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Current and future directions for cancer immunotherapy

Theory and potential of immunotherapy

Cancer immunotherapy aims to exploit and maximise the body’s own immune system in order to target and destroy cancer cells. The immune system is a complex and effective integrated network of specialised cells, organs and factors (cytokines and antibodies) that can quickly and efficiently identify and remove foreign agents such as bacteria and viruses, and “self agents” such as cellular debris and malfunctioning cells that are dangerous to the host. There are several mechanisms in place to alert the immune system to these dangerous self cells in order to safeguard against the development of cancer and other diseases. This process is termed immunosurveillance, and it allows for constant screening by the immune system for malfunctioning cells in order to eliminate them before they can cause harm. However, when cancer develops, immunosurveillance mechanisms have been averted and the harmful cells are allowed to survive. Furthermore, cancer cells no longer respond to appropriate growth controls and therefore multiply without constraint and become dangerous to the host. Therefore, the coordinate failure of cells to respond to growth control signals and the failure of the effective immunosurveillance mechanisms to alert the immune system to destroy aberrant cells can lead to malignant disease.

Cancer poses a particularly difficult problem to the immune system, as these cells have overcome immunosurveillance mechanisms and are recognised as self and therefore do not illicit an immune response. Cancer cells can alter their behaviour in many ways to avoid detection and deletion. Firstly, they can overcome programmed cell death (apoptosis) mechanisms that cause cells to die when they have acquired mutations that inappropriately signal the cell to cycle and proliferate. Furthermore, many chemotherapy agents work by triggering apoptotic pathways in cycling cells and thus some cancers are resistant to these types of chemotherapeutic agents due to alterations in their apoptotic machinery. Secondly, cancer cells can evade detection of the immune system by altering the expression of cell surface molecules. MHC molecule expression is essential to trigger an immune response by activating T lymphocytes through the T cell receptor (TCR). Therefore, it is common for cancer cells to down-regulate expression of its MHC molecules7. Finally, cells can secrete immunosuppressive soluble cytokines such as IL-10 and TGF-β that can down-regulate the immune response. Generally, these cytokines act as brakes on the immune system to control the immune response in order to prevent damage that can be caused by the immune system when unregulated. Therefore, when immunosuppressive cytokines are inappropriately expressed, it can dampen immune responses and allow for cancer cells to avoid attack by the immune system.

Malignant cells can also up-regulate the expression of certain cell surface molecules that may not be innately antigenic but may be useful as tumour associated antigens (TAA) in future therapies such as prostate specific antigen (PSA). An example of well-studied tumour-associated antigens is the MAGE and GAGE families of genes8. While these antigens were initially described in melanoma, they have been demonstrated to be present in a variety of tumour types including lung and bladder carcinoma, sarcomas, and head and neck tumours9. They are, however, non-detectable in a large range of normal tissues, including brain, bone marrow and peripheral blood. Therefore, they may be used as potential targets for future therapies.

Types of immunotherapy

The aim of immunotherapy approaches is to prime the immune system to target these cancer cells specifically and without creating an autoimmune response. Immunotherapy can refer to any method in which the immune system is being altered creating an autoimmune response. Immunotherapy can refer to any method in which the immune system is being altered to become more effective. Generally, there are three modes of immunotherapy that are currently being utilised – antibodies, cytokines and cellular immunotherapy.

Antibodies have been used in a variety of ways to affect cellular behaviour. They can be administered to replace naturally-occurring ligating events. When antibodies bind to cell surface molecules they can have activating, inhibiting or null effects on cell signalling. It is possible to use activating antibodies to ligate death receptors on cancer cells in order to cause these cells to die (ie Fas)10. It is also possible to ligate lymphocyte surface receptors in order to induce lymphocytes to expand and activate an immune response (B7.1, LFA-3, ICAM-1)8. In addition, blocking antibodies can be used to interfere with naturally-occurring ligation events that are activating. Using a blocking antibody to the epidermal growth factor receptor (EGF-R) has been effective in reducing the growth of several tumour types that have amplified EGF-receptor expression10. Further, as described in this paper by Dr Frazer, anti-viral vaccines can be administered to produce neutralising antibodies against the papilloma virus, which is responsible...
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The development of genetic engineering has been central to the clinical use of antibodies. This conventional vision of chimeric mAbs (constructed from variable regions derived from murine Ab, and constant regions derived from human Ab) and humanised mAbs (mAbs constructed with only the complementarity-determining regions from a mouse, and the remainder of the variable and constant regions derived from a human source) has been more active in the advent of human/mouse chimeric and humanised antibodies. Antibodies have several potential advantages over small molecules, including fewer unwanted side effects as a result of high specificity for the disease target, and in ability to deliver various payloads, including drugs, radiation and toxins, to specific disease sites, as well as an ability to elicit an immune response, principally through Fc function.

**Tumour antigens recognised by monoclonal antibodies**

Significant progress has been made in the last few decades in the detection and classification of defined tumour-associated antigens (TAAs) recognised by monoclonal antibodies. Most of these antibodies are not only specific by malignant cells, but also by at least one subset of normal adult cells. However, tumour cells express these antigens at higher levels than normal tissues (often up to 100-fold). In addition, accessibility of antigen on tumour to circulating mAbs may be greater than on normal tissue. Therefore, these antigens are not tumour-specific, but often referred to as tumour-associated.

Identification and characterisation of TAA reactive to mAbs involves comparative serological, immunohistochemical and proteome-based approaches to analysis of normal tissues and tumours. It is often the case that the molecular nature and function of the reactive antigens (especially those on surface antigens in solid tumours) are poorly defined. They represent a diverse group of molecules, including proteins, glycoproteins and glycolipids. The expression of TAA is often heterogeneous, and loss of expression may be observed in anaplastic transformation and as a result of immune escape.

Importantly, tumour-associated antigens recognised by antibodies are potential targets for antigen-specific cancer immunotherapy. We refer to them as immunogenic, and often serve as prognostic markers in cancer. Different categories of tumour antigens have been identified in a variety of malignancies: receptor-ligand interactions; initiating cellular adhesion via recruitment of effector cells and/or complement; and cross-linking target molecules and triggering transduction of control cell cycle progression and/or inducing apoptosis/cell death.

**Mechanisms of action of unconjugated antibodies**

Unconjugated mAbs may induce therapeutic effect by a variety of mechanisms, including interference with receptor-ligand interactions; initiating cellular adhesion via recruitment of effector cells and/or complement; and cross-linking target molecules and triggering transduction of control cell cycle progression and/or inducing apoptosis/cell death.

**Receptor binding and signalling inhibition**

The binding of mAbs to growth factor receptors expressed on tumour cells may result in blocking of ligand binding to the receptor, and subsequent inhibition of receptor protein tyrosine kinase (RTK) phosphorylation. Activation of RTKs may prevent receptor homodimerisation or heterodimerisation, and result in inhibition of downstream signalling events. Important example of this mechanism of action of mAbs include ErbB2 (eg Herceptin), EGFR (eg C255), and VEGFR (eg MC111). The binding of mAbs against these receptors induces measurable changes in the phosphorylation status of the receptor and key signalling molecules, and results in signaling inhibition in these events including apoptosis, therapy resistance, and angiogenesis. Herceptin has been approved for the treatment of patients with advanced breast cancer, and a number of antibodies against the EGFR are being developed (Table 1). Anti-angiogenesis has been progressively integrated into the treatment of cancer, and mAbs are also being studied in clinical trials to prevent the interaction between VEGF and its receptors.10 The cross linking of VEGF and its receptors and induction of signalling inhibition by mAb has also been reported with other antigen systems, including CD20.

Tumour cell killing via Fc function

A key component of mAb-based therapy of cancer is dependent upon Fc function. This mechanism of cell killing may be through binding to and crosslinking FcγRs on cellular effectors, or through the recruitment of cellular effectors against target tumour cells, and the induction of apoptosis and phagocytosis. The relative contribution of induction of tumour growth and enhanced antibody-dependent cellular cytotoxicity (ADCC). There are a number of examples of mAbs with highly potent Fc function that have demonstrated biologic efficacy in the clinic, including mAbs against GD2, GD3 and Lewis-α antigens.11,12 Campath1H, a humanised version of rat anti-CDS2 mAb, which is licensed for treatment of refractory chronic lymphocytic leukaemia in the USA. Clinical trials have been shown to be a potent recruiter of effector cells in vitro, and is thought to operate via this mechanism in cancer patients.13

Anti-idiotypic network cascade

Monoclonal antibodies can also serve as immunogens for cancer vaccines through the generation of anti-idiotype network cascade. Anti-idiotype antibodies bind to the antigen-binding sites of antibodies, thus effectively mimicking the three-dimensional structure of the tumour antigen. Antibodies with low or no Fc function may serve as surrogate antigens for active specific immunotherapy. Numerous studies in animal models have demonstrated the efficacy of the anti-idiotype antibodies as vaccines for triggering specific anti-tumour responses, and clinical trials are underway in a number of tumours (eg ovarian, melanoma) with this approach.

**Recombinant antibodies as targeting systems**

Conjugated monoclonal antibodies Some antibodies, which target neoplastic cells, do not induce cell death by themselves. Instead, they deliver natural toxins, radioisotopes, chemotherapeutic drugs or cytokines that require cell surface presentation for activity to be effective.14,15 Conjugated mAbs and antibody fragments have been developed for solid tumours and hematological malignancies, and intensively studied in clinical biological activity in vitro, as well as in vivo animal models. Radioisotopes can be chemically linked to anti-tumour mAbs and administered to patients to deliver radiation selectively to tumour sites. Radioligand conjugates are either constructed by covalent attachment of the radionuclide to the antibody, or by crosslinking through a chemating agent or chemical. The cytotoxic efficacy of a given radioligand conjugate depends on the physical-chemical properties of the radionuclide. Lymphoma cells are particularly sensitive to radiation. The anti-CD20 mAb radiolabelled with yttrium 90Y (Zevalin) has been shown to increase delivery of radiation to neoplastic versus normal tissue by nearly 1000-fold16,17, and is now approved for treatment of B cell lymphomas. Another anti-CD33 mAb conjugated to 90Y has lead to its preclinical development, and to the initiation of clinical trial protocols in patients with cancer refractory to traditional ways of treatment. The linking of calicheamicin to an anti-CD33 mAb has achieved success in the treatment of elderly patients with AML, and Mylotarg has been approved for this indication. Another strategy for mAb-mediated drug delivery involves a two-step approach known as ADEPT, or antibody-drug conjugate. Small molecules tend to have short half-lives, and are rapidly eliminated from circulation. Some of the small therapeutic Ab fragments have been modified by linking to various agents, such as polyethylene glycol and albumin, to block reabsorption in kidneys.18

Bispecific antibodies

Bispecific antibodies (bsAbs) or scFv/Ab fragments and diabodies can overcome the natural specificity of an effector cell for its target, and re-direct the lysis towards a cell population it would otherwise ignore. Most bsAbs can potentially be recruited by bispecific agents include granulocytes, macrophages, natural killer and T cells. For example, cytotoxic T lymphocytes can be re-directed against a tumour by bsAbs that have specificity for a constant component of the T cell antigen receptor complex, or chimaeric antigen receptors (CARs) that are expressed on the neoplastic cells surface. This technique was pioneered in the 1990s and confirmed in many recent animal studies and in clinical trials.19-21 The combination of tumour cell specificity with T cell receptor mechanism has led to the development of a potential approach that has shown encouraging preclinical results. Recent clinical trials of bsAbs using both TCR and Fab's as triggering molecules have also been reported.

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Monoclonal antibodies in combination with other treatment modalities

The combination of monoclonal antibody therapy with other therapeutic agents, particularly chemotherapy and radiotherapy, has been shown in in vivo models and in clinical trials to have potential additive or synergistic effects. The mechanisms of this effect are complex, and related to the interactions between conventional tumor therapy mechanisms of action, and the effect of Fc function or signalling inhibition on tumor cell proliferation and repair mechanisms. The majority of data comes from experiments combining mAbs-based immunotherapy with chemotherapy. The combining of radiotherapy with EGFR-targeted mAbs, and chemotherapy with radioimmunotherapy, has also been shown in in vivo models – and in early phase clinical trials - to have synergistic effects. This approach of combination therapy will in in vivo models – and in early phase clinical trials – to have

Summary and future directions

It is now apparent that the choice of target antigen, immunogenicity of antibodies, extent of antibody half-life, potential of antibodies to recruit immune effectors, decisions on conjugation partners and mAbs manufacturing processes are critical in the development of monoclonal antibodies for cancer therapy. Advances in hybridoma technology, and more recently developments in antibody engineering, have been essential for progress in targeted immunotherapies. Optimisation of monoclonal antibody therapies will be directed towards design of better antibodies and immunoconjugates, enhancement of tumour-specific cytotoxicity, and the development of more effective combination therapy approaches. Approaches, particularly the full potential of mAb-based immunotherapy is yet to be reached.

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The dendritic cell (DC), an uncommon type of bone marrow-derived leukocyte, is widely acknowledged as the most effective antigen presenting cell (APC) and has the unique capacity to initiate and control immune responses against naive and tumour antigens. These cells have generated intense interest in the scientific community because of their potential use as "autologous adjuvants" in cancer vaccination.

**DC biology**

DC differentiate from early myeloid and lymphoid progenitors. In at least two broad subgroups are described – the CD11c+CD123+ "myeloid" DC and the CD11c+CD123- "lymphoid" DC. They have different properties. Current suggestions are that the latter group is more immature and non-reflective and migrate to regional lymph nodes through the afferent lymph. The CD11c+CD123- DC migrate directly to the lymph node from the bloodstream via high endothelial venules. Monocytes may contribute directly to both populations.

DC integrate signals from the environment to link the innate and adaptive arms of the immune system. Through the expression of various surface molecules and cytokines, DCs provide signals that allow T cells to activate, expand, and differentiate into effector cells (Th1, Th2, Th17) depending on the context of the antigen presented.

**DC in cancer**

Abnormalities in cancer

An effective immunologic response to tumour is reliant on a coordinated immune response, a major component of which is the tumoural role played by CD8+ cytotoxic T lymphocytes (CTLs). In a normal individual, tumour antigen from transformed cells is taken up by DC, processed, and presented to T and B lymphocytes in secondary lymphoid tissues. The ensuing interaction between DC and an antigen-specific naive CD8+ T cell results in clonal proliferation and expansion of CD8+ effector and memory T cells. Effector CTL are then able to recognise and kill antigen-bearing tumour cells in the periphery, preventing the growth of the tumour.

Once a malignancy becomes established, it is clear that DC, along with the immune system, have failed in their role of immunosurveillance. There is a multitude of reasons for this to have occurred. Abnormal DC numbers have been described in some cancer patients and abnormal DC function has been noted in breast adenocarcinoma, renal cell carcinoma, prostate adenocarcinoma, basal cell carcinoma, multiple myeloma, melanoma and transitional cell carcinoma of the kidney and bladder.

DC function can be suppressed by the release of tumour-derived inhibitory factors. Interleukin-10 (IL-10), multiple myeloma and bronchogenic carcinoma may impair DC function. IL-6 and macrophage colony stimulating factor (M-CSF) released by renal cell carcinoma inhibited the differentiation of CD14+ derived from CD34+ progenitors. Vascular endothelial growth factor (VEGF) release from human tumours can alter dendritic cell maturation, and high levels of VEGF have been observed in patients with a high number of immature myeloid cells in the blood, which in turn were closely correlated with the stage and duration of clinical neoplastic disease.

In multiple myeloma, DC numbers are relatively normal but CD8+ T cell induction, antigen presentation, and viral control, there was low or absent expression of the costimulatory molecules CD10 and CD80 on DC obtained from the tumour site. In addition, data from analysis of tumour-infiltrating cell populations show that functional DC are impaired in the presence of myeloid cells. In the blood, which in turn were closely correlated with the stage and duration of clinical neoplastic disease.

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In addition to immune evasion, as a result of abnormalities in DC, it is possible to understand the mechanism of immune escape. It is now widely accepted that DCs have a crucial role in regulating the immune response.

**Tumour antigens**

In addition to the choice of DC preparation for vaccination, the selection of tumour antigen for vaccination is of great importance. The ideal tumour antigen for vaccination is one that is highly specific for tumour tissue and not expressed on normal tissues. It should be processed by the tumour cell and contain immunogenic epitopes that are presented in conjunction with MHC molecules. It should be stable and not rapidly degraded. Although not entirely necessary, targeting a tumour antigen that is of vital functional importance to the tumour would be a considerable advantage.

Unfortunately, at the current level of knowledge, we are only able to identify tumour antigens that fulfil some of these ideals.

The form of antigen preparation is also of vital importance. There is a spectrum of options from peptide antigen encoding a single MHC-restricted epitope to various forms of whole tumour antigen, which encompasses a range of epitopes specific for multiple different MHC alleles. As the range of antigens and epitope coverage increases, so does the likelihood of autoimmune responses. Despite the theoretical risks, there is relatively little evidence to suggest that autoreactivity will pose a major impediment to anti-tumour vaccination.

**Clinical trials**

Since the first clinical trial of DC immunotherapy2 was published in 1996, a large number of trials in many different diseases has been undertaken. Virtually all of these trials have been phase I trials and only recently have phase II studies commenced (for a review of current clinical trials see reference 3). Perhaps the most common malignancy to be examined thus far is melanoma. Although comparatively few of these studies have been formally published, trials using MoDC27 and CD34DC23,24 have generated encouraging results with objective clinical responses in 20-30% of patients with late stage disease. Some of these responses have been complete and long-lasting. Associations have been noted between the clinical response (including cutaneous vitiligo) and immunologic response. In one trial, in which subjects were vaccinated with CD34DC pulsed with four melanoma-derived peptides, clinical responses (albeit in an early stage follow-up) were correlated with the number of peptide-specific immunologic responses. The clinical response rate of DC trials in melanoma certainly seems more promising than other investigations by randomised controlled trial, particularly in early stage disease.

Another tumour in which promising results has been seen is renal cell carcinoma. This tumour has been historically associated with responses to non-specific immunotherapies such as IL-2 and lymphokine activated killer cells (LAK). Excellent results were achieved (4/17 attained complete remission) in renal cell carcinoma patients through vaccination with allogeneic DC/tumour hybrids. Characterisation of the cell preparation used in this trial is under further study.

Multiple myeloma and non-Hodgkin's lymphoma are promising candidates for immunotherapy, particularly in the setting of minimal residual disease post-autologous transplant. A recent phase II study with allogeneic DC/tumour hybrids vaccination with MoDC have been noted in vivo in breast, ovarian and colon adenocarcinoma amongst others, demonstrating the feasibility of this approach.

**Vaccination protocols**

One of the problems with assessment of the accrued data is that large, well-controlled trials have studied small numbers of patients treated with multiple different vaccination protocols. As a consequence, a consensus on the optimal choice of DC preparation has not been forthcoming. The vast majority of clinical responses occur in patients who have an immunological response. This may be due to the fact that the immune response in the patient does not always reflect that seen in the local tumour environment.

Some tentative conclusions regarding DC preparation can be made. It appears that DC, MoDC and CD34DC are all feasible alternatives for an immunotherapy program. No head-to-head comparisons have been made in an in vivo setting, and there is only limited in vitro data2 to support one preparation over another. Available evidence suggests that immature MoDC may not be the optimal preparation for tumour immunotherapy. Human vaccination studies have suggested that the use of immature MoDC should lead to antigen-specific tolerance, clearly an undesirable outcome for tumour immunotherapy. Certainly,
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accumulating data suggest they may be less efficacious. Data on DC dose has not been established, however information regarding route of administration is coming to be highly influential. Coadministration of agonist (id) or antagonist (il) agonist is preferred for intravenous (iv), as the id and il routes produced interferon-γ (IFN-γ) responses, however only to elicit an antibody response. T cells examining direct intranodal injection of DC under ultrasound guidance have also shown clinical and immunological responses.

Vaccination frequency is another contentious issue. Most current schemes involve two injections, however this has been based largely on data obtained from patients with infection with disease. Whether this data will translate to the field of immunotherapy remains to be seen. In tumour immunotherapy, particularly if the subject is vaccinated in a state

Intravenous (iv), as the id and il routes produced interferon-γ (IFN-γ) responses, however only to elicit an antibody response. Techniques such as the 51-chromium release cytotoxicity assay

It would be prudent at this early stage to avoid vaccination of patients with a tendency to autoimmune disease. Far, it would be prudent at this early stage to avoid vaccination of patients with a tendency to autoimmune disease. Further directions

Future directions

Paradoxically, the future of DC immunotherapy requires some backtracking in the laboratory. A plethora of clinical trials have been completed with great initial enthusiasm, however it is now becoming apparent that use of inappropriate DC preparations may be quite detrimental. Clearer characterisation of the intrinsically critical requirements to break tolerance to self-antigen is critical. The challenge is different:

Future directions include targeting antigen to various cellular compartments, including helper epitopes or constructs, improving antigen presentation and maturation signals to improve in vivo induction of immune responses. The promising beginning indicates that the effort expended in optimising the many aspects involved may yield great dividends.

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References


Vaccines to prevent and treat cervical cancer

Vaccines to prevent HPV infection and cervical cancer

VLP-based vaccines to prevent HPV infection are now in late phase clinical trials. One such trial, sponsored by Merck, is evaluating a recombinant L1 virus-like particles (VLPs) vaccine. The vaccine is currently in phase III trials, and results are expected to be available in the near future. The vaccine is designed to induce an immune response against the L1 capsid protein, which is present in all HPV genotypes. The vaccine is expected to be effective against a broad range of HPV genotypes, including those that are most prevalent in cervical cancer. It is also expected to be effective against HPV genotypes that are not currently included in the vaccine.

Vaccines to treat HPV infection and cervical cancer

There is currently no vaccine available for the prevention of cervical cancer. However, there are several vaccine candidates in clinical trials. One such candidate is the Gardasil vaccine, which is approved for the prevention of cervical cancer. The vaccine is administered in two doses, and it is expected to provide long-term protection against HPV infection. The vaccine has been shown to be effective in preventing cervical cancer in clinical trials. It is also expected to be effective against other HPV-related cancers, such as anal and oropharyngeal cancer.

Vaccines to prevent and treat papillomavirus infection

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References

Immunotherapy of melanoma

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Why?

Melanoma is a cruel disease. The most recent Australian figures indicate that over 8000 cases of melanoma were reported in 1997 and that approximately 900 people died of the disease that year.1 Of all the statistical data, perhaps the most disturbing is that melanomas are diagnosed early, the five-year survival for melanoma is more than 90% and Australia in fact leads the world in this respect. However, for the patients who do develop a tumour, may their condition is usually metastatic disease or metastatic disease, the outlook is very poor. The one-year survival of metastatic melanoma is 41.5% and the median survival is approximately 7.5 months, although this varies according to the site of metastasis.2 No intervention has been shown to improve the outcome of patients with metastatic disease. Clearly, better treatment approaches are required.

There is tantalising evidence that immune responses may alter the outcome of patients with melanoma. Many of these patients have circulating antibodies or T cells specific for particular tumour antigens. This does not prove a cause and effect relationship, since it is possible that these patients simply have indolent melanomas and that the immune response is an epiphenomenon. However, it is a consistent observation and the hypothesis that immune responses help to control some cancers is reasonable.

Interleukin-2 (IL-2) is approved for use for patients with metastatic melanoma in the USA but not in Australia. Although responses are infrequent and toxicity is high, the small proportion (about 6%) of patients who achieve a complete response to IL-2 have a high probability of long-term complete remission and presumed cure.3 This is rare with conventional chemotherapy and indicates an important qualitative difference in the mechanism of action of this agent – induction of immune memory. Many of these patients develop vitiligo due to T cell-mediated killing of normal melanocytes, indicating that the immune response is specific for antigens in cells of the melanocyte lineage. The development of vitiligo in these patients indicates a higher probability of rejection of tumour tissues that express these antigens.4,5 Combination chemotherapy regimens that achieve long-term disease remission almost certainly involve an immunological component.6-8 Although there is no correlation between memory responses to viral antigens and memory responses to tumour antigens, the latter group is particularly appealing since their development of vitiligo in these patients indicates a higher probability of rejection of tumour tissues if they can be induced, they are probably the worst group to study if the aim is to optimise the vaccination approach. Patients with advanced cancer are often inherently immunosuppressed due to their disease, their poor nutrition or in some cases their treatment. Their cancers are usually progressive, sometimes rapidly. Because an immune response can take weeks to months to become evident it will become apparent – a risky assumption, it is likely that these patients will encounter problems due to their progressing cancers before an immune response has time to mature. Patients with metastatic melanoma means that if a course of vaccination lasts for three months, many patients will not be able to complete it. In one sense, it is surprising that clinical effects of immunotherapy have ever been seen in this population.

Early immunotherapy studies in melanoma used approaches that were thought to be good ideas but had not been validated in humans. Clinical responses were rare, but significant toxicity was also a problem. Because of the infrequency and unpredictability of clinical responses to treatment, valid immunological surrogate endpoints were required. Until recently these assays were not available. Newer assays are now available that are more reproducible and sensitive (reviewed in reference 16). For the first time, immunological responses can now be characterised and measured, finally raising the possibility of optimisation of vaccine protocols.

For this reason, several investigators including our group are now turning to patients with earlier stages of disease. We are performing a series of small studies involving patients who have had cancers that express the antigen of interest but which have been removed. These patients are likely to have an autoimmune disease or resected distant metastases have a higher risk of recurrence and are also eligible. Depending on the nature of the study, it is sometimes necessary to limit eligibility to patients with a particular HLA type. Patients in these studies are usually able to finish a three-month course of vaccination without a significant risk of relapse of their melanoma. This then provides the opportunity to determine whether a vaccination strategy that seemed a good idea on paper is in fact able to elicit measurable immunological responses. The underlying assumption is that only if an immune response is measurable will it be able to be extended to human melanoma. This assumption has never been proven, but it provides a reasonable starting point.

Where to now?

As a result of these observations at both the preclinical and clinical level, it is possible to conceive of a strategy that is most likely to be effective. It is important to identify antigens that are widely expressed and are important to the malignant phenotype so that tumours are not easily able to down regulate their expression. These antigens then need to be delivered in such a way that effective antigenic peptide pools are recognised and a vigorous immunological response can be elicited. Our understanding of the basic biology of the process suggests that this will be best done in a context that provides an inflammation to the region, a vaccine remains in place and a vigorous immunological response can be elicited. Our understanding of the basic biology of the process suggests that this will be best done in a context that provides an inflammation to the region, a vaccine remains in place and a vigorous immunological response can be elicited. Our understanding of the basic biology of the process suggests that this will be best done in a context that provides an inflammation to the region, a vaccine remains in place and a vigorous immunological response can be elicited. Our understanding of the basic biology of the process suggests that this will be best done in a context that provides an inflammation to the region, a vaccine remains in place and a vigorous immunological response can be elicited.
Breast cancer and pregnancy: What we know and where we go

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Abstract

While breast cancer is a high profile disease, its association with pregnancy is less often reported. Pregnancy-associated breast cancer or gestational breast cancer (GBC) is defined as breast cancer diagnosed during pregnancy or in the 12 months post-partum. GBC is uncommon, but likely to become more common as women delay pregnancy until they are in their thirties and forties when the chance of developing breast cancer begins to rise. Delays in diagnosis mean that the prognosis for GBC is often poor. Women who become pregnant later in life also run the risk of developing breast cancer before they conceive. These breast cancer survivors then have difficult choices to make about conception.

Research in these areas is based mainly on reports from single institutions. Further research is needed, and in Western Australia a population-based study to evaluate the epidemiology and management of breast cancer and pregnancy is underway. This work will provide fresh evidence on which to base future practice recommendations, and will enable further research to be conducted about the pathological, biological and imaging characteristics of the malignancies in the pregnant and lactating breast.

Introduction

Because of the high incidence and mortality of breast cancer in the developed world, research in this area has been given a high priority and been widely reported to the general community. Breast cancer’s association with pregnancy, while uncommon, has been less often reported. More women are choosing to delay pregnancy until their thirties and forties, when the incidence of breast cancer rises. This is likely to lead to an increased risk of pregnancy-associated breast cancer, and more women are likely to develop breast cancer before they conceive. This has major implications for both women and the healthcare system.

At present, the association between breast cancer and pregnancy is uncommon, with estimates of it affecting between one in 3,000 and one in 10,000 pregnancies. Historically breast cancer concurrent with pregnancy, also known as gestational breast cancer (GBC), was thought to carry a poor prognosis. This adverse outlook, and the fact that most clinicians’ experience and knowledge of GBC is limited, has continued to impact upon the medical psyche. It has also meant that subsequent pregnancy in breast cancer survivors has not been widely recommended. In this paper we will discuss the evidence available, on which clinicians can base their management of women with GBC and breast cancer survivors who may want to conceive. We will also report on a population-based study of these two groups of women, recently commenced in Western Australia.

Gestational breast cancer (GBC)

GBC is defined as breast cancer diagnosed during or in the 12 months post-partum (including lactation). The reported incidence of GBC, based on mainly single institution reports, ranges from 0.76 – 3.8% of all diagnosed breast cancers. Overall, the incidence appears low, but in premenopausal women, incidence of GBC is reported to be between 7-14%.[11] Pregnancy-associated breast cancers have been reported to have a worse prognosis and are commonly more advanced at presentation (larger tumours and lymph node positive) than non-pregnancy associated breast cancers.[12,13] However, when matched for age and stage at diagnosis, there is no difference in survival between pregnancy-associated and non-pregnancy associated breast cancers. Ezzat reports on a seven-year survival
even in such an uncommon condition, may have medico-legal implications. The rarity of GBC means that a randomised controlled trial is not an appropriate method of evaluating the clinical epidemiology and outcomes of the disease. In general, most studies published to date relating to breast cancer and pregnancy have been descriptive, consisting of retrospective, single institution series, where over a long period of time only small numbers of women have been recruited. There are only four published series involving more than 100 women each. The results of these studies have given us a greater appreciation of how pregnancy may influence the outcome of breast cancer, but have also led to conflicting and confusing information.

The Gestational Breast Cancer Project that commenced in Western Australia (WA) will be the first to use a population-based data set to investigate breast cancer and pregnancy. The project involves collaboration between the WA Safety and Quality of Surgical Care Project and the WA Breast Cancer Research Alliance. Initially this study is descriptive, and has used the wa Record Linkage Project to identify women who were diagnosed with GBC or have survived breast cancer and subsequently conceived since 1982. The WA Record Linkage Project brings together all of the major population-based hospital morbidity data, birth and death records, mental health services data, cancer registrations and midwives’ notifications, linked back to 1980. This linkage system is one of the most complete in the world.

The use of population-linked health data enables us to explore community outcomes and provides additional information for the knowledge base required for evidence-based practice, in areas where it is difficult to gain such data from randomised clinical trials.6 We expect to identify about 300 cases (approximately 10 GBC and seven subsequent pregnancies per year). The information obtained will be supplemented with data from patient medical records and cancer registry data to provide information on diagnosis, treatment and outcomes of the breast cancer and pregnancy. The project has approval to access named data from the WA Department of Health, and ethics approval from the University of Western Australia and all participating hospitals. The data file will be de-identified for research purposes.

This work will enable further research to be conducted in the pathological, biological and imaging characteristics of the malignancies in the pregnant and lactating breast. Future prospective studies are envisaged that will look at changes in the management of breast cancer related to pregnancy, and the psychosocial issues (including fertility) which surround such a diagnosis. We anticipate that this study will lead to a greater understanding of breast cancer and pregnancy, providing new, population based evidence to contribute to the body of knowledge regarding management and outcomes of pregnancy.

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**References**


Cancer Forum – Volume 26 Number 2 – July 2002
Living with cancer in Australia

Report of a conference held in Canberra on 4 February 2002

K Kirke AM
Chair, Patient Support Committee,
The Cancer Council Australia

The Charter of Paris Against Cancer is a global call to action against cancer. Its purpose is to foster improved cancer treatment and research worldwide. The Charter was signed on 4 February 2000 by representatives of many nations, including Australia. The preamble to the Charter sets out its purpose.

REPORTS

PREAMBLE

Deeply troubled by the professional and universal impact of cancer on human life, human suffering, and on the productivity of nations,

Committed to the humanitarian treatment and equal partnership of people with cancer in the ongoing effort against this disease,

Anticipating the rapidly rising tide of cancer incidence throughout the globe, in developed and developing nations alike,

Recognising the need for intensified innovation in all avenues of cancer research, prevention and healthcare delivery,

Believing that quality healthcare is a basic human right,

Acknowledging that currently achievable improvements in cancer survival remain unmet, due to inadequate emphasis on prevention, inadequate funding and unequal access to quality cancer care,

Certain that lives can and will be saved by increasing access to existing technologies,

Aspiring to nothing less than an invincible alliance – between researchers, healthcare professionals, patients, government, industry and media – to fight cancer and its greatest allies, which are fear, ignorance and complacency

On the first anniversary of the signing, an inter-faith event was hosted by The Cancer Council Australia (TCCA) in the Great Hall of the University of Sydney.

With the Charter as its lodestar the Patient Support Committee of TCCA, through its national network of Cancer Councils, organised regional seminars for people living with cancer and their supporters, to explore, discuss and document their expectations and experiences with the healthcare system. In 2001, 42 urban and rural seminars were held, attended by over 900 people in all. From these, 129 priority issues were identified. The themes were grouped in categories as:

1. Coordinators of cancer care
   - Specially trained, defined role, funded, qualification
   - Based in treatment centres and regional areas
   - Members of multidisciplinary team/liaison
   - Networked, in service, relieved, supported

2. Education
   (i) Healthcare professionals
      - "The ideal oncology curriculum"
      - Early involvement of palliative and supportive experts
      - Better communicators
      - Understand survivorship
   (ii) Community
      - Cancer as chronic, controllable disease
      - Reduce stigma and discrimination

3. Information (and helpful advice)
   - Quality assurance, accessibility, availability
   - Public and professional awareness of the CIS
   - Business cards with 13 11 20 and "tips" for GP referral point

4. Infrastructure (and practical matters)
   - Review of patient, accommodation and transport scheme (PATS) and isolated patient, transport and accommodation scheme (IPTAAS)
   - Accommodation near treatment centres
   - Parking near treatment centres
   - Schedule appointments conveniently
   - Financial relief and respite care

5. Empowerment (patients and carers)
   - Information about options
   - Explanation about possible implications
   - Help with formulating questions

6. Support (for support groups)
   - Guidelines and "tips sheets"
   - Evidence-based guidelines eg narrative therapy
   - Support for informal carers
   - Practical help at community level

7. Standards for care
   - Minimum national standards defined
   - Routine best practice
   - Take luck out of process

8. Research
   - Option to participate in clinical trials
   - Encourage translational, psychosocial, behavioural and epidemiological research to inform Cancer Councils
   - Evaluate existing programs
   - What works and what does not
   - Monitoring quality of life indicators

9. Prevention and early detection
   - Participation rates in screening programs
   - Advocacy for application of current knowledge

Some examples are:

- National review of PATS/IPTAAS by end of 2002
- Increase number of medical schools using the Ideal Oncology Curriculum (all by 2005)
- Training program for cancer care coordinators by 2004
- Increase GP referrals to the CIS by 10% per annum

Table 1 – Action points

- Access to information and support
- Practical issues
- Communication
- Coordination and multidisciplinary care
- Service development
- Community education
- Equity
- Survivorship

With information gathered through this process, a national conference was convened in Canberra on the third anniversary of the signing of the Charter. Called "Living With Cancer", the meeting brought together consumers and health professionals to discuss the issues raised, seek consensus and develop an action plan.

The conference keynote address on “Survivorship” was delivered by Professor Miles Little, from the University of Sydney. The conference then broke into workshops to tackle the priority issues identified at regional seminars by affirming their importance and proposing ways in which deficiencies might be addressed. These were brought back to a plenary session for general scrutiny and endorsement.

The draft report of the conference identified nine areas for attention, and within each area checkpoints for detailed action (Table 1).

The draft report was circulated for comment/sign off by all participants and is now the blueprint for Cancer Councils and consumer groups in initiating action collectively and independently to ensure that all cancer patients in Australia, irrespective of where they live, have access to an acceptable level of advice and support. In this way the aims of the Charter of Paris will be realised in Australia.

Prof Miles Little addressing the Living with Cancer conference

* A copy of the proceedings of the Living with Cancer conference is available on request from The Cancer Council Australia.
In February, Australia’s cancer researchers meet at Erskine House, University of Queensland, for the 14th Lorne Cancer Conference. Over 350 delegates listened to a selection of top national and international speakers present their latest data. As usual, the talks covered a wide range of topics, including signal transduction, tumour suppressor genes, immunology, apoptosis and animal models of human cancers. However, a recurrent theme throughout the meeting was the role of the p53 tumour suppressor pathway.

From p53 to therapy

The plenary lecture was delivered by Sir David Lane from the University of Dundee and Cyclacel Ltd, Dundee, Scotland, who discussed ‘P53: A target for anticancer therapy’. p53 is a tumour suppressor protein with potent cell cycle arrest and apoptotic functions. In normal cells, the wild type p53 protein is believed to be maintained in a latent state. Upon exposure to a wide variety of stress signals, this latent wild type p53 becomes activated. The p53 pathway is inactivated in most cancers (including breast, lung, stomach and colorectal) and provides multiple opportunities to develop new anticancer drugs.

Lane discussed potential therapeutic strategies based around the p53 pathway. A key regulator of the p53 pathway, Mdm2, which binds to p53 and diminishes its degradation via the proteasome. In tumours in which the p53 gene is intact but its function is compromised by loss of upstream signalling pathways, small peptide inhibitors, which block the interaction between p53 and active Mdm2, can be used to activate p53 and trigger a full p53 response. In the case of human cervical cancer, the human papilloma virus (HPV) uses a protein known as E6 to inactivate p53. HPV E6 interacts with and inactivates p53 by using Actinomycin D and Leptomycin B to selectively inhibit E6 mdm2 levels. Together, these two drugs can reduce E6 expression and reactivate the p53 response in HPV-expressing tumour cells.

In tumours that lack a functional p53, a number of approaches can be used, including gene therapy to reintroduce the wild type p53 and drugs designed to mimic the downstream effectors of p53. Lane’s group has taken the latter approach. In cells, p53-mediated cell death can be induced via the apoptotic pathway by blocking the function of cyclin A/Cdk2. Using rational drug design and “in silico” screening, the group has identified small molecule inhibitors of cyclin A/Cdk2 function. Lane said they show clear anti-tumour activity in normal cells, but they often also kill normal cells – resulting in unwanted side effects and morbidity. However, a number of groups have suggested that mutant adenoviruses may be used to selectively target p53-deficient tumour cells. Mature adenoviruses have evolved proteins (encoded by the E1a and E1b genes) that are able to deregulate the cell cycle of the host cell to provide an environment conducive to viral replication. Since cancer cells already have defective p53 pathways, these adenoviruses may be engineered to remove the E1 proteins so that they can be replicated in cancer cells but will be unable to replicate in normal cells. Such E1-deficient adenoviruses should, in theory, eventually cause the lysis of tumour cells while leaving normal cells intact.

However, Antony Brashiwate from the University of Otago in Dunedin, New Zealand, is not convinced that such viruses are cancer-specific. He has been testing some of the predictions concerning cancer cell selectivity of adenoviruses using the ONYX-015 virus that is currently in phase III clinical trials. This virus has the E1B-55k protein deleted, which should mean it can only replicate in cells with a mutant p53 protein. Brashiwate presented data showing that the ability of this virus to cause cell death was not restricted by the status of the p53 pathway. Indeed, he found that the virus killed p53 wild type cells with similar efficiency to the p53 mutant cells. His results thus do not support a case for the ONYX-015 virus being cancer cell selective. He concluded that the therapeutic benefit of ONYX-015 might be due with its selectivity for growing tumours at a stress response pathways and not due to the original premise of tumour-specific viral replication.

Complex roles for MMPs in tumour progression

Lynn Matrisian from Vanderbilt University in Nashville presented an excellent overview of the role of the matrix metalloproteinase (MMP) family of extracellular proteases in tumour progression. The concept that tumour-produced MMPs contribute to invasion and metastasis by virtue of their ability to degrade extracellular matrix has been widely accepted for many years. However, Matrisian argued that the role of MMPs is much more complex, and discussed data which challenged some of the early assumptions of how MMPs are involved in tumour progression. Firstly, Matrisian pointed out that MMPs are not, as previously thought, produced by the tumour cells – rather it is the stromal cells that produce the MMPs in response to tumour cells. Matrisian then went on to question the assumption that the primary role with MMPs is to invade the extracellular matrix to invade the tumour. Recent work has indicated that MMPs are involved in the growth of primary tumours, including benign tumours such as colonic polyps. The assumption that MMPs act by degrading extracellular matrix also came under scrutiny. While there is little doubt that MMPs do degrade matrix, an increasing number of non-matrix substrates are being described. These include proteins such as tumour necrosis factor a, E-cadherin, CD44 and many more, indicating the potential for MMPs to have a much broader influence on the tumourogenic process. All this raises the question as to whether or not MMPs really are appropriate targets for anti-cancer therapies. Certainly the concept that inhibition of MMPs will have clinical efficacy by stopping cells migrating into the vasculature and out into the tissues would seem a very narrow and simplistic view. Indeed, Matrisian noted that some cell types in vitro and in vivo that make tissue-degrading MMP inhibitors have so far been disappointing, although there is some indication of efficacy in early stage cancer. This was somewhat surprising in that there is a large amount of preclinical data suggesting that MMP inhibition should have clinical efficacy. Matrisian put this down to differences in the way that preclinical and clinical data is obtained. She pointed out that preclinical experimentation is driven primarily by the availability of these compounds, whereas clinical trials are more likely to be driven by clinical and/or financial considerations. Furthermore, clinical trials are often carried out on late stage disease, whereas preclinical models can more easily test the benefit of early intervention.

Matrisian concluded by stressing the need for cooperation between basic scientists, clinicians, academics and the pharmaceutical industry to close the gap between preclinical experimentation and clinical trials.

Time to pass the baton

Ashley Dunn, who has been the driving force guiding the Lorne Cancer Conferences since their inception in 1989, announced at the conference that he would step down as chairman of the organising committee. Dunn said that while he had “enjoyed immensely” chairing the conference, it was “time to pass the baton” to the younger generation. He indicated he was confident that the conference will be in good hands with Doug Hilton and Warren Alexander taking over the reins.

Australian Behavioural Research in Cancer

This is a regular feature in Cancer Forum describing behavioural approaches to cancer control. Australia has five behavioural research centres: the Centre for Health Promotion and Cancer Prevention Research (CHPPR) of the University of Queensland; the Cancer Education Research and Prevention Program of the University of Western Australia; the Centre for Behavioural Research in Cancer (C2CRC) of the University of Auckland; the Centre for Behavioural Research in Cancer (C2CRC) of the Curtin University of Technology, Perth; and the Centre for Cancer Control Research (C2CRC) of the Cancer Council South Australia.

This report has been edited by Anne Gibbs (C2CRC) from the reports received. No report was provided from the C2CRC.

New Results

n Centre for Behavioural Research in Cancer (C2CRC), VIC

Socially cued smoking in bars, nightclubs and gaming venues: A case for introducing smoke-free policies

Knowing that restrictions on smoking in the workplace and at home reduce levels of smoking in adults, Lisa Trotter, Melanie Wakefield and Ron Boland sought to determine if this may also be the case for recreational venues such as pubs and clubs. A cross sectional survey found that 69% of smokers reported that they would quit smoking if smoke-free policies were to be introduced, 77% of smokers endorsed the potential for smoke-free policies to reduce smoking among young adults and 75% of those who patronise social venues at least monthly report smoking more in these settings (socially cued smokers). These people are aged under 30 years, have made previous quit attempts, are more likely to have a higher number of cigarettes that can be smoked before their health can be affected. Further, 25% of smokers who frequently patronise social venues report that they would be more likely to quit altogether if there were bans in these venues. These people are likely to be aged under 30 years, contemplating or preparing to quit, and approve of bans in social venues. These findings suggest that smoking restrictions in social venues may reduce smoking among young adults who smoke more socially than in any other setting.

The surgical management of ductal carcinoma in situ in Australia in 1995

Data on surgical management of ductal carcinoma in situ (DCIS) of the breast in females were collected as part of the National Survey of the Management of Breast Cancer in Australia in 1995. Surgeries identifying patients with DCIS in their patient registries as having treated a new diagnosis of DCIS between 1 April and 30 September 1995 completed a questionnaire on the presentation and management of each case. The study was conducted by a national steering group and funded by the National Breast Cancer Centre. The report was prepared by Victoria White and Mye Pyden from the C2CRC in collaboration with Dale Shugg from the Menzies Centre for Population Health, Tasmania and Melbourne surgeons Paul Kitchen and John Collins.

Two hundred and five surgeons supplied treatment details on 418 DCIS tumours in 415 women. Half of all tumours were detected at BreastScreen clinics, and a further 25% were...
Reports

Breast care: Improving women’s access to a quality breast prostheses service. A research study to inform policy development.

An intervention study led by Trish Livingston was undertaken to evaluate prostheses use among 102 women who had a mastectomy. Women were recruited through 13 major public hospitals in metropolitan Melbourne. The 64 women in the intervention group received full funding for the prostheses of their choice ($395), while the 34 women in the control group received the hospitals’ usual funding ($150-$395). An evaluation of the quality of women’s experiences in relation to their first prostheses was conducted, with the women being interviewed shortly after receiving their prostheses and then again three and six months later.

Over 80% of women found the administrative procedures to be extremely easy. Compared to women in the intervention group, women in the control group reported that cost was an important influence on their choice of prostheses. Women in the intervention group rated the funding level significantly higher (86%) than women in the control group (50%). The most important factors for women choosing a prostheses were the shape of the prostheses, whether it looked natural and how comfortable it was.

The results of this research, which was funded by the Department of Human Services and BreastCare Victoria, will inform recommendations on policy development and administrative arrangements in order to improve equity and satisfaction for women who purchase breast prostheses.

n Cancer Education Research Program (CERP), NSW

Community attitudes and practices in relation to environmental tobacco smoke

Environmental tobacco smoke (ETS) has been identified as a serious cause of acute and chronic health problems in both adults and children. Given recent legislative changes in NSW to reduce smoking, it is important to understand the current views of the community regarding ETS. For this purpose, Dr Raoul Walsh and colleagues conducted a telephone-based support service for people with breast cancer.

The fourth in this monograph series, entitled Cancers of the skin and lip, is expected that females – like males – will show a decreasing incidence of lung cancer. The monograph shows socio-demographic components of the South Australian population at an elevated risk of cancers at these sites. This information is relevant for the planning of preventative initiatives, including initiatives to reduce the incidence of smoking, to reduce excess alcohol consumption, dietary improvements, and maintaining good workplace practices and environments.

The fourth in this monograph series, entitled Cancers of the female breast and gynaecological organs, has been drafted. As with the earlier monographs, the aim is to inform the public, as well as secondary school and tertiary students with a range of information on cancer trends in South Australia, and opportunities for prevention in the future.

A monograph supplement was also prepared – at the request of staff of the Foundation and South Australian screening services – on risks of cancers of the breast, cervix and skin (malignant), and stages of progression of these cancers at diagnosis, by country of birth. This is also being used to evaluate primary and secondary preventative initiatives and to plan future services. Community support for smoking bans in bars and gaming venues over time.

Passive smoking has many known negative health effects, including lung cancer. The only way to fully protect staff and patrons in bars and gaming venues from exposure to second-hand smoke is by implementing complete smoking bans in these venues. Evidence of community support for smoking bans is important in reassuring governments which are considering implementing smoking bans, and also to counter hostility incurred by arguments of reduced patronage in these venues. The Tobacco Control Research and Evaluation Program conducted representative surveys of approximately 2000 adults throughout South Australia in July 2000 and October 2001, to measure changes in community support for smoking bans in bars and gaming venues over this period. Support for bans in bars and gaming venues significantly increased from 37% overall, and the largest increase in support was seen among smokers. Support for bans in gaming venues similarly increased (significantly) to 73%, with the largest increase again observed among smokers. Regular patrons showed high levels of support for bans in both types of venue.

Research in the Pipeline

n CBRC

Referral of men newly diagnosed with prostate or colorectal cancer to a telephone-based support program

The compelling evidence that providing information, education and counselling services is beneficial to cancer patients adapting to their illness, has led to the development of a mobile telephone-based support service for newly-diagnosed prostate and male colorectal cancer patients to a telephone outcall service provided by The Cancer Council...
Victoria’s Cancer Information Support Service (CISS). The research aims to determine whether the strategy of having cancer specialists actively refer newly-diagnosed patients to an outcall program starting shortly after diagnosis, leads to improved psychological adjustment to cancer diagnosis and treatment.

The three research arms of the block-randomised control trial comprise:

- specialist referral with CISS outcalls within one week of diagnosis and again at six weeks, three months and six months post-diagnosis;
- specialist referral with one CISS outcall; and
- specialist referral to CISS with contact to be initiated by the patient.

The CISS outcall program will be conducted by nurse counsellors who will follow a standardised agenda to capture the range of issues and needs facing newly-diagnosed cancer patients. To assess the effectiveness of active and passive referrals, patients will be interviewed by telephone at four, seven and 12 months after diagnosis. Specialists’ experience and acceptance of the referral procedure will be assessed, as well the impact of the outcall program on CISS staff and resources.

CERP

Coordinated care for advanced cancer: evaluation of two models

Patients with advanced cancer often have long-term complex health needs and complicated treatment regimes. To ensure patient care is optimised, the coordination of cancer care services must be a priority. Afaf Girgis, Sibihah Breen and colleagues are undertaking a study of the effectiveness of two models of coordinated care for advanced cancer (an oncologists/GP model and a telephone caseworker) against current “usual care”. Newly-diagnosed patients with advanced (non-localised) cancer will be recruited from across NSW via the NSW Central Cancer Registry and randomly allocated to one of the three groups. Data will be collected by computer-assisted telephone interview (CATI) at three and six months, and will be used to provide feedback to appropriate care coordinators on issues of concern and recommended strategies for addressing these. In the oncologist/GP model, tailored feedback will be sent directly to clinicians about patient outcomes, for use during routine visits by that patient. In the telephone caseworker model, feedback will be sent to the patient’s nominated caseworker, who will proactively phone the patient at six-weekly intervals (including at the three and six month data collection points). The focus of the call will be to provide phone support to patients and to link them to local support strategies and community services via a cancer services directory. Patients can call their caseworker at any time, with a 24-h answering machine available to leave messages if a call is made after hours. Patient-oriented outcomes including quality of life, prevalence and severity of symptoms and unmet needs, will be the focus for assessing the efficacy of the interventions. Patients in all three groups will receive a hand-held Cancer Care Record to assess referral to and utilisation of services and resources. An incremental cost-effectiveness ratio will also be calculated for each model compared to usual care. If found to be effective in improving patient outcomes compared to usual care, it is anticipated that the two models will be particularly useful in rural areas (especially the caseworker model) and should easily be implemented on a national level in conjunction with existing mechanisms in a cost-effective manner.

CERP

Enhancing the multidisciplinary care of women with breast cancer (Breast Cancer Project)

It is well-recognised that best practice in the management of breast cancer involves a multidisciplinary approach to care. This approach has been found to have a positive influence on the psychosocial well-being and survival of women with breast cancer. GPs would like to be more involved in the continuing care of their breast cancer patients, and play a key role in the multidisciplinary team. In the primary care setting, GPs are uniquely placed to provide to the breast cancer patient appropriate information, referral, treatment options, support and, if appropriate, specialist referral with one CISS outcall; and

This 18-month project was initiated by Queensland Health in conjunction with the Brisbane North Division of General Practice and the Centre for Health Promotion and Cancer Prevention Research at the University of Queensland. The project aims to explore ways to enhance the current role of the GP in the care of women with breast cancer.

CCCR & TCRC

Analysis of hysterectomy rates in South Australia

Using hospital separation data, the prevalence of a hysterectomy status among South Australian women has been estimated across different age groups and regions. These data will be used to assess cervical screening coverage, adjusting for differences in hysterectomy rates by area and age group.

Follow-up survey of local governments in relation to sun protective policies and practices

This survey follows one undertaken in 1999 to assess sun protection activities of councils from the perspectives of shade provision at outdoor facilities/parks and gardens, and building and planning approvals to incorporate shade requirements to protect the public as well as occupational health and safety of council workers. Data have been collected for 2002 and will be compared with results from 1999 to determine progress in the Local Government sun protection program.

Support needs of people at risk of genetically inherited cancers (clients of the Familial Cancer Service)

A study is being planned to assess the support needs of familial cancer registry clients and their preferences for various modes of support services. Results from this survey will be used to inform the development of a support program for these people, who are not currently able to access many support services because they don’t have cancer.

Quitting smoking and physical activity

Previous research has suggested a relationship between quitting smoking and engaging in increased levels of physical activity. Physical activity has been viewed as a potential quitting aid, a way to counter weight gain associated with quitting, or a natural consequence of quitting smoking and beginning to feel more fit and healthy.

The Tobacco Control Research and Evaluation Program is investigating this relationship amongst a cohort of callers to the Quitline, through a follow-up survey conducted 12 months after the initial call to the Quitline. Some population survey data may also be used to investigate this relationship.

News

CERP

In April, CERP hosted the 6th Behavioural Research in Cancer Control Conference that was attended by approximately 70 delegates from across Australia. The conference began with a thought-provoking keynote presentation delivered by Professor Rob Sanson-Fisher from the University of Newcastle, giving an overview of behavioural science’s contribution to cancer research and directions for the future. This was followed by a lively and entertaining conference dinner which, among many things, explored delegates’ joke repertoire and miming abilities. Plenary sessions included: a presentation by Professor Mark Elwood, Director of the National Cancer Control Initiative, on the National Cancer Control Initiative’s program; ‘Tobacco Control and the Future’, presented by Dr Ron Borland, Director of the VicHealth Centre for Tobacco Control and the Cancer Council Victoria, and; ‘Understanding and influencing physical activity within a cancer prevention research agenda’, presented by Professor Neville Owen, Director of the Health Promotion and Cancer Prevention Research Centre, University of Queensland. A wide range of papers were presented showcasing the quality of work being undertaken by researchers across Australia. Sessions included cancer prevention; smoking uptake and cessation; tobacco policy research; cervical and breast cancer; and psychosocial care. Overall, the three-day conference proved to be an excellent forum for discussion and exchange of ideas and provided many opportunities for the establishment of collaborative links. Copies of the conference proceedings are available from CERP.

CERP

Copies of CERP’s annual report for 2000-2001 are now available from CERP.

Tobacco Control Research and Evaluation Program

Alaf Girgis gave an invited keynote presentation on preparing patients for medical imaging at the 53rd Annual National Conference of the Australian Institute of Radiography and the 20th Radiation Therapy Symposium at Coffs Harbour. Janice Perkins and Jill Cockburn ran an interactive session on ‘patient care and medical imaging’ and Janice delivered an invited keynote presentation on the ‘definition and measurement of quality of life’.

CCCR & TCRC

The Tobacco Control Research and Evaluation Program has recently published its triennial Tobacco Control Research and Evaluation Report Volume 1, 1998-2001, which summarises research and evaluation projects undertaken over the three year period. Hard copies of the report will be distributed soon, and an online version is available at the new TCRC website. This is accessible via The Cancer Council South Australia website (www.cancersa.org.au) by clicking on the TCRC link under ‘Research’.

With thanks to Narelle Mills (CERP), Cathy Swart (CHPCPR) and David Roder (CCCR & TCRC) for contributions to this report.
Falling between the Stools?
A consumer-initiated survey of cancer patients’ experiences

Cancer consumers are increasingly trying to influence the cancer research agenda, urging investigation of those aspects of cancer prevention and treatment which are of most interest to them. Sometimes this is pursued through influencing the usual channels of scientific and behavioural inquiry and sometimes by undertaking a study themselves. We think Cancer Forum readers will be interested to hear about an example of the latter, which we believe to be the first of its kind in Australia.

Last year the Breast Cancer Action Group NSW, in order to more formally assess gaps and problem areas in the health care system for women with breast cancer, designed and circulated a questionnaire to its members. The principal aim of the survey was to ask for members’ qualitative views on the most positive and negative aspects of their cancer journeys. Some quantitative information was also sought. Although the respondents were not randomly selected, being BCAG members, they brought to the study views that were considered and informed.

The results, analysed and reported by Julie Billett, Policy Officer at The Cancer Council NSW, highlight common deficiencies and gaps in the breast cancer journey, and the areas most frequently seen as well served. Amongst the key service improvements that consumers wanted to see were:

- Patient communication and information—need for more accessible, timely and authoritative information tailored to women’s needs, and communication skills training for health professionals.
- Integrated, multidisciplinary, specialist care spanning the treatment pathway—need for a stronger multi-disciplinary approach to care, provided by a team of clinicians with specialist training in breast cancer care including breast nurses.
- Supportive care—need improved services and support mechanisms to address women’s psycho-social, practical and information needs.
- Accessible services for all patients—need for improved links and coordination between referral centres and local services to ensure seamless, accessible care for all women, backed up by practical support to meet the particular needs of remote and rural women.

The impetus for the survey came from BCAG’s participation in The Cancer Council NSW’s Breast Cancer Services Development Group, in turn set up at the request of consumers. The Cancer Council’s willingness to assist with the analysis with the assistance of the survey’s findings was much appreciated and shows the synergy that can be generated through partnerships with consumer groups. Very cost-effective too.

Consumer initiated and designed research can contribute valuable insight into the treatment experiences of people living with cancer. These insights in turn provide consumer groups with an evidence-based platform for their advocacy and lobbying activities.

We intend to present the results to cancer conferences such as COSA. A copy of the report is available from either The Cancer Council NSW or from BCAG NSW.

Yours faithfully

SALLY CROSSING
Chair

4 April 2002

Eat & Run nutrition conference

The first Australasian Nutrition, Physical Activity & Cancer Conference was held in Sydney between 24–26 June 2002. Attended by around 250 people, the Eat & Run conference was convened by The Cancer Council Australia and the New Zealand Cancer Society and hosted by The Cancer Council New South Wales. The conference helped guide and influence what cancer societies can do about nutrition, physical activity and obesity. The forum addressed the epidemiology of nutrition, physical activity and cancer, the efficacy of nutrition and physical activity interventions and the potential role of policy and advocacy.

Australia’s Biggest Morning Tea

Australia’s Biggest Morning Tea (ABMT) is The Cancer Council Australia’s second largest fundraising event. The event provides an opportunity for communities to build awareness of cancer while raising funds to help fight this disease.

Throughout May, more than 37,000 hosts nationwide held morning teas and had a cuppa for cancer research with their friends or co-workers.

At the time of publication, ABMT had already raised more than $5.1 million, and TCCA is confident of reaching this year’s national target of $5.5 million.

Thank you to the event’s national sponsor, Bushells, whose backing means that money raised by the community goes directly to support vital cancer research programs.
John Fahey and friends support The Cancer Council Australia

The proceeds of a special tribute dinner for former Commonwealth Finance Minister and NSW Premier the Hon John Fahey, who retired from Federal Parliament last year, have been donated to The Cancer Council Australia. The dinner was hosted by NSW Senator Marise Payne and NSW Opposition Leader John Brogden.

Mr Fahey decided to retire from politics after being diagnosed with lung cancer. In presenting the $10,000 cheque to The Cancer Council Australia Chief Executive Officer Professor Alan Coates last month, he said: ‘When you’re directly affected by cancer, the importance of quality information and support — and the need for ongoing research — really hits home. I, and all my friends who attended the dinner, are very pleased to be able to make a contribution to reducing the impact of cancer through this donation to the TCCA.’

New TCCA Communications Manager

Jennifer Denholm has been appointed Communications Manager of The Cancer Council Australia. Jennifer comes to The Cancer Council Australia from a specialist healthcare communications agency in London, where much of her time was spent working with oncologists and patient-focused cancer organisations. Previously she was PR and media officer for the pharmaceutically benefits branch of the Commonwealth Department of Health and Aged Care.

Jennifer replaces Lisa-Maree Hennon who is currently on maternity leave.

TCCA moving

The Cancer Council Australia is moving from its current William Street address to the University of Sydney’s Medical Foundation Building in Camperdown. The move, anticipated to take place in mid-September 2002, will also involve the Clinical Oncological Society of Australia (COSA) and the Australian Cancer Network (ACN).

Who will you buy a daffodil for?

Daffodil Day
FRIDAY 23 AUGUST

1300 65 65 85
www.daffodilday.com.au

ANTI CANCER DRUG DEVELOPMENT

Baguley and Kerr (ed)
Published by Academic Press (2001)
Distributed by Harcourt Australia Customer Service
ISBN: 0120726513. 384 pages plus index
RRP: $243.10

This book gives an overview of the stages of drug development. The first four chapters deal with underlying mechanisms of tumour development and how basic information about the cell cycle, cell signalling and death pathways can provide targets for therapeutic attack. The next section is mainly about approaches to block tumour progression and includes a useful summary of tumour antigens, an area with which tumour biologists and drug designers should become more familiar. This first half of the book together with the three chapters on drug screening should be of wide interest to chemists, biomedical researchers and oncologists because of the concise, comprehensive descriptions of pathways, with clear diagrams. The results given for some of the lead compounds highlight the complexities of signalling pathways and the importance of context, but at the same time provide a framework for further development. The inclusion of chemical structures, often omitted in such reviews, is welcome. The chapters on drug design, xenobiotics and peptide libraries are more specialised in appeal.

The areas of biology and clinical trials highlight strategies important to the eventual clinical testing of an anticancer drug. The expectations of funding sources, researchers need to recognise and cope with issues of drug development beyond their own specialty, for example pharmacology, surrogate markers for efficacy and toxicology, and trial design. There is little mention of the rapidly expanding use of genomics and proteomics to address some of these problems. However, the book will be a starting point for unravelling the molecular correlations emerging from gene expression profiling of tumours, and for designing tests for functional validation. Well-referenced and indexed, with some colour plates, this text would be a useful addition to the clinic, research laboratory and institution library.

P Parsons
Queensland Institute of Medical Research
Herston, Qld
This book provides the most comprehensive source of both key information and data supported by references to current literature, major trials and landmark articles. The information contained covers all aspects of breast cancer including sections about adjuvant therapy, chemotherapy and scheduling, treatment protocols, physical dose distributions alone. The treatise concludes with a light-hearted poem entitled Shades of Gray, to re-enforce the point that physical dose is only the first layer of therapy. The prevention chapter includes most of the recent data related to breast cancer prevention and although not clinically orientated, describes the current situation regarding prevention strategies. The breast imaging chapter is comprehensive and in particular the mammography is beautifully illustrated. The chapter describes the limitations of imaging techniques, and in particular it introduces the new imaging techniques – such as MRI – and describes its use. The surgical section is comprehensive and includes diagnostic techniques and well-illustrated pictures of the basic surgical techniques in the early treatment of breast cancer, utilising both mastectomy and breast conservation. The principles of early breast reconstruction including tissue expansion and flap reconstruction are well illustrated. A brief pictorial chapter on the pathology of benign and malignant disease is a short of detail but clear to the point. The chapter on breast radiotherapy is quite comprehensive for a book of this size, with a very useful, comprehensive reference of current information in a handy, concise format and easy-to-read format. Such information in paper-based format will, of course, require regular updates, and this is acknowledged by the editors. This 2000 edition represents an updated and revised version of the first edition, published in 1999. This is an issue for all guidelines and information sources which aim to maintain currency and must be borne in mind by the readers.

Although this handbook is written for an American audience and contains information which is specific to the American health care system, it is a good overview of the current status of breast cancer in Australia. The breadth and depth of information make this a suitable text for experienced clinicians and for those interested in the role of Campath-1H in breast cancer. The book is 128 pages in length and divided into five chapters, details the dosage regimens and previous studies in refractory disease. These studies were performed over a number of years and often with relatively small numbers of patients. However, they certainly confirmed the drug is both highly active and relatively safe, with the main side effect being immunosuppression and infection. The final chapter – chapter five – discusses the role of Campath-1H as a preparative regimen and T-cell depletion method prior to bone marrow transplantation in refractory B-CLL, and includes both myelo-ablative and non-myelo-ablative marrow transplant strategies. The book gives an excellent, up-to-date, concise, comprehensive, and authoritative review of the role of Campath-1H in chronic lymphocytic leukaemia by leading authorities in the area. It would be a very useful book for someone planning to use the drug for patient treatment in the clinical setting, and also those with a wider interest in B-CLL or monoclonal antibody therapy.
The initial four chapters are about generic disciplines in the field, covering agent identification and preclinical testing; intermediate biomarkers; tissue microdissection and processing; and basic pharmacokinetics and pharmacodynamic principles. The first of these chapters, by Jim Crowell at the National Cancer Institute (NCI), is a striking account of the systematic approach taken by the Division of Cancer Prevention in its Chemopreventive Agent Development Research Group. First there is a careful scouring of the literature and, quite admirably, media accounts around the world, for clues about agents whose scientific basis may be a lot more than folklore. This approach has the benefit of ready-made “proof of concept”. However, there may well be centuries of human exposure information, though not well compared with a placebo. So there develops an understanding of the mechanisms of action and pharmacodynamics of agents like curcumin (in India), polyphenols (from green tea in the Far East) and others. Of course, the NCI also supports more traditional approaches to agents identified through observational epidemiology in humans. For example, after Professor Gabriel Kune’s groundbreaking observation of the possible protective role of aspirin in the Melbourne Colorectal Cancer Case-Control study in the early 1980s, the single largest risk factor for the 50% risk reduction, was found to be a 50% reduction in colorectal cancer rates in those who took aspirin. Aspirin has made aspirin an obvious target for the NCI’s attention. This approach has the benefit of ready-made “proof of concept”. The balance of the book is organ-specific chapters on chemoprevention. This is particularly impressive to this non-dermatologist. Throughout the organ-specific chapters, there was a surprising lack of references to basic biology of cell and tissue organisation; the role of oncogenes and the downstream (prostanoids) metabolic products in cancer promotion is a theme throughout the book – as well as possible non-cox inhibitor mechanism of action of aspirin and the nonsteroidal anti-inflammatory drugs. The agency is also engaged in carrying ideas forward that may emerge from “high tech” discoveries such as DNA microchip technology, or functional proteomics. The steps that follow are impressively comprehensive, including mechanistic pre-screening of putative standard agents (as signal transduction modulation, including those targeting growth factors, oncogenes and tumor suppressors; -anti-hormones, -anti-inflammatory drugs, -apoptosis, -angiogenesis). In vitro efficacy models, in vivo short-term screening using intermediate endpoints and animal model efficacy testing are all described in the systematic process of candidate selection before clinical trials. Safety and dosage information is collected in the later phases of toxicity and pharmacology studies in an equally systematic fashion.

The initial biomarker chapter highlights the gap between the need for biomarkers to hasten the drug evaluation process in humans, and the difficulty of such markers as truly surrogate for the cancer endpoint. Despite millions being spent in this area by the NCI, there is lingering uncertainty about most markers: markers anywhere less true than aspirin’s alone its relevance as cancer immunology. The chapter leads one to the excitement and real prospects of cancer control through immunological strategies, particularly with respect to the use of vaccines and the (so-called) “immunotherapy”. Its observation also holds promise and reality as we see that BCG vaccination in bladder cancer is one of the few strategies surviving the rigorous development process through to randomized controlled trials.

In fact, despite all the effort, very few other approaches have reached this far to be exposed as “mainstream medicine”. Celecoxib, in the field of colorectal carcinogenesis, is another. With its efficacy established in an RCT in familial adenomatous polyposis. With a meritorious force of large trials of agents already “through” extensive preclinical testing, currently in progress, we can look forward to an exciting decade ahead. Importantly, the risk or at risk will be the next challenges, with the implementation hurdle perhaps even higher than the simpler negative (but so important) truths already well entrenched in the public health message (don’t smoke, for example).

From a technical standpoint, this book left something to be desired. Firstly, it was completely devoid of illustrations (cartoons, as our Pacific neighbours would have it) that are so informative to the reader in the complex field of molecular pathogenesis. That is a lost opportunity to spread contemporary understanding to a whole cohort of young investigators and causing intellectual capacity (many advances come this way). Secondly, simple proofreading seemed overlooked with glitches that threatened the reader’s comfort and confidence in the book. Even the printing left out sentences and lines in a few pages rendering a few sections as non-sectors.

Overall, this is an excellent reference book painting a good picture of the state of the art of the science of chemoprevention for the first few years of the century, and will provide all readers with a critical look at the opportunities for investigation within the cancer control and immunology. The chapter leads to the excitement and real prospects of cancer control through immunological strategies, particularly with respect to the use of vaccines and the (so-called) “immunotherapy”. Its observation also holds promise and reality as we see that BCG vaccination in bladder cancer is one of the few strategies surviving the rigorous development process through to randomized controlled trials. As the editor-in-chief is Head of Experimental Oncology, it was a considerable surprise that rather than simply reproduce the state of the art, what was really needed was to provide an overview with a critical look at the opportunities for investigation within the cancer control and immunology. The chapter leads to the excitement and real prospects of cancer control through immunological strategies, particularly with respect to the use of vaccines and the (so-called) “immunotherapy”. Its observation also holds promise and reality as we see that BCG vaccination in bladder cancer is one of the few strategies surviving the rigorous development process through to randomized controlled trials. As the editor-in-chief is Head of Experimental Oncology, it was a considerable surprise that rather than simply reproduce the state of the art, what was really needed was to provide an overview with a critical look at the opportunities for investigation within one’s own realm of resources – intellectual, laboratory or clinical. The balance of the book is organ-specific chapters on chemoprevention. This is particularly impressive to this non-dermatologist. Throughout the organ-specific chapters, there was a surprising lack of references to basic biology of cell and tissue organisation; the role of oncogenes and the downstream (prostanoids) metabolic products in cancer promotion is a theme throughout the book – as well as possible non-cox inhibitor mechanism of action of aspirin and the nonsteroidal anti-inflammatory drugs. The agency is also engaged in carrying ideas forward that may emerge from “high tech” discoveries such as DNA microchip technology, or functional proteomics. The steps that follow are impressively comprehensive, including mechanistic pre-screening of putative standard agents (as signal transduction modulation, including those targeting growth factors, oncogenes and tumor suppressors; -anti-hormones, -anti-inflammatory drugs, -apoptosis, -angiogenesis). In vitro efficacy models, in vivo short-term screening using intermediate endpoints and animal model efficacy testing are all described in the systematic process of candidate selection before clinical trials. Safety and dosage information is collected in the later phases of toxicity and pharmacology studies in an equally systematic fashion.

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There is, however, very little on current therapeutic modalities. The one chapter focussing on this area is the excellent chapter on hyperthermia for breast cancer, but its omission begs the question of what happened to the other chapters on the current treatment of important cancer types.

Overall, this book would be useful for a cancer clinician wishing to have a ready reference of molecular biology, carcinogenesis and pre-clinical models and how they relate to cancer. However, as a book on the clinical aspects of cancer, this text does not fulfil its aim of bridging the gap between researchers and clinicians.

R Judson
Parkville, Vic

CANCER OF THE HEAD AND NECK

Author: J Shah
Published by B C Decker (2001)
RRP: AS441.08

To cover, in a meaningful and comprehensive manner, as vast and diverse a topic as cancer of the head and neck in 477 pages would clearly require an expert in the field. It would thus come as little surprise that this goal has been so successfully achieved in this text under the editorial leadership of Jatin Shah, Chief of Head and Neck Services, Memorial Sloan-Kettering Cancer Centre. All the authors are present or past members of the Head and Neck Disease Management Team from the Memorial, some of whom have clearly spread the gospel throughout North and South America. The author freely acknowledges the impossibility for a text of this nature to be either complete or permanently up-to-date, but shortcomings in achieving either of these goals are not obviously manifest.

The book commences with introductory chapters on epidemiology of head and neck cancers, common basic pathology and imaging modalities. This is followed, using a systematic format, by a more detailed description of the anatomical regions of the upper aerodigestive tract. With each region the important anatomical considerations, disease processes, clinical presentations, diagnostic tests and treatment options are discussed. Further chapters cover skull base, salivary tumours, thyroid and parathyroid glands, vascular tumours of the head and neck and soft tissues and bony tumours. The concluding chapters cover more comprehensively bone and soft tissue reconstruction, radiation oncology, chemotherapy, rehabilitation and quality of life assessment. Each chapter is masterfully crafted and covers a specific topic or region comprehensively. Treatment recommendations are based on an analysis of a vast literature base and address all available modalities, particularly emphasising the role of multimodality therapy in advanced or biologically unfavourable disease and the importance of an appreciation of the functional disability associated with the various treatment options. Whilst not purporting to be a textbook of operative surgery, broad principles relating to surgical technique and goals are included in an insightful manner.

This is a beautiful text that was a joy to read, being clearly written in a concise style and glittering with photographs, illustrations, radiographs, charts and tables of the very highest standard. Good things do not come cheaply, but it is hard to put a price on quality. This is a text that those interested or practising in any region of head and neck cancer treatment would enjoy. For those involved in teaching the accompanying CD-ROM, containing the complete texts and illustrations, offers many exciting possibilities.

R Judson
Parkville, Vic

CANCER OF THE LUNG: FROM MOLECULAR BIOLOGY TO TREATMENT GUIDELINES

A Weitberg (ed)
Published by Humana Press (2002)
RRP: US$125.00

This book is edited by Alan Weitberg with a foreword by Jokin Klastersky, and was published this year. It contains five parts. Part I includes some background epidemiology, basic science including pathology, molecular biology and diagnostic techniques as well as lung cancer staging. Part II details surgical, multimodality treatment of regionally advanced non-small cell lung cancer, stage IV non-small cell lung cancer and new treatments. Part III looks at the treatment of small cell lung cancer including chemotherapy, surgery, radiation and novel approaches, whereas part IV includes a section on the novel uses of radiation therapy. Part V is a short section on the availability and potential benefits of using lung cancer guidelines.

The chapter on techniques for the diagnosis of lung cancer is also well-written, and included a section on endobronchial ultrasound aspiration. The newer technique for endobronchial ultrasound appears to be absent although autoimmuno-fluorescence bronchoscopy is mentioned. To its credit, the potential role of Helical CT scanning is briefly discussed. Much has been published in this promising area since the book’s publication.

Overall, the book is well-written, and provides brief but quite comprehensive summaries of the relevant areas. In particular, the section on pathology is well-written for non-pathologists and includes a mention of atypical adenomatous hyperplasia as a precursor for bronchoalveolar cell carcinoma. As a book, the reviewers unavoidably suffer the disadvantage of not having the latest information, for example DPNHEC as the precursor for carcinoids. Nevertheless, this part is quite concise and well-written.

The parts of treatment are similarly easy to read and are as up-to-date as possible. For instance, there is good discussion on the follow-up studies from the often quoted Roth and Rosell studies of neoadjuvant chemotherapy for non-small cell lung cancer. There is also a brief discussion on the potential future of small molecules and biological therapy, though it would have been nice to have more information on this rapidly advancing field.

Nonetheless, this book should be generally well-written, and certainly well worth reading for all those with an interest in the important biological and clinical issues in lung cancer management.

K Feng
Dept of Thoracic Medicine
Prince Charles Hospital
Chermside, Qld

CANCER SCREENING: A PRACTICAL GUIDE TO

PHYSICIANS

K Azei and G Wu (eds)
Published by Humana Press (2002)
RRP: US$99.00

This is a very interesting and useful book. It covers a wide variety of cancers and gives a thorough overview of the treatment options available. The way the book is set out is interesting. Each chapter starts with key principles and then goes through the methods of the particular cancer. Under consideration, biology of the cancer, rationales of screening and methods of screening. Finally there is a summary, which includes cost effectiveness and controversial issues.

The final two chapters of this book ‘Future prospects in cancer screening’ and ‘Medico-legal aspects of cancer screening’ are a challenging part of this book. The future looks to be an exciting place to be in the area of cancer screening and a worrying place to be for medico-legal issues!

For a cancer specialist there is, I feel, insufficient detail. This is more a text for the interested generalist. Some general practitioners who have a particular interest in cancer disease may wish to purchase it.

H Fardy
Shellharbour, NSW

CANCER TIPS: A HANDBOOK FOR CANCER PREVENTION AND MANAGEMENT

J M Metz
Published by Lippincott Williams & Wilkins (2002)
RRP: A$55.00

In the preface, the author describes the purpose of the book as to ‘provide clear, concise information that can always remain at a cancer patient’s fingertips’. By its concise nature, the information does not include much detail but rather, focuses on the most important points. The book arose from the author’s work on the OncoLink website, a site that provides information on cancer care.

The book meets its stated purpose and, in my view, is a good initial resource book for people diagnosed with cancer. There is also a section on prevention and screening for individuals interested in this area.

Other areas covered in the text are: dealing with the side effects of cancer treatments; sexuality issues, physician and patient communication, issues for breast cancer, and alternative medicine. New, current topics are described in the section on ‘miscellaneous topics’. In section eight, a guide on how to use the Internet is described. Throughout this section, the author offers criteria or parameters to be used in the evaluation of a ‘medical’ website. The final section is a workbook that encourages the reader to keep a record of medications, vitamins, herbs, unconventional treatments, medical history, surgical history, past hospitalisations, etc. Such a personal record would be very helpful for the individual who seeks more involvement in their medical care.

As an American text, there are inevitably some differences in terminology. Most of the language that would not be used in Australia, such as drug names, can be quickly clarified by a doctor or nurse. Other terms will be familiar to Australians who watch American television programs or regularly read American books. As the book is written from a medical perspective, the reader is referred to as the ‘patient’ - this may make some readers uncomfortable.

The author presents a section on unconventional medical treatments. There is a constant theme through this section that it is important to share with the physician any unconventional treatments. This is repeated in the workbook section. The tone of this section is clinically focussed, with recommendations by the author against most of the treatments described. Although inclusion of this section is a positive step toward resolving the issues around patients not sharing their non-prescribed treatments with their doctor, patients may continue to be reserved about sharing such information for fear that they will be judged harshly by the doctor.

Overall, this book is highly recommended for people who are undertaking treatment for cancer. It provides information that people consistently state that they need and a framework for discussing issues with their doctor.

L Greenish
School of Nursing, Canberra University
Canberra, ACT

CANCER TREATMENT

C Haskell (ed)
Published by Saunders (2001)
RRP: A$474.10

As stated by the editor, Charles M Haskell, “The goal of cancer treatment is to provide an authoritative, comprehensive appraisal of contemporary therapy. Because of advances in molecular medicine and therapeutics, this appraisal requires a more extensive understanding of the basic science of oncology than in the past. An introduction to essential basic concepts is now included to meet this need.”

This weighty tome is divided into 22 parts.

Part I: covers the principles of cancer treatment (including the biology of cancer, principles of cancer genetics, and principles of biologic therapy).

Part II: provides detailed information on drug therapy, including a series of monographs for chemotherapy and biological agents.

Part III: provides an overview of haematologic considerations in cancer treatment.

Part IV: covers the principles of cancer treatment (including the biology of cancer, principles of cancer genetics, and principles of biologic therapy).

Part V: provides detailed information on drug therapy, including a series of monographs for chemotherapy and biological agents.

Part VI: provides an overview of haematologic considerations in cancer treatment.
no marmography or ultrasound illustrations are given), early disease, through to locally advanced disease, localised (single site) metastatic disease and widespread metastatic disease including palliative cases. The book has been supported (although it is unclear to what extent) by the drug company AstraZeneca. Each case occupies approximately two pages, and nearly all have clinical and radiological illustrations (some occupying the entire page). The clinical details are brief and to the point and are followed by the question: “What management/treatment/advice would you recommend?” The author then details what actually happened to the patient. In many cases, not all the prognostic information is available. Some of the cases have a very brief conclusion to the end. The illustrations are of high quality. The use of arrows to demonstrate the clinical radiological abnormalities would have been useful. Some of the illustrations are repeated and there are even some personal photos of one of his patients playing golf and sking. I am unsure of the style of the book (narration is conversational and sometimes a little disjointed and lacking in scientific depth. There is variability in the details of treatments (from “steroids were given” to “where to buy “goat skin gloves” in patients with lymphoedema. There is no standardisation of drug nomenclature (trade versus generic names). Editorial advice and proof reading is missing. There are inappropriately labelled pages, eg 137. The appendices at the end of the book are not useful – the trials mentioned are not explained; the list of chemotherapy, hormonal and supportive drugs is not complete and is inaccurate. The recommended reading includes five articles and three textbooks.

One cannot be critical of the way a particular case was treated, and certainly some management decisions are controversial and some go against current clinical evidence. The author does not make any attempt to calculate the risk benefit assessment of treatments given, particularly in the adjoining setting.

I believe the usefulness of this book as presented is limited. Breast cancer management is a multidisciplinary effort and a book even of this type can no longer be written by one individual. Perhaps co-authorship with other individual cancer specialists would have avoided some of the variations and lack of detail in the modalities of therapy discussed. The usefulness of these cases in terms of teaching students and junior staff is also limited unless they are supplemented by additional information either by the author (not done) or by a tutor using the cases as a starter for discussion. For example, what would the differential diagnosis be; were the investigations appropriate; what is the prognosis in this setting; what are the risks and benefits of treatment; what are the treatment options; and if the patient was treated differently, why? The sum of a model answer supported by referenced evidence would make this a far more useful text. In the absence of these additional features, then I suggest that most clinicians would have similar cases from their books. A key strength is the raw clinical material and use as resource material such as an atlas of diagnostic oncology from which to obtain appropriate histological, radiological and clinical illustrations. As it stands, at the recommended price of $140.00 who should buy this book? Probably no one.

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ENCYCLOPEDIC REFERENCE OF CANCER

M Schwab (ed)

Published by Springer (2001)
ISBN: 3-540-66527-7
992 pages plus index and CD-ROM
RRP: US$195.00

In the words of the editor, this reference text is designed to close the language gap between clinical and basic scientists and provide basic information to students and the informed layperson. The aim is to provide readers with an entry point to a panoply of knowledge, and entries are written in a very accessible style. The encyclopedia covers a broad range of cancer-related topics and represents a huge effort of cooperation with over 250 contributors, all internationally recognised experts in their field.

The format is reader-friendly, consistent and well-presented. The terms are arranged alphabetically, with each entry consisting of a concise definition and, where appropriate, a list of synonyms. A menu of entries on syndromes, genes and molecular processes also provide further information written in an essay format with reference to key publications. The terms are cross-referenced and, in some cases, are accompanied by helpful illustrations. The entries range from definitions of common acronyms, to concise description of cancer processes including tumour initiation, progression and the cell cycle (particularly useful topics for students and to those new to the field of cancer research), to descriptions of molecular techniques, such as microarray analysis.

Although the encyclopedia includes a number of excellent entries, a useful feature is the expert review or test by laboratory researchers wishing to understand terms used by clinical cancer research colleagues, it was clear that the encyclopedia is heavily weighted towards explaining basic science terms. Nevertheless, the author does not make any attempt to calculate the risk benefit assessment for the investigators but also for basic scientists researching reading out of their field of expertise and, as designed, an excellent reference for students. The book is accompanied by a useful CD-ROM, which contains the full text in PDF format.

A DeFazio

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FARNESYL TRANSFERASE INHIBITORS IN CANCER THERAPY

S Sebbi and A Hamilton (eds)

Published by Humane Press (2001)
ISBN: 0-89630-619-4
273 pages plus index.
RRP: US$125.00

The Ras GTPases operate as molecular switches that link extracellular stimuli with a diverse range of biological outcomes, including cell proliferation and differentiation. Some 30% of human tumours carry mutations in one of their Ras genes that renders the mutant Ras protein insensitive to normal regulation. The Ras on and delivers a potent proliferative signal that contributes to tumour growth. Ras therefore constitutes an excellent target for drug discovery. Starting with this premise, the book by Sebbi and Hamilton catalogue the work of many research groups and pharmaceutical companies that has led to the first generation of therapeutically active Ras inhibitors, which are now undergoing phase I and II clinical trials. This is very much a sequential “basic science to bedside story” that clearly illustrates how in vitro biochemical and cellular activity can be translated to the groundwork for pharmacological exploitation. Here it is a relatively simple set of three observations. Ras must be localised to the inner surface of the plasma membrane to function. A C-terminal membrane anchor to the plasma membrane post-translationally mediates plasma membrane localization, and the first enzyme involved in the ras anchor is farnesyltransferase (FTase). The book goes on to examine the rationale for developing farnesyltransferase inhibitors (FTIs).

The first chapters cover some of this background, but the non-expert would probably be advised to read the last chapter as well to fully appreciate the basic science. Thereafter the book tackles the detailed biochemical of FTase, plus the two complementary approaches that have been used to identify FTIs – rational drug design based on the minimal FTase substrates, and random screening of compound libraries. Each class of FTI that has been developed is then dealt with separately, together with detailed descriptions of the relevant biological chemistry. Subsequent chapters cover the cell biological and animal model testing of the various FTIs followed by a collation of the various phase I trial results with some of the featured compounds. A summary chapter then pulls together what can be gleaned from these studies and sets out future directions for clinical trials. The final chapter also covers similar ground, but gives an overview of the whole story and sets out some of the biological questions surrounding the future use and development of the FTIs. In particular, how to deal with accumulating data that the Ras-related protein Rhob, or some other prenylated protein and not Ras, may actually be the molecular target of FTIs. The implications from such work are far-reaching and clearly impact on the design of future clinical trials. On the other hand the rather lack of targeting of FTIs opens up possible uses outside of oncology. This is touched on earlier in the book, with an examination of the possible use of FTIs and the related GGTase inhibitors as anti-trypsinomalous drugs.

Inevitably in a multi-author book, there is replication of introductory material between chapters. This is not an exception. The structure of the book could also have been given a little more thought and the chapters presented in a more logical sequence, but these are very minor gripes. There is no doubt that the book contains most of the whole FTI story and is to be commended for the exhaustive bibliographies that are a feature of every chapter. So who should read it? For the non-Ras expert, it presents a nicely illustrated story of biotechnology at work, from basic biology through rational drug design to actual clinical therapeutics, highlighting the development steps that are required along the way. To the Ras expert it is a very useful and comprehensive review of a rapidly moving and increasingly intriguing field.

J F Hancock

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GROWTH FACTORS AND THEIR RECEPTORS IN CANCER METASTASES

W Jiang, K Matsumoto and T Nakamura (eds)

Published by Kluwer Academic (2001)
The next three chapters deal with primary and metastatic malignancy. The clinical and radiological evaluation of previously unsuspected liver lesions, but as advances in imaging have occurred, so has the delineation of the nature of the lesion. This has allowed a rational approach to treatment. The next chapter on techniques of hepatic resection in a book of this size is of necessity somewhat limited in detail, but with line drawings and operative photographs, the principles are well outlined for the following up-to-date review of the surgical and non-surgical management of hilar cholangiocarcinoma and gall bladder cancer. The next chapter is in two parts, incorporating chemotherapy for liver tumours and isolated hepatic perfusion. The concentration is on chemotherapy by hepatic artery infusion with a good summary of trials, complications and outcome. A review of the data to date shows the limited place of the complicated procedure of isolated hepatic perfusion. The potential for gene transfer in the treatment of hepatic malignancy is outlined in a chapter. It is in the preliminary phases of investigation and is yet to enter the clinical arena. The final chapter is a comprehensive overview of the potential of liver transplantation for hepatobiliary malignancy – indicating it has a limited, but very definite, place for highly selected candidates.

Overall, the book is well presented and beautifully illustrated, with extensive and comprehensive references. By necessity, the magnitude of the topic limits how much can be accomplished, but it is easy to read, the surgical subjects are well covered, and it includes a CD-ROM disc.

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**Hepatobiliary Cancer**

L H Blumgart, Y Fong and W R Jarnagin (eds)
Published by American Cancer Society (2001)
RPP: A $ 253.55

The first two chapters cover benign liver lesions and incidentally-found hepatic lesions. This may seem strange in a book on hepatobiliary malignancy, but it is entirely appropriate. Modern radiology has increased the identification of previously unsuspected liver lesions, but as advances in imaging have occurred, so has the delineation of the nature of the lesion. This has allowed a rational approach to treatment in asymptomatic patients as in patients at risk of primary or metastatic malignancy. The clinical and radiological evaluation of different lesions is covered.

The next three chapters deal with primary and metastatic malignancies. There is a good review of the epidemiology of hepatocellular cancer and cholangiocarcinoma. Diagnosis and treatment strategies are clear and well presented, and the chapter covers some aspects of rarer tumours. Metastatic liver cancer is well-covered in two chapters. The first chapter is a first-rate account of colorectal metastases with a short discussion on non-colorectal metastases while the second chapter presents an overview of hepatic surgery for metastatic gastrointestinal neuroendocrine tumours. The determination of resectability and the results of resection are outlined in these two chapters.

The two succeeding chapters cover surgical and non-surgical ablative therapy for liver tumours. The pathophysiology of cryoablation is considered in detail, as is the role of transcatheter arterial chemembolisation. The cytotoxic molecules interleukin-2 and interleukin-2 are also included. Gene therapy of prostate cancer with interleukin-12 is discussed as well as treatment of tumour invasion with the hepatic growth factor antagonist, NK4.

Each review focuses on the normal physiological roles of a particular factor, its receptor and relevance to cancer growth, tumour invasion and metastases. The chapters are well-written, easy to read, current and extremely well-referenced. They enable the reader to access original articles and pursue in depth any particular topic or aspect of a molecule’s function. The basic contrast is made between normal, provided, a rapid, yet comprehensive introduction to each subject.

I found the chapters on leukemia inhibitory factor, interleukin-2, interleukin-12, IGF-1 and TGFs particularly useful, and this collection of reviews is rounded up nicely by the excellent last chapter on growth factors and their receptors and cell adhesion complexes in cytoskeletal assembly.

This book should be compulsory reading for any investigator, undergraduate or postgraduate seeking knowledge about, or pursuing research into, cancer. The breadth and depth of each topic is outstanding.

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**Metastasis Research Protocols, Vols I and II**

S A Brooks and U Schumacher (eds)
Published by Humana Press (2001)
RPP: $ 525.00

Cancer metastasis – that is, the spread of tumours to secondary sites in the body – is the major cause of cancer mortality. Metastasis is a complex, multi-stage process which remains poorly understood. Better definition of this process at the molecular level is essential for current cancer research and should lead to new approaches to therapy. This pair of volumes provides a valuable resource for experimentalists in the field. It is a laboratory guide providing detailed descriptions of a wide range of procedures, ranging from basic biochemical methods through to in vivo models for evaluating metastatic potential. In general, the chapters have the format of an introduction followed by the step-by-step methods, notes commenting on the choice of reagents, troubleshooting etc, and references. The extent of the introduction varies considerably between the chapters – in some it consists of brief comments on the history and applications of the methods in question, in others (eg Vol I, chapter six) an excellent, concise review is provided.

Volume I, ‘Analysis of cells and tissues,’ describes methods for cell culture, cryopreservation, isolation and purification of protein expression, tumour proliferation and vascularisation. It also provides protocols for a range of methods for evaluating nuclear acids in tumour specimens, including in situ hybridisation, basic techniques for studying nuclear acids, analysis of methylation, and the use of the polymerase chain reaction for the detection of circulating tumour cells. Finally, there is a chapter on mathematical modelling of metastasis (which is in its infancy). In general, the protocols are clearly presented and easy to follow. In some instances I would have liked to have seen some discussion of the factors that make some reagents suitable as to suitable reagents. For example, there are many antibodies to interrogate on the market, which give very variable results. As these are enormously expensive, trial and error to find the best reagents is generally not possible. A major disappointment was the lack of discussion of molecular markers known to be associated with progression (eg Erb-B2 in breast cancer, and CD9 and CD82 down-regulation in various esophageal cancers). In addition, the advent of microarray technology is set to have a profound effect on the field of tumour classification and prognosis. Hopefully this will be addressed in any new edition. Another disappointment was the limitation of methods for the study of cell proliferation to cell cycle analysis and DNA synthesis. Flow cytometric methods that use fluorescent dye linked antibodies (FITC and PKH26) are widely used but to my mind the most valuable part of these volume is that dealing with animal models of metastasis. Given the complexity and the multidisciplinary nature of the process, it is ultimately necessary to study it in vivo. Starting with a chapter on basic principles for the study of metastasis using animal models, different systems are described, including the chick embryo and various types of transgenic, syngeneic, transgenic and orthotopic. Finally, the application of green fluorescent protein-labelled cells for the study of metastasis is described.

Overall, these volumes are a valuable addition to any laboratory interested in studying metastasis in defined cell systems through to evaluation in physiologically relevant animal models.

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**Methods in Mammary Gland Biology and Breast Cancer Research**

Mip and B Asch (eds)
Published by Kluwer Academic (2000)
RPP: US$125.00

This volume came together under the auspices of the Committee on Mammary Gland Biology, a group formed over two decades ago and whose membership includes many of the originators of our current knowledge of mammary gland biology and the methods used for its study. The impetus for publication of this book came from the realisation that progress in understanding mammary gland biology relied on appropriate deployment of well-characterised animal models, but that the current generation of animal models were difficult to source. Moreover, the emergence of gene knockout techniques and animals with selective ablation of particular genes has opened out a new potential for mammary gland research to unravel basic mechanisms in mammary development and carcinogenesis. The editors have assembled an outstanding collection of contributors, many of who are leaders in the mammary gland field.

This book presents a compendium into one practical guide of methods that are well established in mammary gland biology as well as methods whose potential has yet to be fully realised. The book is in four sections: in vivo model systems; special techniques in vivo studies; in vitro model systems; molecular analysis; and gene transfer techniques. The in vivo sections cover all established models of mammary cancer and include a very helpful comparison of tissues of mouse, rat and human mammmary carcinogenesis – essentially evaluating which aspects of rodent carcinogenesis are sufficiently similar to the human for these models to be used. They also include very helpful descriptions of fundamentally important methods in mammary gland biology such as mammary fat pad clearance, transplantation, whole mount preparation, and hormonal treatment. The in vitro section covers methods for culture of mammary cells, both normal and malignant, including methods to grow mammary cells under conditions which recapitulate growth in structures similar to those found in the mammary gland in vivo. The final section covers gene transfer by viral and non-viral methods, conditional gene deletion, and more recent viral techniques such as tissue recombination and intraductal injection.

The volume is extremely well presented. The chapters are clear, detailed and very well referenced. They are primarily practical guides, and the material is clearly presented and beautifully illustrated with diagrams and pictures. The volume is designed to be a laboratory manual, and is bound in spiral for easy opening. This volume would be an outstanding practical guide for researchers engaged in research on mammary gland biology. Very highly recommended.

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**The Molecular Basis**
OF HUMAN CANCER

W Coleman and G Tsongalis (eds)  
Published by Humana Press 2002  
RRP: US$145.00

This book is intended to provide a source of current information on the molecular mechanisms underlying tumorigenesis in the practical context of medical oncology practice. The authors state that it is primarily directed at advanced graduate students, medical students, postdoctoral trainees and established investigators with basic research interests.

The book is divided into seven sections including: cancer epidemiology; basic molecular biology concepts; molecular themes in oncogenesis; mechanisms of mutation, etiology of human cancers; human tumor systems and future directions.

The section on human tumor systems focuses on major organ system cancers including colorectal, hepatocellular, breast, prostate, lung and skin, as well as haematopoietic malignancies. Future directions includes chapters on genetic diagnosis and counselling, novel molecular targets and gene therapy.

Since the majority of the 24 chapters were written by different authors, there is at times a predictable overlap in content. However, this does not detract from the value of the book, as it is most likely to serve its purpose as a reference manual for those interested in gaining insights into a specific area. Each chapter is generally clearly written, providing succinct and up-to-date information. Although general concepts and major signalling pathways are clearly written, providing succinct and up-to-date information, the book would require more detailed coverage, given that these are currently topics of intense laboratory and clinical investigation.

The primary aims of this book are well met. It would be a good resource for clinicians with basic research interests, and well as a departmental reference for clinicians.

In conclusion, this book is a good summary of the current thinking in the management of urological cancers. There is a comprehensive overview of the broad topic of prostate cancer, with chapters on surgical pathology, genetics, and clinical management. The book also includes chapters on molecular biology, genetics, and clinical management of urological cancers. The book is divided into three sections dealing with clinical issues, psychosocial care and broader issues such as research and ethics respectively. The clinical section focuses on pain, other symptoms, cancer treatments, spirituality and complementary therapies. The section on using cancer treatments in palliative care offers an excellent site-specific overview of this often-controversial topic.

The psychosocial section focuses on hope and communication. There is a fairly comprehensive overview of the broad hope literature, which will interest most nurses. The grief and bereavement chapter offers a useful conceptual overview that departs from traditional approaches and will assist with planning interventions. Overall, this section offers a supportive, human approach to the difficult issues of working with people who are dying.

The final section offers fairly standard ethical and research chapters, a good overview of the issues of providing palliative care in non-malignant disease, and a non-clinical approach to enhancing quality of life, and ends with the important topic of health professional self-care.

Overall, this is a worthwhile addition to the nurse’s cancer library, offering opportunities for reflection and thought rather than a clinical guide for practice.

S Aranda
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THERAPEUTIC GUIDELINES

PALLIATIVE CARE

M Mashford et al  
Published by McPherson’s Printing Group (2001)  
RRP: A$33.00

As a palliative care physician I thought reading this type of “review book” would constitute a pleasant interlude and some light reading. I was very pleasantly surprised as it is a book full of little gems, for example “Medications that are non-essential for symptom control should be ceased” (often overlooked, especially when started by a different specialist). It was well worth the time to read. Of particular value is the Australian relevance of the material, with regard to medications and services available in this country.

The book covers all the basic facets of palliative care. Palliative care is about total care – that is, physical and psychological – of the patient and family/carers. This book covers the “circle of care” from diagnosis, treatment, and palliation to death. The chapters covering the self-care of palliative care providers are very pertinent, as we often forget to look after ourselves and burn out. The book touches on communication, ethics and bereavement issues in a holistic approach.

A comprehensive list of common symptoms (fatigue, neurological, mucositis, dermatological and urogenital) and their management in a palliative care setting is useful for the full-time palliative care physician and the general practitioner.

Where symptoms have multiple possible causes, often with more than one solution, alternative management strategies are presented so if one drug doesn’t work then second or third line drugs are suggested.

The book has a very useful section on analgesia, dealing with the pharmacology of analgesics and adjuvants and with pain management. The different types of drugs used for different types of pain are clearly set out. Useful are the tables setting out the conversion between different types of opioids.

My only regret is that the book does not stress enough that all symptoms are an “SOS” for help and there should be a sense of urgency by the treating medical team to respond quickly – as there may be no tomorrow.

For completeness the book has excellent chapters on HIV/AIDS palliative care and paediatric palliative care, including appropriate pain charts and drug doses. There is an excellent list of resources in the appendix.

In summary, I found this book easily readable with good information on diverse aspects of palliative care and well worth having in my library. I would like to finish with a quote from the book: “Patients should be left in no doubt that distressing symptoms like pain and nausea can almost always be controlled provided continuous and competent care can be assured.”

P Redelman  
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TREATMENT OPTIONS IN UROLOGICAL CANCER

J Waxman (ed)  
Published by Blackwell Science 2002  
ISBN: 0632 05589 8. 382 page plus index  
RRP: A$264.00

If you have the urge to write a summary about urological cancer, don’t bother, since this excellent book has done so for you. Edited by John Waxman and boasting an international line-up of expert authors this book is a well-balanced account of the current thinking in management of urological cancers without getting bogged down in unnecessary detail.

The section on renal cell cancer has a heavy leaning towards the molecular biology of the disease. The immunotherapy is a good review without being ponderous. However, the surgical treatment for renal cell cancer was lacking, not discussing new techniques such as laparoscopic nephrectomy or the possible survival benefit of nephrectomy in the face of metastatic disease.

The section on bladder cancer also has a heavy emphasis on molecular biology. The chapter on treatment options were generally up-to-date, especially the section on an adjuvant chemotherapy by Connie Steinberg. Surprisingly there was no discussion about combined radiotherapy/chemotherapy as an alternative to cystectomy despite this predominantly being a UK textbook.

The section on prostate cancer was probably the climax of the book with Waxman giving us a glimpse of the complex interactions of disease and therapies. The section on using synthetic androgen deprivation therapy was particularly interesting with Kirk having a chance to answer some of the criticisms of the MRC study giving additional detail not available in the original publication.

In conclusion, this book is a good summary of the current status (2001) for urological cancers. The chapters are detailed enough to be informative but not too long for the uninstructed to lose interest. I suggest it is an excellent starting point for those wanting a quick update, such as advanced trainees and oncologists who are branching into this area as a sub-specialty. It will need to be updated next year.

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PALLIATIVE NURSING: BRINGING COMFORT AND HOPE

S Kinghorn and R Gamlin (eds)  
Published by Baillière Tindall (2001)  
ISBN: 0 7020 2422 8. 270 pages plus index.  
RRP: A$162.50

This book represents an eclectic collection, principally arising from a conference of the same title. The book is aimed at a nursing audience and aims to offer a foundation for nurses involved in the delivery of palliative care as part or all of their work. The book is an exploration of issues, rather than a clinical text, dealing with contemporary literature in the field – although not always making a clear distinction between research-based and opinion-based work. There is excellent use of case studies throughout, helping with the clinical application of the largely literature based material.

The book is divided into three sections dealing with clinical issues, psychosocial care and broader issues such as research and ethics respectively. The clinical section focuses on pain, other symptoms, cancer treatments, spirituality and complementary therapies. The section on using cancer treatments in palliative care offers an excellent site-specific overview of this often-controversial topic.

The psychosocial section focuses on hope and communication. There is a fairly comprehensive overview of the broad hope literature, which will interest most nurses. The grief and bereavement chapter offers a useful conceptual overview that departs from traditional approaches and will assist with planning interventions. Overall, this section offers a supportive, human approach to the difficult issues of working with people who are dying.

The final section offers fairly standard ethics and research chapters, a good overview of the issues of providing palliative care in non-malignant disease, and a non-clinical approach to enhancing quality of life, and ends with the important topic of health professional self-care.

Overall, this is a worthwhile addition to the nurse’s cancer library, offering opportunities for reflection and thought rather than a clinical guide for practice.

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East Melbourne, Vic

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**TUMOR-SUPPRESSING VIRUSES, GENES, AND DRUGS**

H Maruta (ed)

Published by Academic Press (2002)


RRP: A$249.70

The target audience for this compact book includes research scientists, academics, undergraduate and graduate students. There are twenty chapters, comprising topics ranging from cell surface receptors, integrins, to signal transducers and nuclear proteins including cell cycle regulators, as well as useful chapters on oncolytic viruses, key tumour suppressors and angiogenesis.

Each area is comprehensively addressed—the text places each molecule of interest in the context of its signalling pathway(s), and describes the mechanisms by which these gene products are deregulated in cancer. Experimental models aimed at restoring growth control using target-specific molecular biology are summarised. Where available, in vivo models are also described, including information on agents entering phase I and II clinical studies. In the latter case, the basic science, rather than clinical outcome data is the main focus. Detailed attention to referencing is notable.

There is a good deal of local content; several chapters were written by Australians with recognised expertise in their respective fields. Authors include Tony Burgess, Marc Achen, Steven Stacker and Hiroshi Maruta (also the editor).

This book would be a suitable reference source in a research institution or clinical trials group library. It should appeal to basic scientists curious to understand diverse areas of tumour biology and where each field is heading in terms of translational research.

G Lindeman
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<td>Website: <a href="http://www.haematology.org/meeting/">www.haematology.org/meeting/</a></td>
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<td>8-11</td>
<td>18th World Congress of Digestive Surgery</td>
<td>Hong Kong</td>
<td>Congress Secretariat</td>
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<td>8-11</td>
<td>9th Hong Kong International Cancer Conference</td>
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<td>11-14</td>
<td>25th San Antonio Breast Cancer Symposium</td>
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<td>6-9</td>
<td>56th Annual Cancer Symposium of the Society of</td>
<td>Los Angeles</td>
<td>D.K. Kubel, Society of Surgical Oncology</td>
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<td>Surgery of Surgical Oncology</td>
<td>USA</td>
<td>85 W Algonquin Rd, Suite 55</td>
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<td>Arlington Heights, IL, 60055, USA</td>
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<td>12-15</td>
<td>Adjunct Therapy of Primary Breast Cancer</td>
<td>St Gallen</td>
<td>St Gallen Oncology Conferences</td>
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<td>c/o Prof H J Senn</td>
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<td>Post Office Box St Gallen – CH 9006, Switzerland</td>
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| 16-19    | ICTR 2003: 2nd International Conference on Translational Research and Pre-Clinical Strategies in Radiation Oncology | Lugano, Switzerland | Jacques Bernier  
Oncology Institute of Southern Switzerland  
San Giovanni Hospital  
Bellinzona – CH-6904, Switzerland  
Fax: +41 91 820 9044  
Email: bernier@usi.ch  
Website: www.icsg.ch/ict2003.html |
| 2-5      | 8th Congress of the European Association for Palliative Care | The Hague, The Netherlands | KENES International  
PO Box 5006  
Tel Aviv – 61500, Israel  
Ph: +44 22 908 0488 Fax: +44 845 127 5944  
Email: sacdp@kenes.com |
| 5-9      | 94th American Association for Cancer Research Annual Meeting | Toronto, Canada | AACR  
Public Ledger Building, Suite 816  
150 South Independence Mall West  
Philadelphia – PA 19106-3, USA  
Ph: +1 215 440 9300 Fax: +1 215 351 9165  
Email: meetings@aacr.org  
Website: www.aacr.org |
| 1-4      | Oncology Nursing Society 28th Annual Congress | Denver, USA | Oncology Nursing Society  
Meetings Services Team, 501 Holiday Drive  
Pittsburgh – PA 15220-2, USA  
Ph: +1 412 921 7373 Fax: +1 412 921 6565  
Email: member@ons.org  
Website: www.ons.org |
| 21-24    | 12th Reach to Recovery International Conference “Bridging the Gap: the Needs and their Assessment” | Lisbon, Portugal | Vencer a Viver De Henrieta Nobibit de Almeida Lima  
Nucleo Regional Do Sul Da Liga Portuguesa Contra O Cancro  
Rua Professor Lima Basto  
Lisboa – P-1099-023, Portugal  
Ph: +351 21 726 5786 Fax: +351 21 726 3363  
Email: cmatos@dpp.pt |
| 3-8      | 12th World Conference on Tobacco or Health: Global Action for a Tobacco Free Future | Helsinki, Finland | CongCreator CC Ltd  
Ms Aira Raudasso/Ms Hanne Heikkinen  
PO Box 762  
FIN-00101 Helsinki Finland  
Ph: +358 9 454 2190 Fax: +358 9 454 2193  
Email: wctoh2003@congcreator.com  
Website: www.wctoh2003.org |
| 10-14    | 10th World Conference on Lung Cancer | Copenhagen, Denmark | International Conference Services  
Suite 604, 650 West Hastings Street  
Vancouver – V6C 1E1, Canada  
Ph: +1 604 681 2153 Fax: +1 604 681 1049  
Email: conference@2003worldlungcancer.org  
Website: www.2003worldlungcancer.org |
| 21-25    | ECCO 12 – the European Cancer Conference | Copenhagen, Denmark | FECS Conference Unit  
Ms Kris Vierotegelen  
Federation of European Cancer Societies  
Av E Mounier, 83  
Brussels – B-1200, Belgium  
Ph: +32 2 775 0205 Fax: +32 2 775 0200  
Email: ecco12@feics.be  
Website: www.feics.be |
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 South Australia
The Cancer Council Tasmania
The Cancer Council Victoria
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
Cancer Forum  n Volume 26 Number 2  n July 2002

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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Prof 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 2002
Ordinary Members: $110
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(Paediatric Oncology
(ANZ Childhood Cancer Study Group)
Palliative Care
Pharmacy
Psycho-Oncology
Radiation Oncology
Regional & Rural Oncology
Social Workers
Surgical Oncology

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