humana Press (2001)
ISBN: 0-89603-828-9. 399 pages plus index.
RRP: $US119.00

According to the Editor Renal Cancer: Methods & Protocols provides an introduction to the surgeon, clinician, investigator and research scientist to the basic methods employed in the diagnosis and treatment of renal cancer. Indeed this aspect of the book represents less than 10% of its content. The bulk of the book describes in vitro and in vivo experimental techniques ranging from telomerase assays through to laser-capture micro dissection and experimental models of antibody targeting. A number of angiogenesis assays and murine animal models are described. Each of these techniques is described in laboratory manual detail with precise description of experimental strategies.

There is a proportion of the book focussed on immuno-therapeutic and monoclonal antibody approaches to this type of cancer which again describe in detail the laboratory basis for such work rather than the clinical trial results themselves.

There is little to interest the clinician, and I suspect most laboratory researchers have their own protocols and this book will be of passing interest to those wishing to compare their strategies with those of the selected techniques.

This book would have very limited interests to investigators both in the clinic and the laboratory and I cannot see it being a worthwhile acquisition.

M Rosenthal
Private Medical Centre
Royal Melbourne Hospital
Melbourne, Vic

Skin Cancer

Sober and Haluska (Eds)

Published by Sober and Haluska (2001)
ISBN: 1-55009-108-5. 339 pages plus index.
RRP: $253.55

This American Cancer Society Atlas of Skin Cancer is one of a series of 23 volumes, each covering cancer of an organ system. The contributors to the skin cancer volume are very much from the Harvard Medical School/Massachusetts General Hospital with the eminent Arthur Sobers and Frank Haluska as editors. It is pleasing to see that there is an Australian contribution in the shape of the important section on prevention of skin cancer by Robin Marks, Professor of Dermatology at Melbourne University, and David Hill from the Centre for Behavioural Research in Cancer at Melbourne University.

According to the publisher, the readership is "undergraduate, postgraduate, research and professional". Inevitably such a broad target audience will leave everyone a little dissatisfied.

Although promoted as an "atlas", this volume is really more a profusely illustrated monograph with full text and bibliography. Anyone hoping to see a host of illustrations of the different ways skin cancer can present will be disappointed. There are only nine clinical photographs of basal cell carcinoma (BCC) in the relevant chapter. BCC is extremely common and quite variable in presentation and a couple of dozen photographs would be in order in an "atlas". Amelanotic melanoma gets no mention in the index and there is only a single illustration of this difficult diagnostic entity.

Tumours such as angiosarcoma and dermatofibrosarcoma protuberans are seen rarely even by dermatologists and therefore an effort to collect a number of illustrations of these tumours would seem to be a major objective for a book of this type. Indeed there is no photograph of atypical fibroxanthoma or malignant fibrous histiocytoma. The latter is mentioned only in the treatment section and is never described clinically in the text. Paget's disease of breast or extramammary sites as well as cutaneous metastases from internal organs get no mention whatsoever. Some photographs, even of common entities such as BCC, are surprisingly poor in quality as are reproductions of bar charts and diagrams.

As is now happening with a number of textbooks, the volume comes with full text and illustrations on CD-ROM, a handy facility.

T White
Dermatologist
Bondi Junction, NSW

Somatostatin Analogs in Cancer Management

C Scarpignato

Published by Karger (2001)
ISBN: 3-8055-6931-9. 196 pages plus index.
RRP: $US97.50

This is a brief book. It is not a compilation of papers presented at an international symposium but, as the editor indicates in his preface, it is a collection of 11 commissioned monograph reviews. The authorship interestingly is predominantly European without one US contributor. Whether this represents a bias in selection of the authors or whether truly only investigators in Europe have ever contributed substantially to this field is not addressed. However the collection of papers comprehensively reviews the Somatostatin Analogs and especially octreotide.

The first chapter, which is an overview of Somatostatin Analogs, I certainly found useful. The chapter was well written and the author had obviously invested a significant effort in the writing. However other chapters were not as well constructed and only addressed the questions of biology pharmacology and therapy somewhat superficially. Moreover many of the chapters which discussed the clinical use of octreotide are somewhat dated and written in a fairly perfunctory manner. Specific chapters addressing some of the newer issues in Somatostatin Analog research would have been worthwhile. A detailed discussion on the use of octreoscans and the use of radiolabeled octreotide would have been fascinating.

I wonder whether specialised books such as this are becoming dated and whether the types of issues would be best addressed on a specific Internet website where they could be updated and published in a timely fashion.

There is no doubt this book would be of interest for someone working in the field of Somatostatin Analog research but whether the cost of $US97.50 is worth the investment for somewhat dated book is questionable. I'd rather pay this amount to an updated website rather than a book of this vintage.

M Green
Department of Haematology & Clinical Oncology
Royal Melbourne Hospital
Parkville, Vic

Targeted molecular imaging in oncology

E Kim et al (Ed)

Published by Springer (2000)
ISBN: 0-387-95028-1
RRP: $US169.00

This book explores the current state of imaging techniques using targeted agents for the imaging of a variety of malignancies. Its aim is to demonstrate how targeted imaging is impinging on oncology practice as well as research and it foreshadows what potentially lies in the future with these agents.

The book is organised into 21 chapters. The first four chapters discuss the basic principles of cancer metabolism and molecular biology, imaging strategies in oncology and the basic nuclear medicine principles of single photon emission computer tomography (SPECT) and positron emission tomography (PET) as well as magnetic resonance imaging and magnetic resonance spectroscopy.

The next 12 chapters deal with radiopharmaceuticals, antibodies, contrast agents and targeted SPECT, PET and MRI applications. Biochemical mechanisms of a wide variety of tumour targeted imaging agents, including monoclonal antibodies, peptides and non-specific radiopharmaceuticals are explained. The last five chapters discuss new imaging approaches about angiogenesis, apoptosis/hypoxia, signal transduction/antisense, gene delivery and expression, and optical imaging. The book is well illustrated throughout with examples using animal models as well as imaging in humans. The book summarises the current state of application of these techniques and acknowledges the continuous evolution in this field due to technical development.

This book is of primary interest to medical oncologists who seek a book summarising the current status of imaging in the evaluation of a variety of malignancies, both in patients with disease as well as in animal models. It may also be of use in the library of nuclear medicine departments with a large oncology referral base. The book is well written and well illustrated but its target audience is not broad.

M Rossleigh
Associate Professor of Medicine
University of New South Wales
Chairman, Department of Nuclear Medicine
The Prince of Wales and Sydney Children's Hospital

Tumor angiogenesis & microcirculation

E Voest & P D'Amore (Eds)

Calendar of meetings

Calendar Of meetings – AUSTRALIA AND NEW ZEALAND

Date	Name of Meeting	Place	Secretariat
2001			
November			
9-10	The Australian and New Zealand Head & Neck Society	Melbourne Vic	Head & Neck 2001 Secretariat Abacus Management Pty Limited PO Box 77 Pymble NSW 2073 Ph: +61 2 9439 7477 Fax: +61 2 9439 5616 Email: abacus@abacusconf.com
28-30	28th COSA Annual Scientific Meeting	Brisbane Qld	Lawrie Wright Clinical Oncological Society of Australia GPO Box 4708 Sydney NSW 2001 Ph: +61 (0) 2 9380 9022 Fax: +61 (0) 2 9380 9033 Email: cosa@cancer.org.au
2002			
February			
4	"Cancer – We Care" Conference	Canberra ACT	Lawrie Wright The Cancer Council Australia GPO Box 4708 Sydney NSW 2001 Ph: +61 (0) 2 9380 9022 Fax: +61 (0) 2 9380 9033 Email: info@cancer.org.au
21-22	4th National Breast Care Nurse Conference	Adelaide SA	Sylvana DiMaria Ph: +61 8 8222 4618 Email: sdmaria@mail.rah.sa.gov.au
28 Feb – 3 Mar	Inaugural Quality In Practice Conference	Gold Coast Qld	Conference Convenor Quality in Practice PO Box 2058 Milton BC Qld 4064 Ph: +61 (0) 7 3876 6370 Fax: +61 (0) 7 3876 6373 Website: www.agpal.com.au www.conferenceonline.com.au
June			
21-22	5th Winter Congress of the Cancer Nurses Society of Australia	Canberra ACT	Samantha Barabasz Creative Logic 477 Warrigal Road Moorabbin Vic 3189 Ph: +61 3 9555 5001 Fax: +61 3 9555 5002
July			
5-6	Familial & Genetic Aspects of Cancer: 2002	Barossa Valley SA	Teresa Fisher Familial Cancer Conference 2002 Email: directorate@nbcc.org.au Ph: +61 2 9334 1708
October			
21-23	International Clinical Trials Symposium 2002	Sydney NSW	ICMS Pty Ltd Ph: +61 2 9290 3366 Fax: +61 2 9290 2444 Email: trials@icms.com.au Website: www.ctc.usyd.edu.au
November			
25-29	The Australian Health & Medical Research Congress	Melbourne Vic	Initiative of Australian Society for Medical Research Website: www.ahmrcongress2002.conf.au
28-30	29th COSA Annual Scientific Meeting	Sydney NSW	Lawrie Wright Clinical Oncological Society of Australia GPO Box 4708 Sydney NSW 2001 Ph: +61 2 9380 9022 Fax: +61 2 9380 9033 Email: cosa@cancer.org.au
2003			
November			
15-19	6th International Symposium on Paediatric Pain – "Pain in Childhood: The Big Questions"	Sydney NSW	Dianna Crebbin DC Conferences Pty Ltd PO Box 571 St Leonards NSW 2065 Ph: +61 2 9439 6744 Fax: +61 2 9439 2504 Email: mail@dcconferences.com.au

CALENDAR Of MEETINGS – INTERNATIONAL

Date	Name of Meeting	Place	Secretariat
2001			
November			
7-10	XIXth Chemotherapy Foundation Symposium: Innovative Cancer Therapy for Tomorrow	New York USA	J Silverman, Medical Onocology Dept Mount Sinai Medical Centre New York, New York, USA Fax: +1 212 369 5440 Email: J_silverman@smtplink.mssm.edu Website: www.neoplastics.mssm.edu/CTF/sympbrochure.html
9-11	Oncology Nursing Society 2nd Annual Institute of Learning	St Louis Missouri USA	Oncology Nursing Society Pittsburg, Pennysylvania, USA Fax: +1 412 921 6565 Email: member@ons.org Website: www.ons.org
16-18	3rd International Conference on Cancer-Induced Bone Diseases	Awaji Island Hyogo Japan	T Matsumoto, MD, First Dept. of Internal Medicine, University of Tokushima School of Medicine, Tokushima, Japan Fax: +81 88 633 7121
18-21	16th Asia-Pacific Cancer Conference: Cancer in the New Millennium	Manila Philippines	16th APCC, Philippine Cancer Society Manila, Philippines Fax: +63 2 735 2707 Email: 16apcc@pcsi.com.ph Website: www.philcancer.org
26-30	Data Management in Cancer Clinical Trials	Brussels Belgium	D Zimmerman, EORTC Education Office Brussels, Belgium Fax: +32 3 772 62 33 Email: dzi@eortc.be Website: www.eortc.be
December			
7-11	43rd Annual Meeting of the American Society of Hematology (ASH)	Orlando Florida USA	ASH, Washington DC, USA Fax: +1 202 857 1164 Fax: +1 202 857 1164 Email: ASH@haematology.org Website: www.haematology.org.meeting/
10-13	24th Annual San Antonio Breast Cancer Symposium	San Antonio Texas USA	L Dunnington San Antonio Cancer Therapy and Research Center San Antonio, Texas, USA Fax: +1 210 949 5009 Email: ldunning@saci.org Website: www.sabcs.saci.org
2002			
January			
23-27	Molecular Imaging in Cancer: Linking Biology, Function, and Clinical Applications In Vivo	Lake Buena Vista, FL USA	American Association for Cancer Research Ph: 215 440 9300 Fax: 215 351 9165 Email: meetings@aacr.org Website: www.aacr.org
February			
13-17	Apoptosis and Cancer: Basic Mechanisms and Therapeutic Opportunities in the Post-Genomic Era	Waikoloa, HI USA	American Association for Cancer Research Ph: 215 440 9300 Fax: 215 351 9165 Email: meetings@aacr.org Website: www.aacr.org
March			
7-10	The Molecular Genetics of Colon Cancer	Philadelphia, PA USA	American Association for Cancer Research Ph: 215 440 9300 Fax: 215 351 9165 Email: meetings@aacr.org Website: www.aacr.org
14-17	55th Annual Cancer Symposium of the Society of Surgical Oncology	Denver Colorado USA	D Kubis, Society of Surgical Oncology Arlington Heights, Illinois, USA Fax: +1 847 427 9656 Email: diannekubis@acaai.org Website: www.surgonc.org

Date	Name of Meeting	Place	Secretariat
2002			
15-16	4th International Conference on the Adjuvant Therapy of Malignant Melanoma	London UK	CCI Limited, London, United Kingdom Fax: +44 207 720 7177 Email: cci@confcomm.co.uk Website: www.fecs.be/Conferences
19-23	3rd European Breast Cancer Conference	Barcelona Spain	K Vantongelen, FECS Conference Unit Brussels, Belgium Fax: +32 2 775 02 45 Email: EBCC-3@fecs.be Website: www.fecs.be/Conferences
April			
6-10	93rd Annual Meeting of the American Association for Cancer Research	San Francisco California USA	American Association for Cancer Research Ph: 215 440 9300 Fax: 215 351 9165 Email: meetings@aacr.org Website: www.aacr.org
12-13	3rd European Oncology Nursing Society Spring Convention	Venice Italy	K Vantongelen, FECS Conference Unit Brussels, Belgium Fax: +32 2 775 02 45 Email: EONS3@fecs.be Website: www.fecs.be/conferences
17-20	11th Congress of the European Society of Surgical Oncology (ESS0)	Lille France	ESSO 2002 – FECS Conference Unit Brussels, Belgium Fax: +32 2 775 02 00 Email: ESSO2002@fecs.be Website: www.fecs.be/Conferences/esso2002/
18-21	Oncology Nursing Society 27th Annual Congress	Washington DC USA	Oncology Nursing Society Pittsburgh, Pennsylvania, USA Fax: +1 412 921 6595 Email: member@ons.org Website: www.ons.org
May			
1-5	Oncogenomics 2002: Dissecting Cancer through Genome Research	Dublin Ireland	American Association for Cancer Research Ph: 215 440 9300 Fax: 215 351 9165 Email: meetings@aacr.org Website: www.aacr.org
18-21	2002 Annual Meeting of the American Society of Clinical Oncology (ASCO)	Orlando, Florida USA	American Society of Clinical Oncology Alexandria, Virginia, USA Fax: +1 703 299 1044 Email: info@asco.org Website: www.asco.org
June			
6-9	7th Congress of the European Haematology Association (EHA)	Florence Italy	Eurocongres Conference Management Ph: +31 20 679 3411 Fax: +31 20 673 7306 Email: eha2002@eurocongres.com Website: www.eurocongress.com/eha2002
8-11	EACR- XVII: European Association for Cancer Research	Granada Spain	L Hendrickx, FECS Conference Unit Brussels, Belgium Fax: +32 2 775 0200 Email: infro@fecs.be Website: www.fecs.be/conferences/eacr17
30 June – 5 July	18th UICC International Cancer Congress	Oslo Norway	Congrex Sweden AB Stockholm, Sweden Fax: +46 8 661 91 25 Email: canceroslo2002@congex.se Website: www.oslo2002.org/

Date	Name of Meeting	Place	Secretariat
2002			
August			
28 Aug – 1 Sept	12th International Conference on Cancer Nursing 2002	London Arena Docklands, London UK	Liz Piem/Claire Manning The Conference Office Ph: +44 0 20 7874 0294 Fax: +44 0 20 7874 0298 Email: healthcare.conference@emap.com Website: www.isncc.org
September			
1-4	9th Central European Lung Cancer Conference	Vienna Austria	Mondial Congresss Vienna, Austria Fax: +43 1 586 91 85 Email: congress@mondial.at
17-21	21st Annual Meeting of the European Society for Therapeutic Radiology and Oncology (ESTRO)	Prague Czech Republic	ESTRO Office, Brussels, Belgium Fax: +32 2 779 54 94 Email: info@estro.be Website: www.estro.be
18-21	SIOP 2002: The 34th Meeting of the International Society of Paediatric Oncology: Brain Tumours	Porto Portugal	Congress Secretariat Congrex Holland BV Amsterdam, The Netherlands Fax: +31 20 50 40 225 Email: siop2002@congrex.nl
29 Sep – 4 Oct	World Assembly on Tobacco Counters Health 2002 (WATCH 2002)	New Delhi India	Fax: +91 11 694 4472 Email: cancerak@ndf.vsnl.net.in Website: www.watch-2000.org/
October			
6-9	44th Annual Meeting of the American Society for Therapeutic Radiology and Oncology (ASTRO)	New Orleans, Louisiana USA	G Smith, ASTRO Fairfax, Virginia, USA Fax: +1 703 502 7852 Email: gsmith@astro.org Website: www.astro.org
13-17	Frontiers of Cancer Prevention Research: Genetics, Risk Modeling, and Molecular Targets	Boston, MA USA	American Association for Cancer Research Ph: 215 440 9300 Fax: 215 351 9165 Email: meetings@aacr.org Website: www.aacr.org
18-22	27th European Society for Medical Oncology (ESMO) Congress	Nice France	ESMO Congress Secretariat Lugano, Switzerland Fax: +41 91 950 27 07 Email: 16apcc@pcsi.com.ph
November			
1-3	Oncology Nursing Society 3rd Annual Institute of Learning	Seattle Washington	Oncology Nursing Society Pittsburgh, Pennsylvania, USA Fax: +1 412 921 6565 Email: member@ons.org Website: www.ons.org
10-16	9th Hong Kong International Cancer Conference	Hong Kong China	9th HKICC Secretariat Fax: +852 2818 1186 Email: mededcon@hku.hk Website: www.hku.hk/
19-22	2002 Meeting of the European Organisation for Research and Treatment of Cancer (EORTC), the American Association for Cancer Research (AACR) and the National Cancer Institute (NCI): Molecular Targets and Cancer Therapeutics	Frankfurt Germany	L Hendrickx, FECS Conference Unit Brussells, Belgium Fax: +32 2 775 02 00 Email: info@fecs.be Website: www.fecs.be

Date	Name of Meeting	Place	Secretariat
2002			
December			
6-10	44th Annual Meeting of the American Society of Haematology (ASH)	Pennsylvania USA	American Society of Haematology Washington, DC, USA Fax: +1 202 857 1164 Email: ASH@haematology.org Website: www.haematology.org.meeting/
8-11	18th World Congress of Digestive Surgery	Hong Kong China	Congress Secretariat Ph: 852 2818 0232/852 2855 4235 Fax: 852 2818 1186 Email: isdshk@hkucc.hku.hk
11-14	25th San Antonio Breast Cancer Symposium	San Antonio Texas USA	L Dunnington San Antonio Cancer Therapy and Research Center San Antonio, Texas, USA Fax: +1 210 949 5009 Email: ldunning@saci.org Website: www.sabcs.saci.org
2003			
August			
3-8	12th World Conference on Tobacco or Health: Global Action for a Tobacco Free Future	Helsinki Finland	Email: wctoh2003@congcreator.com Website: www.wctoh2003.org

THE CANCER COUNCIL AUSTRALIA

The Cancer Council Australia is the peak national cancer control organisation.

Its members are the leading state and territory cancer councils, working together to undertake and fund cancer research, prevent and control cancer and provide information and support for people affected by cancer.

MEMBERS
The Cancer Council ACT
The Cancer Council New South Wales
The Cancer Council Northern Territory
The Cancer Council Tasmania
Anti-Cancer Council of Victoria
Anti-Cancer Foundation of South Australia
Cancer Foundation of Western Australia
Queensland Cancer Fund

AFFILIATED ORGANISATIONS
Australasian Association of Cancer Registries
Clinical Oncological Society of Australia Inc
Palliative Care Australia
Prostate Cancer Foundation of Australia

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Chief Executive Officer
Professor A Coates MD, FRACP, AStat

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Hon S Lenehan BA, DipMan, MBA, FAICD
Professor M Quinn MB ChB, MGO, MRCP (UK), MRCOG, FRACOG, CGO
Ms L Rogan
Dr R Walters RFD BmedSc, MBBS, RACGP
Professor J Zalcberg MB BS, PhD, FRACP

THE CLINICAL ONCOLOGICAL SOCIETY OF AUSTRALIA INC

The Clinical Oncological Society of Australia (COSA) is a multi-disciplinary society for health professionals working in cancer research or the treatment, rehabilitation or palliation of cancer patients.

It conducts an annual scientific meeting, seminars and educational activities related to current cancer issues. COSA is affiliated with The Cancer Council Australia.

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President Elect
Dr L Kenny MB BS, FRANZCR
Council Nominees
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Dr D Goldstein MB BS, MRCP (UK), FRACP
Ms P Yates BA, DipAppSc, MSocSc

MEMBERSHIP

Further information about COSA and membership applications are available from
GPO Box 4708, Sydney, NSW 2001.

Membership fees for 2001

Ordinary Members: $110
Associate Members: $60
(includes GST)

INTEREST GROUPS

Breast Oncology
Cancer Research
Data Managers
Epidemiological
Gastrointestinal Oncology
Gynaecological Oncology
Head and Neck Oncology
Lung Oncology
Medical Oncology
Melanoma and Skin
Oncology Nursing
(Cancer Nurses Society of Australia)
Paediatric Oncology
(ANZ Childhood Cancer Study Group)
Palliative Care
Pharmacy
Psycho-Oncology
Radiation Oncology
Regional & Rutal Oncology
Social Workers
Surgical Oncology