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Ovarian cancer

Overview

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Over the past couple of years, there has been a greater emphasis on ovarian cancer, both in the research setting and also in terms of public awareness.

This is entirely fitting, as, while total numbers of cases of ovarian cancer are not huge, the impact of the disease on society certainly is, with three-quarters of the cases presenting as late stage (stages III and IV) disease. While many respond to chemotherapy, there is a high relapse rate and ultimately, three-quarters of women with advanced cancer will ultimately die from the disease.

An Australian Cancer Network working party has spent the past two years refining the Guidelines for the Management of Ovarian Cancer, and this document has now been sent to the National Health and Medical Research Council for ratification. Dissemination of these Guidelines is expected early in the new year.

At the same time, an expert advisory group, under the umbrella of the National Breast Cancer Centre, is working on strategies to disseminate these guidelines to the profession, and develop a separate consumer version.

On the research front, the Australia New Zealand Gynaecological Oncology Group is collaborating in a multi-centre, multi-pronged study. This study is supported by funding from the Department of Defence, in part.

The three major components include:

(1) An epidemiological study – case-controlled, looking at lifestyles of all women newly diagnosed with ovarian cancer over the next three years, and comparing them with age-matched controls, seeking to tease out any risk factors, lifestyle changes, etc. They expect to recruit at least 1,000 women, making it the largest study of its kind in the world, building on a previous eastern states study conducted in the early 1990s.

(2) A biospecimen collection, with samples of tumour and blood taken from women at the time of their surgery for ovarian cancer. Microassay studies will be undertaken, and there are plans to establish a tissue bank for future collaborative studies also.

(3) A chemotherapy treatment study, comparing in a blinded randomised way four different treatment arms; comparing doublets and triplets of chemotherapy with the "gold standard" of Paclitaxel and Carboplatin. Other drugs to be studied are Topotecan, Gemcitabine and Caelyx.

This review of the current state-of-the-art in ovarian cancer is not meant to be a forerunner of the Guidelines, but rather to highlight areas of change or special areas of interest to Australian researchers.

In compiling these articles, I am also very conscious of the work being undertaken by cancer consumer groups, especially in ovarian cancer, where they are making an impact on women and their families with the disease both in lobbying and in fundraising to assist research.

Ovarian cancer is still a major problem today, but the research effort can be expected to make an impact over the next few years.

I	Control doublet	
	Paclitaxel 175mg/m^2 IV (3 hr	D 1 x 8 cycles (q 21 days)
	Carboplatin AUC 6 IV	D 1
II	Gemcitabine triplet	
	Paclitaxel 175mg/m^2 IV (3 hr)	D 1 x 8 cycles (q 21 days)
	Carboplatin AUC 5 IV	D 1
	Gemcitabine 800mg/m^2/d IV	D 1, 8
III	Modified Doxil triplet	
	Paclitaxel 175mg/m^2 IV (3 hr)	D 1 x 8 cycles (q 21 days)
	Carboplatin AUC 5 IV	D 1
	Doxil 30 mg/m^2 IV (every other)	D 1

IV	Topotecan doublet (module A)		Topotecan doublet (module B)	
	Carboplatin AUC 5 IV	D 3	Paclitaxel 175mg/m^2 IV (3 hr)	D 1
	Topotecan 1.5mg/m^2/d IV	D 1-3	Carboplatin AUC 6 IV	D 1
	x 4 cycles (q 21 days)		x 4 cycles (q 21 days)	
V	Gemcitabine doublet (module A)		Gemcitabine doublet (module B)	
	Carboplatin AUC 6 IV	D 8	Paclitaxel 175mg/m^2 IV (3 hr)	D 1
	Gemcitabine 1000mg/m^2/d IV	D 1, 8	Carboplatin AUC 6 IV	D 1
	x 4 cycles (q 21 days)		x 4 cycles (q 21 days)	

THE NATIONAL OVARIAN CANCER PROGRAM

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Background

Ovarian cancer is the leading cause of death from gynaecological cancers in Australia. In recognition of the impact of ovarian cancer on Australian women, in September 2001 the Federal Government committed $500,000 over two years, to improve the health outcomes for women with ovarian cancer. The National Breast Cancer Centre (NBCC) was chosen to manage a national ovarian cancer initiative.

In November 2001, a strategic plan, Priority actions for ovarian cancer control: a framework for a national approach, was developed by an Interim Ovarian Cancer Steering Group, based on input from key stakeholders in ovarian cancer control. The plan outlined eight objectives, and from these objectives a work plan for the Ovarian Cancer Program was developed, focussing on a number of priority areas:

- Information for women, health professionals, policy makers and the community about aspects of ovarian cancer such as risk factors and diagnosis of ovarian cancer;
- Promotion of optimal management of all women diagnosed with ovarian cancer;
- Strengthening the provision of psychosocial, physical and practical support for women diagnosed with ovarian cancer and their families;
- Developing a national monitoring system for ovarian cancer control in Australia; and
- Encouraging all organisations concerned with ovarian cancer control to work collaboratively to improve ovarian cancer outcomes.

A multidisciplinary Expert Advisory Group was established to guide the work of the Ovarian Cancer Program. The work of the Program is also supported by a number of working groups for specific projects.

This report provides a summary of those objectives and the achievements to date.

Risk factors for ovarian cancer

While much research in Australia and internationally is directed at understanding the causes of ovarian cancer, there are currently no opportunities for community-wide prevention programs. Known risk factors include family history[1], age[2] and previous personal history of ovarian cancer. Pregnancy and oral contraceptive use are associated with a reduced risk of ovarian cancer[3]. Prophylactic oophorectomy[4], tubal sterilisation and hysterectomy[5] have been shown to reduce a woman's risk of ovarian cancer.

To date, the Program has commissioned a detailed review of the research about known risk factors for ovarian cancer and opportunities for prevention. The review will be made available in early 2004 and will provide an evidentiary base for the development of information for clinicians and women.

Information for women with a family history or known genetic risk for ovarian cancer

Up to 10% of all cases of epithelial ovarian cancer are thought to be due to hereditary factors[6]. Women with a genetic mutation in BRCA1 and BRCA2 have a risk of between 15% to 66% of developing ovarian cancer by the age of 70[7,8].

In association with the Genetics Expert Advisory Group of the National Breast Cancer Centre, and in light of recent progress in the understanding of this area, the published advice about familial aspects of ovarian cancer has been reviewed, with a view to simplifying the risk categories.

Encouraging prompt diagnosis for women with symptoms that may be ovarian cancer

It is estimated that about 70% of ovarian cancers are advanced at diagnosis[1] and advanced disease has a poor prognosis. It is difficult to diagnose ovarian cancer at an early stage because early disease is typically asymptomatic, early symptoms are non-specific and there is currently no accepted method for population screening.

In progressing activities in regard to this objective, the Expert Advisory Group has agreed that there is no currently no evidence to support the conduct of a public education campaign about symptoms of ovarian cancer. The group is developing guidelines for general practitioners to assist them with the often difficult assessment and investigation of women who may have ovarian cancer.

Promoting optimal management of all women diagnosed with ovarian cancer

The five-year relative survival of women with ovarian cancer after diagnosis is about 42%[9]. Adverse prognostic factors for ovarian cancer include older patient age, later stage of disease, higher tumour grade, presence of ascites and residual disease.

Most Australian women with ovarian cancer are treated with surgery and/or chemotherapy. There is some evidence that women with ovarian cancer who are treated by a gynaecological oncologist have improved survival rates[10,11], yet a large number of women do not currently receive optimal care.

To address the lack of national evidence-based guidelines about the management of ovarian cancer, the Australian Cancer Network established a working party in 1999 to develop the Clinical practice guidelines for the management of women with epithelial ovarian cancer. This process has been subsequently supported and completed under the auspices of the Ovarian Cancer Program and the guidelines have been submitted to the National Health and Medical Research Council (NHMRC) for approval. The guidelines will be disseminated nationally during early 2004, followed by initiatives to promote the benefits and improved outcomes of multidisciplinary care of women with ovarian cancer.

Research conducted in Australia and overseas indicates that outcomes are improved for women with cancer who are informed about their treatment options[10]. Women with ovarian cancer seek information about a wide range of topics to help them understand and deal with their diagnosis. A consumer guide for women with ovarian cancer is being developed by the Centre, based on the evidence in the Clinical practice guidelines for the management of women with epithelial ovarian cancer. The guide will address topics such as the types and stages of ovarian cancer; treatment options; managing pain and side-effects; the use of complementary and alternative therapies; and support issues.

Strengthening the provision of psychosocial, physical and practical support to all women diagnosed with ovarian cancer and their families

The diagnosis of ovarian cancer has a major impact on women and their families. Of women diagnosed with ovarian cancer, a high proportion has advanced disease[1]. Therefore, providing adequate support for women to improve their quality of life is an important component of patient care. Adequate support and information can improve cancer patients' wellbeing, quality of life and satisfaction with care[12]. Good communication skills, information provision and continuity of care have also been found to improve quality of life for cancer patients[12].

Currently, there is limited access to supportive care services in Australian gynaecological oncology units. The Ovarian Cancer Program is working with the Psychosocial Expert Advisory Group of the National Breast Cancer Centre to investigate the specific needs of women with ovarian cancer and to develop strategies for addressing these needs.

National monitoring system for ovarian cancer control in Australia

While some data are collected about ovarian cancer in Australia, there is inconsistency in the way that data are collected and reported. This makes comparison of data between states difficult. Regular and timely monitoring of ovarian cancer control will enable the targeting of new programs and the evaluation of the effectiveness of current programs. Such a monitoring system should be comprehensive including data about incidence, mortality, diagnosis, treatment and supportive care needs of women with ovarian cancer.

The Ovarian Cancer Program has developed plans to review national data about ovarian cancer and data collection processes to identify gaps in the information available and to direct the development of a strategy to standardise data collection about ovarian cancer.

To provide all women, health professionals, policy makers and the community with access to current, accurate and appropriate information about all aspects of ovarian cancer

Women, health professionals, policy makers and the community should have access to accurate, appropriate and timely information about relevant aspects of ovarian cancer control.

The Program has acted as a clearinghouse for evidence-based information through: a monthly electronic newsletter (Ovarian e-upd@te) disseminated to clinicians, researchers, consumers, cancer councils, state and federal health departments (12 issues to date); and through the establishment of a website for the Ovarian Cancer Program (www.ovariancancerprogram.org.au).

To encourage all organisations concerned with ovarian cancer control to work collaboratively

There are many groups working towards improving ovarian cancer control in Australia. Collaboration between these organisations is vital to improving outcomes for women and maximising the use of resources by avoiding duplication and by introducing varied expertise.

The Ovarian Cancer Program has built relationships to foster a collaborative approach through the establishment of a multidisciplinary Expert Advisory Group to provide advice about the projects and through contact with a range of clinicians, researchers and consumer groups involved in ovarian cancer control. A national ovarian cancer forum, planned for early 2004, will bring together key stakeholders from relevant areas in ovarian cancer control and foster a national information network. It will provide a further opportunity to promote multidisciplinary care and will focus on the delivery of health services and opportunities to improve outcomes.

In summary, the national Ovarian Cancer Program has been active in a broad range of areas. The Australian Government has provided additional funding until the end of 2003, and this will allow further development of these initiatives. With the recent re-funding of the National Breast Cancer Centre for a further four years, the Ovarian Cancer Program is seen as an integral component of the Centre's future work plans.

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Risk factors for epithelial ovarian cancer

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Although in Australia the lifetime risk of ovarian cancer is only one in 107, it is the fifth most common cause of cancer death in Australian women[1]. Over 90% of ovarian malignancies are thought to arise from the ovarian epithelium, while the remaining 10% include germ cell tumours, sex cord tumours and malignant teratomas. Most epidemiological research to date has focussed on the more common epithelial ovarian cancers and the following discussion is restricted to these tumours.

Much remains unknown about the pathogenesis of epithelial ovarian cancer but the two main theories implicate either incessant ovulation or high levels of circulating gonadotrophins. The strongest risk factors are increasing age and a family history of ovarian cancer, but other reproductive, medical and lifestyle factors also appear to have a significant impact on risk. In this review we summarise the current state of knowledge and uncertainty regarding non-genetic risk factors for epithelial ovarian cancer (EOC).

Hormonal and reproductive factors

Oral contraceptive use

Women who have ever taken the oral contraceptive pill (OCP) have an approximately 40% lower risk of EOC than women who have never taken the OCP[2]. Increasing duration of use is associated with a reduction in risk of about 8% per year of use and the decrease in risk may persist for more than 20 years after cessation of OCP use[3]. The different histological subtypes of ovarian cancer have been shown to differ with respect to some risk factors[4] but it remains unclear whether this is the case for the effect of the contraceptive pill. Some have found a similar risk reduction for all histological subtypes[4] but one group reported an increased risk of mucinous EOC associated with ever-use of the OCP[3]. Whether the oral contraceptive pill decreases the risk of EOC in women with BRCA mutations also remains unclear. One case-control study has reported that OCP use was associated with a decreased risk of EOC in non-carriers but not in carriers[5], while a second study found significant reductions in risk with both ever use and increasing duration of use among women with BRCA1 and BRCA2 mutations[6]. Further studies are required to clarify this important issue.

Pregnancy

Women who have ever been pregnant have a lower risk of ovarian cancer than women who have never been pregnant[2]. Moreover, the risk is reduced with increasing numbers of pregnancies such that women who have had six or more children have less than half the risk of developing ovarian cancer compared to women who have had no children. This reduction in risk is likely to be a consequence of both the suppression of ovulation and the altered hormonal milieu during pregnancy. The protective effect appears to be even greater for multiple births than for singleton pregnancies, possibly because of the higher progesterone levels associated with multiple pregnancies[7]. A pooled analysis[2] and a recent case-control study[3] have both suggested that failed pregnancies (spontaneous miscarriage or induced abortion) also reduce the risk of ovarian cancer but other studies have not confirmed these results[8].

There is now increasing evidence that the protective effects of pregnancy are greater for women who had their last pregnancy more recently (OR 0.45, 95% CI 0.30-0.65, for pregnancy in the last year compared to pregnancy 10-14 yrs ago)[9] or at an older age (OR=0.50, 95% CI 0.32-0.77 for >35 vs <25 years)[10]. It has been suggested that pregnancy may have the effect of clearing cells with genetic damage from the ovary. There is some suggestion that younger age at first pregnancy may increase risk of ovarian cancer[11] but these data are less consistent.

The apparent protective effects of both pregnancy and OCP use have been attributed to the fact that both suppress ovulation. A number of studies have observed that an increase in the number of calculated lifetime ovulations is associated with an increased risk of epithelial ovarian cancer[12] with an approximately 6% (95% CI 4-8%) increase in risk for each year of ovulation[13]. Ovulations in the 20-29 years age group were found to be associated with a greater risk (20% increase in risk per year of ovulation, 95% CI 13-26%) suggesting that ovulations at this time in a woman's life may be more important in the carcinogenic process than those either earlier or later in life. The effects of both pregnancy and OCP use on EOC risk are, however, greater than would be expected solely on the basis of their inhibition of ovulation[14].

Breast feeding

There is fairly consistent evidence that women who breast feed their children have a lower risk of ovarian cancer than parous women who do not breast feed, although the effects are modest with about a 1% reduction in risk for each month of breast feeding[15]. This association may also be a consequence of the fact that breast feeding suppresses ovulation.

Age at menarche and age at menopause

As described above, increasing numbers of ovulations are associated with higher risks of ovarian cancer. On this basis, it has been hypothesised that women with an earlier age at menarche or a later age at menopause, and therefore more potential years of ovulation, would be at increased risk of ovarian cancer. The data are, however, highly inconsistent with some studies reporting positive associations, some inverse associations and some no effect at all. It is possible that this inconsistency is a consequence of the effect described above where ovulations early and late in a woman's reproductive life may be less relevant in terms of influencing risk of ovarian cancer[13].

Hormone replacement therapy

The use of hormone replacement therapy (HRT) has been associated with a small but significant increase in risk of EOC and this risk appears to increase with increasing duration of use[16]. Few studies have considered the different types or regimes of HRT but a recent case-control study found that women who took oestrogen alone or oestrogen with sequential progesterone were at increased risk of EOC (OR 1.43, 95% CI 1.02-2.00 and OR 1.54, 95% CI 1.15-2.05 respectively), while those who used oestrogen with continuous progesterone were not at increased risk[17]. Clarification of this issue in future studies may provide important insights into the role of reproductive hormones in the pathogenesis of this cancer.

Infertility and infertility treatment

There is conflicting evidence regarding the effect of infertility treatment on the risk of EOC but a recent pooled analysis of eight population-based case-control studies found no evidence of an association (OR 0.97, 95% CI 0.76-1.25)[18]. Women treated with infertility drugs who do not have a subsequent pregnancy may have a small increased risk but the independent effects of different causes of infertility and the different fertility treatments are yet to be resolved.

Medical procedures, medications and medical conditions

Hysterectomy and tubal ligation

Hysterectomy and tubal ligation have been consistently associated with a 20%-50% decrease in risk of EOC[19] suggesting that both of these procedures confer a protective effect against this cancer. It has been suggested that the apparent protection provided by these surgical procedures might be due to the fact that they block passage of potential carcinogens, such as talc, to the ovary.

Medications

Paracetamol, aspirin and NSAIDs have been associated with decreased risk in EOC in some studies[20], but the effects have been inconsistent and no significant trends of decreasing risk with increasing use have been reported. At this stage it is not possible to draw firm conclusions about the effects of these simple analgesics on the risk of EOC. It also has been suggested that some psychotropic medication may influence the risk of EOC by altering the release of gonadotrophins[21]. Evidence for this is limited and inconsistent so it is not possible to evaluate the effect of these medications on ovarian cancer risk.

Medical conditions

Accumulating evidence suggests that endometriosis of the ovary may progress to EOC, particularly the endometrioid and clear cell subtypes[22]. Endometriosis is a difficult exposure to assess in case-control studies but a pooled analysis of eight such studies of ovarian cancer found a self-reported history of endometriosis was associated with a 70% increased risk of ovarian cancer (OR 1.73, 95% CI 1.10-2.71)[18]. The significance of this association needs further clarification with follow-up studies of women with visually diagnosed endometriosis.

Polycystic ovary syndrome (PCOS) is associated with increased production of androgens and it has been proposed that androgens may be implicated in the pathogenesis of EOC[23]. This association has rarely been studied directly but one study found women with a self-reported physician diagnosis of PCOS had a significant 2.5-fold increase in risk of ovarian cancer compared to women without such a diagnosis[24]. It has also been suggested that inflammatory conditions on or around the ovary may contribute to the development of EOC[25]. Some evidence suggests that pelvic infection may be associated with a modest increase in risk of EOC[26] but further data are required to confirm this association.

Potential effects of diabetes mellitus on steroid hormone production as well as immune function have prompted investigation of the relationship between diabetes mellitus and EOC. Current evidence suggests that such an association is unlikely[27].

Lifestyle and diet

Obesity

Obesity has been associated with changes in circulating hormone levels, particularly oestrogen and testosterone, and elevated levels of these have been implicated in the pathogenesis of ovarian cancer[23]. There is consistent evidence of a small but significant effect of high body-mass index on risk of EOC (RR 1.4, 95% CI 1.2-1.6)[28]. Some studies suggest this association is strongest in women diagnosed with EOC pre-menopausally[29], but further assessment is required to confirm this finding.

Physical activity

The effects of physical activity on risk of EOC have been investigated infrequently and the results that have been reported are inconsistent. Some have reported an increase in risk of ovarian cancer with increased levels of physical activity[30] but others have found either no association or a decrease in risk[31]. Current evidence suggests it does not impact significantly on ovarian cancer risk.

Talc use

Talc use has long been considered a potential risk for EOC because of its structural similarity to asbestos (a known human carcinogen) and the biological possibility that retrograde movement through the genital tract may allow talc to initiate inflammatory changes near or on the epithelial surface. A recent meta-analysis reported a pooled odds ratio of 1.38 (95% CI, 1.25-1.52) for use of perineal talc versus non-use but the authors found no clear evidence of an increase in risk with increasing duration of use[32]. Despite the lack of dose-response, the consistency of the findings across the population-based studies suggests that use of perineal talc is associated with a small increase in risk of EOC.

Tobacco smoking, alcohol and caffeine

Overall, no consistent association has been observed between cigarette smoking and EOC[33] but subtype-specific analyses provide fairly consistent evidence that the risk of mucinous ovarian cancer is increased by cigarette smoking (OR ~3.0 for ≥ 25 pack-years)[34].

There is some evidence that moderate alcohol intake may decrease the risk of ovarian cancer. An American cohort study which followed post-menopausal women for 10 years, reported a significant trend of decreasing risk of EOC with increasing consumption of alcohol up to about one standard drink per day (p=0.01)[35] but this finding was not replicated by a subsequent population-based case-control study[36]. More recently, another American case-control study found that current alcohol drinkers had a decreased risk of ovarian cancer compared to non-drinkers (OR 0.61, 95% CI 0.39-0.94)[37]. A significant trend of decreasing risk with increasing consumption (up to 14 drinks per week) was also observed (p=0.009). The effect was strongest for wine consumption. Further studies considering types of alcohol and examining effects according to histological findings are required to confirm the effects of alcohol on risk of EOC.

Coffee and tea are chemically complex beverages containing

both potential carcinogens as well as chemoprotective agents[38,39]. The weight of evidence suggest there may be a small positive association between coffee drinking and the risk of EOC[40], however many of the associations have been weak and without clear evidence of a dose response. One study has suggested that the effect of coffee may be moderated by menopausal status[36] but this has yet to be confirmed. Tea has been examined less frequently in relation to EOC and most studies have found no effect although one Chinese study reported a strong inverse association between tea consumption and EOC[41]. It is thus possible that any effect of tea may depend on the type of tea (green or black) that is consumed.

Diet

Dietary factors that have been examined in relation to ovarian cancer risk include fruit and vegetables, eggs and dairy products as well as a range of macronutrients, such as dietary fat, and micronutrients. Limited data suggest an inverse relationship between fresh fruit and/or vegetables[35] and, possibly, b-carotene[42] and EOC. A number of population-based studies have examined the effect of egg consumption on ovarian cancer risk and all have found an increased risk associated with eating two or more eggs per week[35,43]. The basis for this association remains speculative but one study has suggested that contamination of eggs by pesticides may provide an explanation for this link[43]. There is less consistent evidence for an association between intake of dietary fat and EOC[44] or between higher consumption of dairy products and ovarian cancer[45], thus no firm conclusions can be reached about the impact of these factors on EOC risk.

Summary and conclusions

A summary of the main risk and protective factors for epithelial ovarian cancer is presented in table one. Aside from increasing age and a family history of breast or ovarian cancer, the most significant risk factors for epithelial ovarian cancer are those related to reproductive history. High parity and long-term use of the oral contraceptive pill confer significant decreases in risk of EOC and it is likely that this is also the case for breast-feeding. Tubal ligation, hysterectomy and possibly a diet high in fruit and vegetables also appear to reduce risk. Factors that may increase the risk of epithelial ovarian cancer include use of hormone replacement therapy, obesity, cigarette smoke (mucinous tumours only), application of talc to the perineal region, regular consumption of eggs, endometriosis and pelvic inflammatory disease.

Much, however, remains unknown about the aetiology of this disease. Many studies to date have treated epithelial ovarian cancer as a single disease and it is now clear that the different histological subtypes may differ with respect to key risk factors[4]. Larger studies are needed in order to evaluate the risk factors for the specific subtypes. Further research is required to clarify the potential role of modifiable exposures such as diet and physical activity in the prevention of this commonly fatal disease. Additional work is also required to clarify the association between factors such as oral contraceptive use, hysterectomy and tubal ligation and ovarian cancer risk among women who carry BRCA mutations and so are at high risk of developing ovarian cancer before we can recommend these measures as preventive interventions in this group.

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Table 1: Summary of risk and protective factors for epithelial ovarian cancer

Exposure		Association[1]	Approximate relative risk
Oral contraceptives		''	0.4-0.6 for ≥ 5 years use
Pregnancy		''	0.5-0.7 for ever vs never pregnant
Breastfeeding		'	0.8 for ever having breastfed
Age at menarche / menopause		–	
HRT		(') for oestrogen +/- sequential progesterone	
Infertility		?	
Hysterectomy / Tubal ligation		''	0.5 – 0.8
Analgesics		?	
Endometriosis		'	1.7-1.9
Polycystic ovary syndrome		(')	
Obesity		'	1.2 – 1.5
Talc		'	1.3
Smoking		' for mucinous tumours only ~3.0 for ≥ 25 pack-years	
Alcohol		(')	
Coffee/Tea		?	
Diet	Fat	?	-
	Eggs	(')	2-3 for 2+ eggs per week
	Vegetables	(')	-

[1] Direction and approximate strength of likely and (possible) associations

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MANAGEMENT OF WOMEN AT INCREASED GENETIC RISK OF OVARIAN CANCER

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Epidemiological studies have identified family history as one of the major risk factors for epithelial ovarian cancer (subsequently referred to as "ovarian cancer") and in recent years we have gained a greater understanding of the specific genes associated with inherited susceptibility to the disease[1,2,3]. This has led to the ability to identify individuals and families who are at significantly increased risk of developing ovarian cancer. These women require counselling about their risks and advice as to what can be done to possibly decrease risk as well as information regarding screening and early diagnosis. This is a specialised area that is rapidly evolving and we strongly recommend that women at increased genetic risk are referred to familial cancer clinics for multidisciplinary management which includes confirmation of the family history and diagnoses, counselling prior to genetic testing, communication and explanation of the results of genetic testing, advice about screening and prophylactic surgery and follow up in high risk management clinics[4,5].

The management of these women at increased risk of ovarian cancer is difficult and presents many challenges. It should be recognised that much of our knowledge regarding the clinical applications and advice to at risk individuals is still preliminary and will undoubtedly change over time. The purpose of this paper is to briefly review the current state of knowledge about the genetics of hereditary ovarian cancer and update interested readers on the genetic epidemiology, prevalence and penertrance of the specific germline mutations associated with ovarian cancer, as well as review the clinical features and overall management of women at increased genetic risk of ovarian cancer.

The majority of women who develop epithelial ovarian cancer do not have a family history and have what is currently termed sporadic ovarian cancer, the causes of which are not well understood. The two major hereditary cancer syndromes associated with a substantially increased risk of ovarian cancer are the hereditary breast/ovarian cancer syndrome (HBOC) and hereditary non-polyposis colorectal cancer syndrome (HNPCC)[2] (table one). It should be noted that the HBOC syndrome also predisposes women to associated gynaecological cancers, specifically cancer of the fallopian tube and primary peritoneal cancer.

Approximately 10% of women who develop ovarian cancer have a germline mutation in either BRCA1 or BRCA2 with a smaller percentage having a mutation in one of the mismatch repair genes associated with HNPCC and are the focus of discussion[6,7]. There are some other rare genetic syndromes associated with increased risk of ovarian cancer, which are beyond the scope of this paper. Germline mutations in BRCA1 and BRCA2 account for the majority of families with hereditary ovarian cancer with about 60% being attributed to BRCA1 and 30% to BRCA2.

The likelihood of finding a mutation in a women with ovarian cancer increases with the number of blood relatives with ovarian or breast cancer in her family as well as ethnicity and other associated cancers (table two). It is not clear what proportions of ovarian cancer in unselected general populations are due to mutations in these genes but the percentage appears to be higher than previously anticipated. In a recent population-based series of 649 unselected incident cases of ovarian cancer diagnosed in Canada, 11.7% of women were found to have pathogenic mutations in BRCA1 and BRCA2, which is more than previous estimates and may even be higher as the genetic tests used would not be expected to detect all mutations[8]. Mutations were found in 19% of women with first-degree relatives with breast/ovarian cancer and in 6.5% of women reporting no family history. No mutations were found in women with borderline tumours, which is consistent with other studies, but there was an association with mutations and the histology of invasive ovarian cancer. Specifically, mutations were detected in 16.4% of serous cancers, 4.3% of endometrioid cancers and in none of the other histological subtypes[8]. This study needs to be confirmed as it raises the possibility that mutations in BRCA1 and BRCA2 may be more common in unselected populations with ovarian cancer than previously anticipated and it also challenges some of the epidemiological data relating family history to risk of ovarian cancer.

First degree relatives with one affected family member with ovarian cancer have generally been advised that they have a 5% lifetime risk which is about three times the 1.4% lifetime risk for women without a family history[1,9,10]. For women with two affected relatives the lifetime risk has been said to rise to about 7%, and these figures have been used to counsel women about risk[1,8,9,10]. However, the confidence values of these risk estimates are wide and studies such as the Canadian population study among others challenge these figures, which may be too simplistic[8]. It is essential that an accurate family history is taken in order to estimate risk of ovarian cancer based on family history and ethnicity should also be taken into account. Women of Ashkenazi Jewish background with a family history of even one case of ovarian cancer and women in the general population with two affected relatives with ovarian cancer should be considered to be at potentially higher risk and be referred to a familial cancer clilnic for further advice and counselling[11,12].

Table 1: Genes associated with hereditary ovarian cancer

Syndrome	Gene	Lifetime risk	Other cancers associated with the syndrome
Breast/Ovarian syndrome	BRCA1 BRCA2	10-60%	Breast, fallopian tube, primary peritoneal cancer.
Hereditary non-polyposis colorectal cancer	MLH1 MSH2 MSH6 PMS1 PMS2	10%	Colorectal, endometrial, gastric, urinary tract.

Table 2: Features in a family history that suggest an increased genetic risk of ovarian cancer

1. Women with a family history of ovarian and/or breast cancer, in two or more women on the same side of the family, particularly if one or more of the following are present:
   - breast cancer diagnosed before the age of 40;
   - the presence of breast and ovarian cancer in the same woman;
   - bilateral breast cancer;
   - breast cancer in a male relative.
2. Women of Ashkenazi Jewish ancestry, with one or more first-degree relatives diagnosed with ovarian cancer.
3. Women with a family history consistent with HNPCC – three or more first or second degree relatives on the same side of the family with colorectal cancer (particularly if diagnosed before the ago of 50), endometrial cancer, ovarian cancer, gastric cancer, and cancers involving the renal tract.

The lifetime risk of ovarian cancer in women with mutations in BRCA1 and BRCA2 varies considerably in different studies and is dependent in part on the ascertainment of families in these studies. Recent results of pooled data from 22 studies demonstrated that women with BRCA1 mutations have a cumulative risk of 39% (confidence intervals 18-54%) of developing ovarian cancer by age 70 while women with BRCA2 mutations have a lower risk of 11% (CI 2.4-19%)[13]. There are age-related differences in the penetration of these genes. The mean age of onset of ovarian cancer in women with BRCA1 mutations is in the mid- to late-forties and for BRCA2-related ovarian cancers about a decade later. BRCA1 and particularly BRCA2-related ovarian cancer are very uncommon under 40 and ovarian cancers under 30 are rarely, if ever, associated with mutations in BRCA1 or BRCA2[13,14,15]. These data have important practical significance as it influences the age at which screening should commence and the age at which prophylactic surgery should be considered. We find it difficult to reconcile these data regarding age of onset of ovarian cancer in mutation carriers with the general advice which has been promulgated by many committees around the world that screening begin at age 25-30 and prophylactic surgery be considered at completion of childbearing or at age 35 years[16,17]. While some may view our comments as heresy, it makes little sense to advise a screening test which is potentially associated with many false positives to young women with a mutation in say BRCA2 knowing that ovarian cancers in such women are rarely diagnosed under 40 and are usually only observed in the late 50s or early 60s. Even women with mutations in BRCA1 rarely develop ovarian cancer under 40 years old[13]. This is in distinct contrast to ovarian cancers that occur in association with HNPCC which are usually seen at a younger age[18,19,20].

Extracolonic cancers occur in 69% of women with MSH2 mutations and 19% of women with MLH1 mutations. There is a 40% risk of uterine cancer in women with HNPCC and a 10% risk of ovarian cancer. The median age of ovarian cancer is 42 years with 30% of invasive ovarian cancer occurring in women under 40. In a review of 120 families entered on the HNPCC register in Victoria, the mean age of diagnosis was 48.3 years with a range of 29 to 74 years[20]. In contrast to BRCA1 and BRCA2-related ovarian cancers which are commonly high-grade serous cancers and at advanced stage at diagnosis, HNPCC-associated ovarian cancers are usually well to moderately-well differentiated and are more likely to be endometrioid or mucinous tumours and are often confined to the ovaries[14,18,19,20]. Furthermore, synchronous endometrial cancers are observed in 20% of women. These differences in biology should influence the advice given to women regarding age to commence screening and the age at which prophylactic surgery should be considered as well as the type of surgery that should be done.

Finally, before discussing management issues it is worthwhile to draw the reader's attention to the importance of ethnicity and risk of BRCA1 and BRCA2 mutations. The overall prevalence of pathogenic mutations in BRCA1 and BRCA2 has been estimated to be 1 in 500 to 1 in 1000 although can be lower in certain populations[1]. A number of founder effects have been observed where the same mutation has been found in multiple, unrelated families and can be traced back to a common ancestor. Founder mutations have been identified in many populations, but have been particularly well studied in the Ashkenazi Jewish population (of central/eastern European ancestry) where three specific mutations (185 delAG and 5382 insC in BRCA1 and 6174 delT in BRCA2) are present in approximately 1 in 40 of the population[21,22,23]. A woman with ovarian cancer and Ashkenazi Jewish ancestry has a 40-60% chance of having a founder mutation identified in BRCA1 or BRCA2 and therefore her relatives are considered to be at potentially high risk and should be offered genetic counselling and testing if a germline mutation is identified in the proband. If the proband is not living it is still worth considering screening first-degree relatives for the three common founder mutations. These mutations may account for up to 25-30% of early onset breast cancers and up to 90% of cancers in families with both breast and ovarian cancers and Ashkenazi ancestry[12,23].

While we are now in the position to better identify women who are at increased genetic risk of ovarian cancer the challenge is how to manage them and their families. Of particular importance is whether it will be possible to modify risk and also be able to diagnose these cancers when they are still confined to the ovaries and would therefore be expected to have a good prognosis. The majority of women with epithelial ovarian cancer have advanced disease at initial presentation and only 25% are likely to survive five years[24]. In contrast, the majority of women with stage 1 ovarian cancer are cured and it has been assumed that early diagnosis would result in a better outcome. There has understandably been a lot of interest in ovarian cancer screening in both women at population risk and increased genetic risk, but there is no evidence to date that screening is associated with a reduction in mortality. There are currently three large population-based ovarian screening studies in progress which will be determine whether regular ultrasound screening and estimation of serum CA125 will result in early diagnosis and improve survival.

Screening studies to date have largely focused on determining the sensitivity and specificity of the various screening modalities. There are problems with specificity and positive predictive value of the screening tests and many women undergo unnecessary surgical exploration[25,26,27]. It is beyond the scope of this paper to review this in detail, but it is clear that there are inherent problems associated with screening tools currently available and we also do not know enough about the natural history of ovarian cancer. While it may sound counterintuitive we really don't know if there is a stepwise progression from stage 1 to 2 to 3 and so on, and if so, what the sojourn time in each stage is. We have not as yet convincingly identified a precursor lesion for serous ovarian cancer, which is the most common histological subtype in the general population as well as being almost exclusively seen in hereditary ovarian cancer. There are very real differences between the various histological subtypes of epithelial ovarian cancer with respect to natural history and biological behavior which seem to be only appreciated by a small number of people with a particular interest in the biology of ovarian cancer[24,28,29]. For example, endometrioid and mucinous cancers are usually confined to the ovaries at initial clinical presentation and have an excellent prognosis. While these may be detected by screening it is unlikely that this will improve their already very good prognosis. In contrast, serous cancers are usually poorly differentiated and widely disseminated within the peritoneal cavity at diagnosis and only 20% are stage 1[24]. Most of the stage 1 serous cancers are well differentiated and may have progressed from serous borderline tumours and biologically are likely to be a distinct subgroup[30]. Indeed, Singer et al have proposed a dualistic model for ovarian serous carcinogenesis with one pathway involving stepwise progression from serous borderline tumours to invasive well differentiated micropapillary serous cancer, and the other more common pathway, from ovarian surface epithelium or inclusion cysts to high grade serous cancer, which seems to develop rapidly and is unlikely to be detected

at an "early" phase with our current technology[30]. A good understanding of ovarian cancer biology is essential if we are to be able to design screening studies and interpret the studies that have been published. A major limitation in all the studies that have been published is the difficulty the interested reader has in trying to determine the histological subtype and grade of screen detected cancers or even their stage. It is not uncommon for the tumours to be listed as "adenocarcinomas" or just stage 1 ovarian cancer, which is inadequate and limits interpretation of the studies. There has also been a tendency to lump all tumours together including non-epithelial subtypes such as granulosa cell tumours and germ cell tumours.

It is important that these limitations are appreciated and also conveyed to women at increased genetic risk of ovarian cancer who are undergoing regular screening. All the guidelines recommend regular ovarian cancer screening, with the usual caveats, and have generally recommended annual screening commence at ages 25-30[16,17,31]. This has been modified in the recently revised Australian guidelines with the appreciation of the ages at which ovarian cancer is likely to develop in women who have germline mutations in either BRCA1 or 2. We would encourage high-risk women to consider participating in the GOG 199 study which will be carried out by the Australian and New Zealand Gynecological Oncology Group (ANZGOG). Women who opt for screening will have a three-monthly CA125 and a yearly ultrasound and in addition blood samples will be stored for newer tests such as proteomics. The mathematical algorithm developed by Skates et al which takes into account the individual's age and the rate of change in CA125 (ROCA) together with the absolute CA125 value and allows women to be triaged into normal, intermediate or elevated risk groups[32]. It is thought to improve the sensitivity and specificity of CA125 as a screening test as it appears to reduce false positives and false negatives that would be generated by a single CA125 set at a cut off level of 35 U/ml. The GOG 199 study is not a randomised study and will also include women who opt for prophylactic or risk-reducing bilateral salpingo-oophorectomy (RRBSO) who will have the surgery performed following a strict protocol and careful pathological assessment. All women will be followed, and in addition will have regular quality of life assessments. This study should allow us to determine what the value of screening is in a high-risk population.

There have been a number of reports of screening in high-risk populations. Dorum et al reported on the results of a screening study of 803 women[33]. Of the 16 ovarian cancers diagnosed five were stage 1 or borderline tumours, one was stage 2 and 10 were stage 3. Liede et al reported on a study that included 290 Jewish women and they diagnosed eight incident cases of ovarian or related cancers (fallopian tube or peritoneal cancer)[34]. Only three were diagnosed at screening and five of the eight women presented with symptoms between screening visits and had advanced cancers. Taylor and Schwartz reported the results of screening 252 high-risk women and diagnosed two advanced cancers, one at screening and one in a symptomatic woman[35]. It is clear from reviewing all the published studies of screening in high-risk women that ovarian cancers are diagnosed relatively infrequently and that most of these women have advanced cancers at diagnosis. In contrast, about 4% of women who have a RRBSO are found with evidence of occult cancers after careful pathological assessment and has been reported to be as high as 13%[36-39]. Microscopic foci of serous cancer have been found in the fallopian tubes, ovaries and at times also in peritoneal washings, and most of these women have had negative screening tests in the 6-12 months preceding surgery. There are recent studies to show that RRBSO in high-risk women significantly reduces the risk of subsequently developing both ovarian cancer and breast cancer (table three). Rebbeck et al reported a 96% reduction in risk of BRCA-related gynecologic cancers in 259 women who had undergone BSO compared with 292 matched mutation carriers who had not had surgery[40]. Six ovarian cancers were identified at the time of prophylactic surgery and all were stage 1. This should be contrasted and compared with the 20% incidence of ovarian cancer in the control group, 11% of which were stage 1. In this study there was a 53% reduction in the risk of breast cancer as well in mutation carriers who had a BSO compared to those who had not. The mean age at BSO was 42 years. In a prospective study reported by Kauff et al there was a 75% reduction in risk of BRCA associated gynaecologic cancer or breast cancer in 98 mutation carriers who underwent RRBSO compared with 72 mutation carriers who opted for screening[41].

It has been appreciated for some years that women who undergo RRBSO may be at risk of subsequently developing peritoneal cancer as the ovarian surface epithelium and peritoneal mesothelium are both derived form coelomic epithelium[42]. The risk of this appears to be much lower than previously thought and only two women in the Rebbeck study subsequently were diagnosed with a peritoneal cancer at 3.8 years and 8.6 years after prophylactic surgery, and one out of 98 women who had prophylactic surgery in the Kauff study was subsequently diagnosed with peritoneal cancer[40,41]. The reasons for this difference are unclear but could be explained by a number of factors including careful pathological assessment at the time of initial surgery including peritoneal washings and complete removal of the ovaries and both fallopian tubes. It is likely that just clamping the broad ligament and removing the ovary as has occurred in the past would leave ovarian tissue remnants in situ and increase the risk of subsequent "peritoneal" cancer.

The available data strongly suggests that women at increased genetic risk should be counseled about prophylactic surgery. As we have mentioned above the risk of ovarian cancer is very uncommon in women under 40 and women with known BRCA1 mutations could have a RRBSO in her late 30s or possibly early 40s depending on her family history and age of onset of ovarian cancer[13,43]. Women with BRCA2 mutations generally only develop ovarian cancer when they are post-menopausal and RRBSO could arguably be delayed until the late 40s or even early 50s in some women. It is difficult to be too prescriptive and the decision regarding timing of surgery can be only made after detailed discussion with the individual woman. The age of onset of ovarian cancer in her family needs to be considered as well as the possibility of genetic anticipation as cancers in subsequent generations tending to occur at a younger age. A small study of anticipation in hereditary breast cancer was recently published by Dagan et al who found that among women with a BRCA1 mutation there was no real difference in age of onset of breast cancer in mothers and daughters, but mutations in BRCA2 were associated with a significantly younger age of breast cancer in the second generation suggesting specific gene environment interactions[44]. The importance of genetic anticipation in BRCA 1 and BRCA2-related ovarian cancer is unclear at present.

The use of hormonal replacement in these women following RRBSO is controversial as these women are also at increased genetic risk of breast cancer and should be individualised with short-term use considered only in women with acute troublesome menopausal symptoms[45]. It is of course important to try to prevent some of the other possible consequences of premature menopause such as osteoporosis[46]. It has been suggested that in women in whom hormone replacement therapy is likely to be requested or used that a hysterectomy is performed as well as a BSO. Estrogen replacement alone is used in women without a uterus rather than combined estrogen and progestagens, which appear to be associated with higher risk of thromboembolic disease as well as breast cancer[45]. This is still an area for which we have no clear answers and detailed individual discussion is required.

Chemoprevention is likely to be a far more acceptable approach to management of high risk women and ideally modification of risk through lifestyle/environmental changes would also be important if we knew what modifications made a difference and at what age they should be introduced. Epidemiological studies have strongly suggested that the oral contraceptive pill (OCP) is associated with a significant reduction in risk of ovarian cancer in the general population[47,48]. Similarly, case control studies have demonstrated that women who have a family history of breast/ovarian cancer also have a similar reduction in ovarian cancer risk of about 50% if they have been on the OCP[49]. However, this was not confirmed in a population study of Jewish women in Israel, which raises some questions regarding the value of OCP in reducing ovarian cancer incidence in the high-risk population[50]. Of particular concern as well is the uncertainty regarding the risk of the OCP on breast cancer risk in women who have germ line mutations in BRCA1 or BRCA2[51]. This also needs to be discussed in detail rather than recommending the OCP to all high-risk women to reduce risk of ovarian cancer. Tubal ligation, interestingly, has been reported to be associated with a reduction in risk of ovarian cancer in the general population as well as in a study of women with known BRCA1 mutations but not BRCA2 mutations[52,53]. The sample size of women with BRCA2 mutations was small and so one cannot be confident in assuming that they would not benefit and this requires more study. While the mechanism is not known it is of interest that Piek et al have recently reported that up to 36% of women with mutations in BRCA1 or 2 have dysphasic changes noted in the tubal epithelium and he has postulated that most serous "ovarian" cancers arise in the tubal epithelium and "spill over" onto the ovarian surface[54]. Supporting this is the relatively common finding of occult cancers in the fallopian tube of women at the time of RRBSO. While the mechanism for the protective benefit of tubal ligation is not known it is tempting to speculate that tubal ligation could alter the micro-environment in the tube and in addition there is vascular impairment and this could result in reduction in risk. This is being further studied but it would seem reasonable to recommend tubal ligation as a means of contraception to high risk women after completion of childbearing and before RRBSO is performed at a later age.

The aim of this paper was to briefly review and summarise a large and complex literature that is rapidly growing. Our increasing ability to identify women at increased genetic risk of developing ovarian cancer has not been matched by good level 1 evidence regarding how best we manage these women and their families. We have briefly discussed the natural history and biology of ovarian cancer, the appeal of screening and early diagnosis as well as the limitations of screening using currently available screening tests. The most convincing data regarding reducing risk is seen in the studies of RRBSO, but clearly this is not an attractive option to many women, and alternative strategies are needed. We have not dealt with the large literature on the psychological impact of being a mutation carrier and the many issues that these women and their families face. This should not be interpreted as lack of importance but rather a lack of space to cover a large and important literature, and the interested reader is directed to papers on this[55-60]. The management guidelines and advice about familial aspects of ovarian cancer recently have been updated and will provide health professionals with a detailed overview of familial ovarian cancer.

Table 3: Ovarian cancer risk reduction strategies for BRCA1 and BRCA2 mutation carriers

Strategy	Risk reduction
Prophylactic salpingo-oophorectomy	96%[40,41]
Oral contraceptive pill	0-50%[49,51]
Tubal ligation	63%[52*]

* Protective effect only seen in BRCA1 mutation carriers

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Molecular prognosis of epithelial ovarian cancer: observations from current literature

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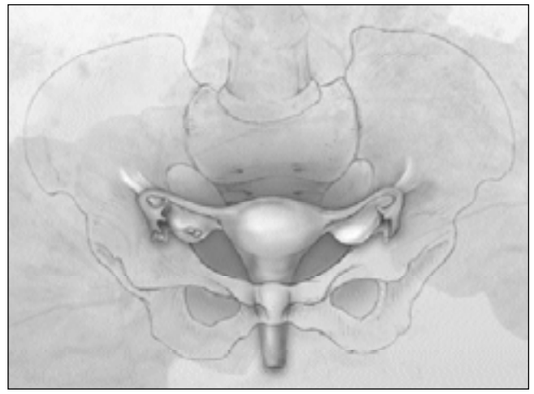
Cancer of the ovary is both the most prevalent and lethal form of gynaecological carcinoma. More than three-quarters of women afflicted have disseminated disease at the time of diagnosis and receive treatment which is usually a combination of debulking surgery and chemotherapy. The most effective chemotherapy agent against ovarian cancer is cisplatin – also used for lung, head and neck, bladder and testicular cancers. Response rates to this drug vary from 40%-80% and it is often used in conjunction with other treatments (eg Paclitaxel) to achieve a subtle increase in the proportion of patients successfully treated.



This disease continues to be a focus of intense research around the world because of the significant fraction of women whose initially responsive tumours develop resistance to all available chemotherapy regimes. Drug-resistant disease is eventually observed in more than 75% of cases after four years from diagnosis and consequently the five-year survival rate in Australia is around 42% – lower than the mean combined survival rate for all female cancer patients of 63%[1]. While survival times have significantly increased over the past 20 years this has unfortunately not correlated with an equally significant improvement in the cure rate[2], thus the genetic changes accumulated by chemotherapy-resistant ovarian cancer cells remain of keen interest.

Alterations in the oncogene TP53 and its downstream targets p21 (cell cycle inhibitor), BAX (apoptosis agonist) and BCL-2 (apoptosis antagonist) are often observed in ovarian cancer, however there is still debate concerning the prognostic function of these changes. Schuyer et al used a range of molecular and immunohistological methods to examine the relationship of these genes and important clinico-pathological variables, including outcome and response to platinum-based chemotherapy drugs including cisplatin[3]. Interestingly, while P53 mutations are present in up to 50% of epithelial ovarian cancers, there was no observed correlation with increased rate of progression or death, nor with expression of p21 or BCL-2 in this study. Higher TP53 protein expression levels could, however, be correlated with shorter overall survival rate (P=0.03). Factoring TP53 mutation and over-expression resulted in a more significant correlation with overall survival than the expression data alone (P=0.08), as observed in other studies[4]. The TP53 target gene, BAX, was significantly linked to progression-free and overall survival (figure one). Furthermore, patients with expression of both BAX and BCL-2 exhibited longer survival times than those whose tumours express BAX alone. The authors conclude that high expression of BAX may therefore be a potential independent prognostic indicator for this disease.

Expression of P21/WAF1, a tumour suppressor gene whose expression is inversely correlated with TP53, has been associated with high tumour grades and late FIGO stages[5]. DNA damaging agents that result in cell cycle arrest in the G1 phase of wild-type P53 cells are capable of inducing the p21/WAF1 gene. Antilla et al used immunohistochemical profiling of over 300 ovarian tumour specimens to explore the relationship between expression of this p21/WAF1 and patient outcome. Statistical analysis of expression levels and patient clinical information revealed that high-level expression of p21/WAF1 resulted in lowered levels of cellular proliferation. In a univariate approach, the gene appeared to be a negative prognostic factor. Patients whose tumours had minimal or no expression appeared to have a higher risk of tumour recurrence after treatment and shorter disease-free and overall survival rates, particularly for those positive for p53 also. While not statistically significant, there was a trend towards higher p21/WAF1 expression in patients who had a complete response to chemotherapy.

Unfortunately none of the variables studied by Schuyer et al[3] could be associated with tumour response to platinum-based chemotherapy, suggesting that chemosensitivity may be controlled by other genetic changes. Variation in chemotherapy regimes between clinicians and hospitals, as well as the complexity of quantifying response, add to the difficulty of relating molecular changes to variations in drug sensitivity. Serial analysis of gene expression (SAGE) profiling

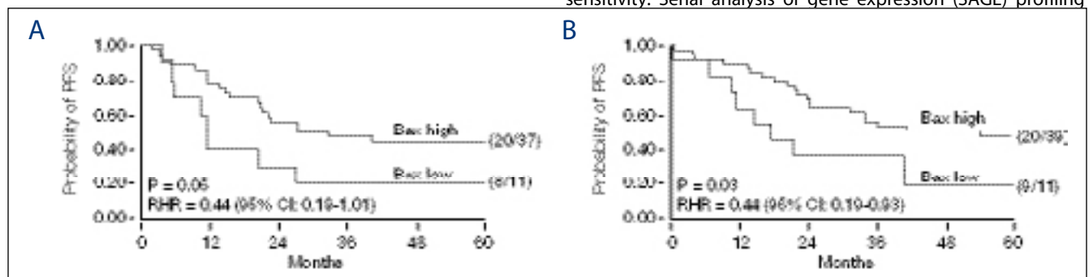


Figure 1: (a) Progression-free and (b) overall survival rates for ovarian cancer patients classified by BAX expression[3]

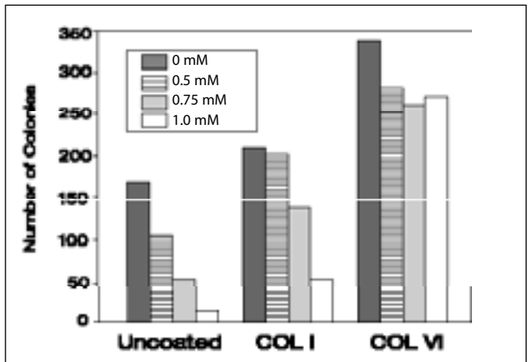


Figure 2: Number of survival colonies of ovarian cancer cell line A2780 plated on collagen substrates after cisplatin exposure[8]

is one method that has been employed to pursue this multi-factorial trait of ovarian cancer. Many of the genes that exhibit differences in expression levels between cisplatin-resistant and sensitive cells are related to cell interactions with their microenvironment[6]. The hypothesis that resistance to chemotherapy may be brought about by direct modifications of the extracellular matrix (ECM) was supported by experiments in which cisplatin-sensitive cells cultured in the presence of collagen VI. This protein is the product of one of the most differentially expressed genes observed by the SAGE (COL6A3)[6]. Cells grown in the presence of collagen VI developed a 15-fold increase in chemo-resistance (figure two)[6], indicating that ECM remodelling may be a key step in the process of a tumour developing resistance to previously effective treatments. Finally

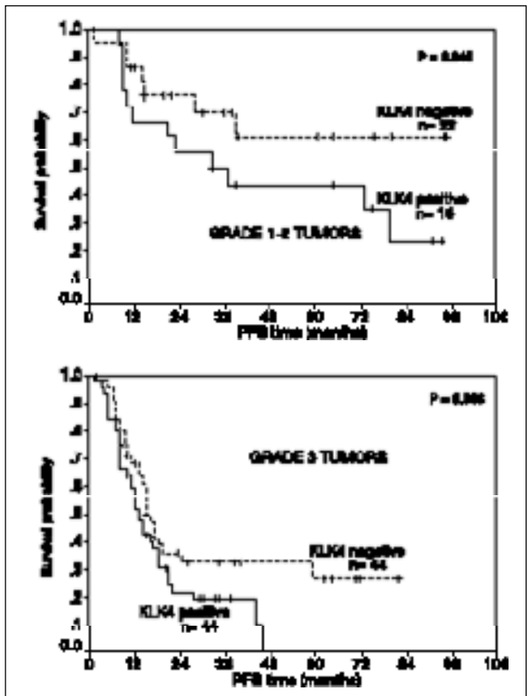


Figure 3: Variation in rate of tumour relapse between grade 1-2 and grade 3 tumours by KLK4 expression[7]

this study showed with the use of tissue arrays (120 cases in total) that expression of COL6A3 in primary ovarian tumours is also correlated with tumour grade. This pathological measure has been shown to relate to chemotherapy response and overall survival rates.

The gene KLK4[7] (Higher Human kallikreien gene 4) has also been associated with disease progression and survival time in ovarian cancer. KLK4 has been implicated in other hormonally-regulated cancers, including those of the breast and prostate. In 147 ovarian cancer samples, expression of the gene was found in 55% of tumours and there was significant association with tumour grade and stage. Overall the authors of this study concluded that KLK4 expression was higher in tumours with a more aggressive phenotype, generally translating to an increased risk of relapse and death. When tested against chemotherapy response rates, a correlation between positive expression and lack of treatment efficacy was detected. Interestingly, it was noted that positive KLK4 expression in grade 1 and 2 cases indicated a 2.5-fold increase in relative risk of relapse, yet the same degree of up regulation was not significantly predictive of relapse in grade 3 tumours (figure 3).

The Fanconi anemia-BRCA pathway has been implicated in the molecular changes occurring in cisplatin-resistant ovarian cancer. Interruption of this genetic pathway ultimately appears to lead to the development and selection of drug-resistant cancer cells[8]. This pathway is comprised of six genes associated with Fanconi anemia syndrome (FANC-A, -C, -D2, -E, -F and -G) plus BRCA1 and BRCA2 and regulates cellular reaction to cisplatin and other DNA cross-linking substances. Cisplatin resistance in ovarian cancer cell lines can be attributed to initial methylation-induced inactivation and subsequent demethylation of FANCF[8]. As this work was carried out using ovarian cancer cell lines it may require validation using other methods such as expression profiling of RNA extracted from human tissue. Indeed, other studies have shown considerable molecular differences between cell lines and ovarian tumours on the basis of hierarchical clustering and multi-dimensional scaling (MDS) with data generated from cDNA microarrays[9] as shown in figure four.

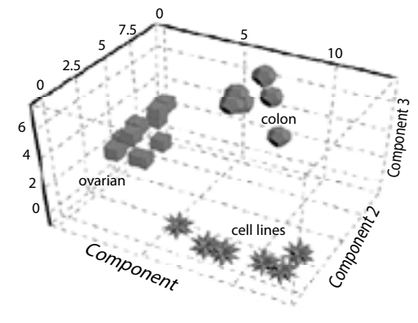


Figure 4: MDS 3D plot of cell line (stars), Ovarian cancer (cubes) and colon (octagonals) tumor samples[9]

The power of microarray analysis to reveal important information about the variation in ovarian cancer patient survival rates is demonstrated by Lancaster et al[10]. TRAIL, a gene identified from array profiling, was demonstrated to be a useful prognosticator. Using RT-PCR profiling of 120 epithelial cancers the authors describe a highly significant relationship between this gene and prolonged survival. Patients who lived for more than five years had 2.2-fold higher expression of this gene than those who died within 12 months of diagnosis. This gene is a member of the "death ligands" and a member of the apoptotic pathway. Another study has demonstrated the combination of TRAIL and chemotherapy lead to a significant increase in apoptosis and growth inhibition of ovarian cancer cell lines and propose the clinical use of this treatment combination[11].

It is clear that the difficulty of successful early detection and high rate of treatment resistance remain two of the key challenges in ovarian cancer treatment and research. If these hurdles can be even partially overcome through an increased understanding and manipulation of the underlying molecular changes many lives may be saved from this aggressive and widespread disease.

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Screening in ovarian cancer

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Ovarian cancer is the leading cause of death from gynaecological cancer in the developed world, comprising 5% of all cancer-related deaths in women. The high mortality rate has been attributed primarily to the difficulty in detecting the disease when it is still confined to the ovary (stage 1). The overall five year survival rate for stage 1 disease is 95%[1], compared with 20% for stage IV disease[2]. However, less than 25% of cases are confined to the ovary at the time of diagnosis. Thus the aim of screening in ovarian cancer has been to detect the disease when still confined to the ovary. However, to date there is no evidence to show an impact on mortality nor is there a test available that predominantly detects early stage disease.

Screening tests in ovarian cancer have until recently relied upon either pelvic ultrasound or the detection of the high molecular weight glycoprotein Ca125 in the serum or a combination of the two modalities (multimodal screening). Transabdominal ultrasound was used in the early screening studies[3-7] but has been replaced by the more sensitive transvaginal ultrasound (TVS) with or without the use of colour Doppler imaging[8]. Problems with utilisation of ultrasound for screening include cost, inter-examination variability leading to decreased sensitivity and specificity and visualisation rates. The latter vary enormously between reports in the literature, depending upon the age of the patient (with visualisation of the ovaries decreasing with age), the skill of the person performing the ultrasound, the presence or absence of a uterus and the presence of bowel gas. Studies to date have based their criteria for malignancy on ovarian volume, outline, the presence of papillary projections and complexity defined by the number of loculations, the cyst wall structure, septa and echogenicity of the cyst fluid. Papillary projections have the highest correlation with a diagnosis of ovarian malignancy and simple cysts and septal thickness have the lowest association with a diagnosis of ovarian malignancy[9]. In terms of operations per cancer detected the figures in the literature range from 9-163, although a systematic review by Bell et al concluded that in annual screening of a population with an incidence of ovarian cancer of 40 per 100,000, if no cancers were missed, between 2.5 and 60 women would undergo surgery for every primary ovarian cancer detected[8].

A number of different molecules detected in the serum of women with ovarian cancer have been investigated. The high molecular weight glycoprotein CA 125 has been the most studied and continues to be the tumour marker used most extensively for screening studies. Bast et al were the first to report an elevated serum Ca125 level in a patient before the diagnosis of ovarian cancer[10]. Since then multiple studies have shown Ca125 to have high sensitivity for ovarian cancer, with the overall sensitivity for all epithelial ovarian cancer in the range of 80% (Urban et al, 2003). Ca125 levels are elevated in greater than 85% of all advanced ovarian cancers but only 50% of early stage disease[1,2]. Elevated levels of Ca125 also occur in 6% of women without ovarian cancer[1] thus reducing specificity. Sensitivity and specificity have been improved by application of a computerised algorithim based on the Bayes theorem for the interpretation of Ca125 in the place of standard cut-off levels[11]. The algorithm compares an individual's serial Ca125 levels with the pattern seen in ovarian cancer cases where the levels tend to rise and in healthy controls where serial Ca125 levels remain static or decrease over time. The closer the individual's profile is to that seen in known cases of ovarian cancer the greater the risk of malignancy[12]. The combination of Ca125 level in the serum followed by TVS (multimodal screening) has also been utilised. Data from prospective studies of screening for ovarian cancer in postmenopausal women have shown that sequential multimodal screening has improved specificity and positive predictive value compared to TVS alone, although TVS may be more sensitive for detecting early stage disease[13].

Ca125 levels fail to increase early in 20-50% of cases of ovarian cancer[1] so other tumour markers have been investigated.

Lysophosphatidic acid (LPA), a bioactive phospholipid, has been reported as a potential discriminating marker for ovarian cancer including early stage disease[14]. High affinity receptors for LPA, Edg4 and Egd7 also have been shown to be increased in ovarian cancer cells[15]. Other molecules that may be potential adjuncts to Ca125 include osteopontin[16], kallikrenins[17] and a panel of markers including OVX1 and M-CSF[18]. Serum inhibin levels may also be a useful adjunct to Ca125 as 80% of mucinous epithelial ovarian cancers and a large proportion of sex cord stromal tumours are associated with increased levels of inhibin[19].

Currently there are two major randomised controlled trials underway to establish the impact of screening on ovarian cancer mortality as well as determining issues of compliance, health economics and physical and psychosocial morbidity. The United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) began recruiting postmenopausal women in 2001 and involves 12 centres in the United Kingdom. The aim of the study is to recruit a total of 200,000 women who will be randomised to either control, screening with ultrasound or multimodal screening. The primary end-point is the impact of screening on ovarian cancer mortality and the results are expected in 10 years. The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial is a two-arm randomised controlled trial involving 74,000 women aged between 55 to 74 who have been randomised to a screening arm (annual screening for ovarian, lung and colon cancer) or to a standard care control arm. Ten centres are involved in this trial which will involve 10 years' average follow-up. Only one screening strategy is being used, namely a combination of TVS and Ca125 performed annually for three years followed by Ca125 alone for two years. The trial has completed enrolment. Clearly the results of both trials will be eagerly awaited although issues pertaining to cost-effectiveness, age at which to begin screening and appropriate screening interval remain unanswered.

The two randomised controlled trials rely upon current technology and run the risk of being out-dated before the data has been analysed. Our understanding of tumour biology would suggest that the progression of a normal cell to a cancer cell involves multiple changes in a number of key pathways in the cell. It would therefore seem logical to question the suitability of single serum markers to identify ovarian cancer. Recent developments in gene expression and more recently in proteomics may well hold the key to new screening tests for ovarian cancer. Petricoin et al have described the use of mass spectroscopy (surface-enhanced laser desorption and ionisation, SELDI) to define a profile associated with sera derived from patients with ovarian cancer[20]. This profile was able to correctly identify 50 out of 50 cases of ovarian cancer, including 18 cases of stage 1 disease and to identify 63 of 66 cases of non-malignant disease, suggesting that this new technology may be a potential tool for screening. Clearly larger and more discriminatory studies will need to be performed but new technologies such as this may well hold the key to the development of an effective screening test for ovarian cancer.

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RAISING AWARENESS: OVCA AUSTRALIA

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Over the past three years the growth of the ovarian cancer consumer movement has raised community consciousness of ovarian cancer and its impact on patients and their families.

Through media campaigns (TV, newspapers, women's and lifestyle magazines), a website, presentations to community groups and the distribution of information leaflets through health centres, ovarian cancer has a much higher profile. Many are now aware that ovarian cancer is the fifth most common cause of cancer death in women; that vague, non-specific symptoms do exist; that family history can highlight additional risk factors; and that for most women knowledge and awareness is their best defence in the absence of an effective screening program. Seeking treatment early could make a major difference in outcome for many ovarian cancer patients.

Involvement of ovarian cancer patients and their families with OvCa Australia has led to the formation of a number of local support groups and networks that have helped patients cope with their condition and overcome the severe isolation that many experience.

OvCa Australia is an active participant in GP education forums, disseminates information through the Divisions of Practice and will be present at the next General Practitioner Conference and Exhibition. A prime objective has been to highlight the need for GPs to consider their approach to the management of women who present with vague abdominal/pelvic disorders and the importance of ruling out ovarian cancer as a cause. An educational project is being planned to target GPs, other clinicians and healthcare professionals.

Ensuring women and GPs understand the importance of appropriate referral when ovarian cancer is suspected has been another key message delivered to the public. Only 50% of ovarian cancer patients are currently being treated by a gynaecologic oncologist. Studies strongly indicate that survival and quality of life are much better in those who are treated by a specialist surgeon.

Consumer advocates have been involved in the development of the Australian Cancer Network Clinical Management Guidelines and an accompanying consumer publication, as well as several projects within the National Breast Cancer Centre's Ovarian Cancer Program. OvCa Australia was a co-host of the first ovarian cancer workshop for researchers and clinicians and will assist in planning and managing a similar event in 2004.

In the past two years National Ovarian Cancer Awareness Week has gained a great deal of public interest as well as the support and involvement of many research institutes and organisations such as the state Cancer Councils. Besides promoting the key awareness messages, the week provides an opportunity to raise much needed funds for research. The awareness week has gained support from corporate sponsors and has led to a number of major cause-related marketing initiatives.

OvCa Australia promotes the importance of effective diagnostic tests and believes that greater investment for research into early detection is paramount. Next year OvCa Australia plans to offer funds to support further research.

A major obstacle to the delivery of health promotion messages has been the lack of study data about ovarian cancer. This should change in the next few years when Australian Ovarian Cancer Study will deliver a quality evidence-base with respect to symptoms, risk factors and prevention.

GASTROINTESTINAL STROMAL TUMOUR PROGNOSTIC PARAMETERS: CASE REPORT AND LITERATURE REVIEW*

T Keith

ABSTRACT

This paper reviews the evaluation of malignancy and prognostic parameters used in gastrointestinal stromal tumours (GIST). Incorporated is a case report of a duodenal GIST treated at our institution. GIST represents a spectrum of mesenchymal tumours from benign to malignant variants, which can arise from anywhere in the gastrointestinal tract. A central pathogenetic event recognised in most GISTs is KIT activation (a tyrosine kinase receptor) believed to be the result of oncogenic mutations. Imatinib mesylate, (a humanised monoclonal antibody), highly effective in vitro in reducing KIT tyrosine activity, has revolutionised the treatment of metastatic GIST, and is discussed along with other treatment options. Traditionally the three key prognostic factors used in GIST have been mitotic rate, tumour size, and anatomic location. However, the unpredictable behaviour of GIST has led to the development of immunohistochemical differentiation markers including CD117 (detecting KIT protein). In addition genetic markers have been used as prognostic parameters, including KIT activating mutations, cytogentic aberrations and telomerase activity.

Case report

A 53-year-old male farmer presented with a three-day history of epigastric pain and melaena, preceded by a syncopal episode. For two weeks previously he had taken an NSAID for a painful shoulder. His GP found him hypotensive and arranged transfer to A & E, where he was haemodynamically stable, blood was found per rectum and Hb was 88g/l. He was commenced on IV omeprazole and underwent gastroscopy that revealed a 1cm dome-shaped tumour with a central bleeding ulcer, in the descending duodenum. This was injected with 10ml adrenaline (1:10,000) and the patient transfused with two units of packed cells. Two days later Hb was 85g/l and he was again transfused two units of packed cells. Repeat gastroscopy enabled biopsy of the tumour, which proved to be a gastrointestinal stromal tumour. CT scan showed a 3cm component of this tumour indistinguishable from the pancreas, at the level of the third part of the duodenum.

The patient underwent laparotomy with local complete excision of the tumour and duodenal repair. Histological examination showed a spindle cell stromal tumour 13mm in diameter, with mitotic rate of 0.5 mitoses per 10HPF and no evidence of necrosis was observed. Immunohistochemistry demonstrated positive staining to CD34, Neuron Specific Enolase (NSE), and Vimentin consistent with diagnosis of GIST. CD117 immunostaining was not available at this institution.

Discussion

GIST were most often classified, until recently, as leiomyomas and leiomyosarcomas, but are now known to represent a discrete neoplastic entity[1]. The term GIST, proposed by Mazur and Clark in 1983, was first used to classify all gastrointestinal non-epithelial mesenchymal tumours[2]. GIST are the most common mesenchymal neoplasms of the gastrointestinal tract, typically expressing KIT (a tyrosine kinase receptor)[3]. GIST arising in the muscle wall usually between the muscularis propria and muscularis mucosae may expand towards the bowel lumen, the serosa or in both directions[4]. Clinically and pathologically, GIST represents a spectrum of tumours from benign to malignant.

GIST incidence peaks in the fifth and sixth decades, is rare before 40 years, but can occur in the paediatric population[5,6,7]. GIST have been estimated to comprise between 0.1% to 3% of all GI malignancies[7,8], 20% of small bowel malignancies and 0.1% of large bowel malignancies[9]. GIST most commonly arise within the wall of the stomach (40-70%) and the small intestine (20-40%) and rarely in the oesophagus, colon and rectum (5-15%)[5,6], or duodenum (4%)[10]. There may be a greater incidence in men[4] while others note no sex difference[3,5]. The effect of gender on tumour behaviour is uncertain; some suggest it does not influence tumour behaviour[11]; others associating male sex with markedly poorer prognosis and increased occurrence of metastases[12].

At diagnosis about 40% of GIST are less than 1.5cm and asymptomatic[4]. Of symptomatic GIST up to 86% are associated with GIT bleeding (acute or chronic)[4,8]. In decreasing frequency the presenting symptoms are abdominal mass, GIT bleeding, anorexia, dysphagia, and obstruction[13,14].

The interstitial cells of Cajal (ICC), localised in the myenteric plexus believed to act as a gastrointestinal pacemaker cell governing peristalsis have been proposed as the cell of origin[5], supported by several immunohistochemical and ultrastructural similarities[3,15,16,17]. Alternatively, GIST may originate from precursor stem cells that can differentiate toward either a smooth muscle or ICC phenotype[7], with KIT expression believed to be crucial in encouraging differentiation of these cells towards an ICC endpoint[18].

Tumours with ultrastructural characteristics of GI autonomic nerve tumours (GANT) are also GIST tumours, based on their KIT positivity and presence of essentially identical KIT activating mutations[3,19]. GANT are believed part of the neoplastic spectrum of stromal tumours, displaying a higher degree of ICC differentiation[16]. GANT should no longer be regarded as a separate entity[20].

GIST are thought to occur by mutations of the KIT gene, located on the long arm of chromosome 4 expressed in the cells of Cajal (ICC)[21]. ICC are immunostained by antibodies against KIT (CD117)[22]. KIT encodes a transmembrane tyrosine kinase receptor, consistently expressed in GIST[6].

Structurally, the KIT receptor can be divided into four principal regions (domains): an extracellular domain; a transmembrane domain; a juxtamebrane domain; and a kinase domain separated into two sections. KIT gene mutations, irrespective of the domain for which they code, cause the receptor to be activated without its ligand (stem cell factor (SCF)), resulting in a continued stimulus for cell proliferation[23].

The KIT gene sequence has 21 exons, and in sporadic GIST, the majority (50-77%) of KIT mutations have been found in exon 11, encoding the juxtamembrane domain of the receptor[3]. A germline mutation identified in familial and multiple GIST has also been identified in the juxtamembrane domain[24]. GIST with exon 11 mutations were originally reported to be of a higher grade, or associated with poorer outcomes[15,25,26]. Subsequently, exon 11 mutations were believed to hold prognostic value. Further, mutations have been described in exons 9 (extracellular domain), 13 and 17 (the two kinase domains)[1,25,27,28] with the majority of exon 9 mutations associated with highly malignant GIST[25,28]. The significance, if any, of exons 13 and 17 is overshadowed by their infrequent[1,25,27] or non-expression[15] in reported GIST series.

Overall, the estimated frequency of KIT mutations is between 21% and 92%[7]. Failure to analyse the entire KIT coding sequence, and limitations encountered with some PCR assays used, as well as genetic differences between series populations may account for this variation[1,15]. A number of GIST, although lacking KIT mutations demonstrate strong KIT activation. Presumably KIT mutations, in these instances, have been detected by conventional screening methods, or, other non-mutational mechanisms may have led to KIT activation. Consequently it has been suggested oncogenic KIT activation occurs in the earliest stages with progression to more malignant behaviour determined by successive cytogenetic and molecular changes[18].

The majority of GIST are the result of somatic mutation. Rare familial cases have been described, however predisposing factors are unknown[3]. A link to EBV infection[4], association with Carney's triad (paraganglioma, pulmonary chrondroma, and leiomyoblastoma of the stomach, a very rare syndrome mainly affecting young women)[29], and association between GIST and Von Recklinghausen's syndrome have been reported[8]. The pathogenetic link between NF1 and GIST may be purely casual[30].

Morphological parameters

While mitotic count appears to be the most reliable indicator overall of GIST behaviour, with a high count correlating to malignant behaviour[31,32] there are accounts detailing GIST, with low mitotic counts behaving aggressively[8,23]. Mitotic count correlates poorly with the malignant potential of small bowel GIST[33]. A major criticism of mitotic counts has been their subjectivity and poor reproducibility[34].

Grading systems have been devised with different cut-off points for the number of mitoses per 10 HPF[6,7]. Mitotic count per 50 HPF is now recommended[19]. Tumours with 0-1 mitoses per 10-50 HPFs will not give rise to metastases, those with more than 5 mitoses per 50 HPFs are considered malignant[13,19]. A mitotic rate ≤ 5 mitoses per 50 HPF is commonly used as a limit for a tumour of predicted benign behaviour. However this cut off point fails to discriminate between benign and malignant small intestinal tumours[33].

Tumour size is suggested as more important than histology in predicting behaviour[4]. Almost all small (<1cm) GIST are clinically benign; tumours more than 5cm are generally malignant[3], however no cut-off diameter predicts malignant behaviour with certainty. For duodenal tumours malignant behaviour is more likely in tumours greater than 4.5cm[31,35].

Prognosis in GIST also varies with anatomic site, but the degree to which this relates to tumour size and/or histologic subtype is not clear. Purportedly, anatomic location is a prognostic factor independent of tumour size, mitotic rate and patient age[36]. Most duodenal GIST occur in the second part of the duodenum, with duodenal and small intestinal GIST more likely to display malignant behaviour relative to gastric GIST[38]. Small bowel tumours have the worst prognosis and oesophageal the best[23,38].

Histologically, GIST express a variety of cell types and growth patterns. Either of two cell types may predominate (spindle cells and epithelioid cells)[5], however a mixed cell type may occur[11]. Spindle cell-type form the majority comprising 70-80% of gastric tumours along with the majority of small intestinal GIST[6]. Epithelioid lesions occur more often in the stomach. Lesions of mixed cell type may exhibit an abrupt transition between spindle and epithelioid cells, however there may an intermediate cytologic appearance[36]. There are some site-specific variations in morphology with spindle cell lesions of the small bowel having

a tendency to contain skenoid fibres[37,38]. Skenoid fibres formerly believed to correlate with neural differentiation, now appear to have no histogenetic significance[36]. Correlation of histologic pattern with prognosis is not established[11], nor is predominant cell type related to pattern of antigenic expression[12].

Rather than using distinct benign and malignant categories, GIST should be regarded as having some malignant potential, described in terms of risk assessment[32] (low, intermediate or high risk), so that no lesion can be definitively labelled as benign.

Immunohistochemical differentiation markers

Immunohistochemistry has been a fundamental tool in the diagnosis of GIST. The antibodies commonly used to characterise GIST are those directed against CD34, CD117 (KIT protein), vimentin, desmin, smooth muscle actin (SMA), S100 protein, and neuron specific enolase (NSE).

GIST are usually positive for CD117 and CD34[36,37], variably positive for smooth muscle actin, and usually negative for desmin[23,36]. Antibodies to CD34 and CD117 differentiate GIST from smooth muscle and other intestinal mesenchymal tumours[6,16].

CD34 reactivity is seen in a wide range of normal tissues and tumours. CD34 is expressed in 60-70% of GIST[36]. A recent large series found CD34 positivity to have no prognostic significance. However, CD34 may aid in distinguishing gastrointestinal leiomyomas and schwannomas, which are negative for CD34[16]. Furthermore, CD34 in combination with CD117 and S100 can be used to differentiate GIST from most other mesenchymal tumours[5]. It also has been shown to demonstrate a reciprocal relationship with SMA expression – CD34 positive tumours are often SMA negative[17]. The variability of CD34 staining among GIST may be due to several phenotypes of GIST precursor cells (ICC)[16].

CD117 is now accepted as the most specific immunohistochemical marker for GIST[39]. CD117 is expressed in 80-100% of GIST and is not expressed in smooth muscle (leiomyoma, leiomyosarcoma) or neural tumours (schwannomas)[3,5]. CD117 positivity is seen in all histologic variants and in benign and malignant GIST of different sites[6]. Nevertheless some maintain that positive CD117 is not absolutely required in all cases of GIST[37]. Interestingly, the detection of KIT expression (by immunohistochemical staining with CD117) does not indicate KIT gene activation.

The lack of unanimity with respect to the immuno-markers used may be a reflection of case selection bias[5]. Although a specificity and sensitivity issue with the antibody(s) used has to be considered.

Genetic markers

Prognoses using genetic markers are currently being defined. The detection of overall net losses and gains of genetic material initially focused on flow cytometry with benign tumours generally diploid and malignant tumours aneuploid. A correlation of aneuploidy with poor prognosis had been suggested[11]. The frequency of aneuploidy in GIST ranges from 22-60%[40]. Ploidy patterns appear to have failed in reliably separating benignity from malignancy. It remains unproven whether DNA ploidy patterns are an independent prognostic marker for GIST. Aneuploidy may be associated with a mere tendency to an adverse outcome[12].

Molecular cytogenetic screening, particularly with CGH, reveals correlations between acquisition of chromosomal aberrations and aggressive clinicopathologic behaviour[18]. CGH enables screening of tumour genomes for gains (representing oncogenes) and losses (suggesting tumour suppressor genes) of DNA and their consequential mapping to chromosomal subregions[41]. Losses are more likely related to the development of GIST, whereas accumulation of additional genetic alterations, particularly gains/amplifications, is required for malignant transformation and metastatic behaviour in GIST[42].

The most convincing support of CGH-detected DNA copy changes as prognostic markers came from a recent series of 95 GIST, including 24 benign, 36 malignant primary, and 35 metastatic tumours[42]. The mean number of demonstrable chromosomal aberrations found were (2.6) benign GIST, (7.5) malignant GIST and (9) metastatic GIST. Deletions of chromosome arms 1p, 14q, and 22q were frequent irrespective of histologic grade. However, 9p deletion, 8q amplification, and 17q amplification were found almost exclusively in malignant GIST. LOH and FISH analyses have also supported the finding of chromosome 9 losses occurring preferentially in malignant GIST[19]. According to El-Rifai et al[42] the absence of gains can be considered a good prognostic parameter, suggesting it can be used as a new complementary diagnostic criterion for GIST. Undoubtedly, some DNA copy changes will prove to have more prognostic significance than others. No correlations between any specific DNA copy number changes and tumour location were found[42].

Although the cytogenetic profile in GIST is often distinctive, with characteristic chromosomal deletions (typically involving chromosomes 14 and 22)[41,42], none of the individual chromosomal aberrations appear specific to GIST. It has been argued for this reason that cytogenetic studies are less crucial than histopathology, KIT immunohistochemistry, and KIT molecular analyses in the routine evaluation of GIST[18].

Telomerase, an enzyme implicated in maintaining the de novo synthesis of the ends of eukaryotic chromosomes is expressed in 80-90% of carcinomas[43]. Its activation is a hallmark of carcinogenesis, with continued renewal of the chromosomal ends by telomerase thought to be a mechanism favouring cell proliferation[44]. Telomerase activity, a negative prognostic indicator, has been investigated in two studies (a total of 42 GIST cases)[43,44]. Unique to malignant GIST, telomerase activity was not detected in benign cases from either series, although not all malignant cases expressed telomerase. Gunther et al[44] showed a primary GIST tumour initially with no telomerase activity, which displayed marked activity in its recurrence. This phenomenon of late activation of telomerase has been reported previously[45]. Telomerase cannot yet be viewed as a reliable prognostic indicator.

Treatment and management

Until recently there was no effective therapy for unresectable or metastatic GIST, which is invariably fatal. A major development in treatment of advanced GIST has been the use of imatinib mesylate (Glivec), approved by the US Food and Drug Administration in 2002, for treatment of patients with CD117 positive unresectable and/or metastatic malignant GIST[46]. Imatinib mesylate works by inhibiting tyrosine kinase activity[47] which is believed to be the basis behind the neoplastic proliferation of GIST. Its use in non-metastatic GIST or for neo-adjuvant therapy is not established.

Complete surgical resection is the primary therapy for GIST, but the required extent of resection, including regional lymph nodes or adjacent organs remains unclear[7]. No benefit has been reported from obtaining wide margins[37]. Failure to obtain histologically tumour-free margins is associated with adverse outcomes[3]. Regional lymph node dissection is of unproven value[36].

Metastases occur in more than 50% of patients diagnosed with malignant or high-risk tumours at the time of resection[37]. Propensity for local recurrence suggests a role for adjuvant therapy, however data is lacking in support of the use of either radiation or chemotherapy[3,13]. Pierre et al[7] found that patients receiving adjuvant therapy had worse outcomes. Radiotherapy is limited by potential toxicity to surrounding structures[23] and is not standard post-operative therapy for GIST.

There is wide variation in five-year survival rates, 19-56% overall and 32-63% following complete resection[7]. Most recurrences occur within five years of primary treatment, but can appear more than 10 years after treatment[3], indicating the need for long-term follow-up.

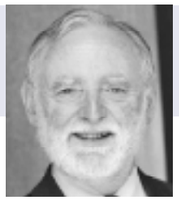
The difficulty in identifying reliable prognostic parameters only adds further confusion to the already controversial topic of gastrointestinal stromal tumours. Classifying GIST based on clinical presentation and morphology alone is difficult if not impossible, with the criteria for malignancy based on tumour size and mitotic count dependant on tumour location. Immunostaining for CD117 (although not entirely specific, but sensitive for GIST) along with a panel of antibodies, supplemented with careful morphologic examination assists the diagnostic process. The reported frequency and prognostic value of KIT activating mutations is uncertain, and in some instances contradictory. Results from molecular cytogenetic studies, suggesting a possible correlation between clinicopathologic behaviour and chromosomal aberrations, have significantly aided the defining of new prognostic parameters. Cytogenetic aberrations appear to be secondary events to oncogenic mutations. The possibility of particular aberrations uniquely affecting signaling pathways, and thereby determining the pathway of GIST progression remains to be seen. Telomerase expression, exclusive to malignant GIST (although not always expressed) may occur as a late event. Its validation as a useful prognostic marker depends heavily on the recruitment of larger numbers of cases and extended clinical follow-up.

This review has highlighted the inconsistencies of current prognostic parameters used in GIST. A multiparametric approach is necessitated, as no sole prognostic indicator has yet been determined reliable. The true test of any chosen parameter is one that can predict outcome on an individual case basis.

* This article is the winning essay in The Cancer Council Australia's cancer-related student essay competition. As the winner, Mr Keith attended the World Health Organisation's Collaborating Centre for Cancer Education's 'Oncology for Medical Students' summer school in Vienna from 28 August-6 September 2003. Mr Keith is a final year medical student at the University of Tasmania, Hobart.

ARTICLES

Constructive collaborations:
The 2003 Medical Oncology Group of Australia Pierre Fabre Cancer Achievement Award Lecture*



A Coates AM

The Cancer Council Australia

It is a pleasure to record my thanks to the Medical Oncology Group, the award selection committee and Pierre Fabre for this unexpected award.

Leonardo da Vinci was one of the foremost contributors to that re-emergence of learning and flourishing of art which we know as the Renaissance, and among the finest exemplars of what we now call Renaissance Man. This term was coined because Leonardo and many of his learned contemporaries aspired to knowledge across what is today an astonishingly wide canvas – painting, engineering, architecture and anatomy. The term is still used as one of approbation.

Robert Heinlein offers a more modern definition along similar lines

> "A human being should be able to change a diaper, plan an invasion, butcher a hog, conn a ship, design a building, write a sonnet, balance accounts, build a wall, set a bone, comfort the dying, take orders, give orders, cooperate, act alone, solve equations, analyze a new problem, pitch manure, program a computer, cook a tasty meal, fight efficiently, die gallantly. Specialization is for insects".

Lazarus Long in Time Enough For Love by Robert Heinlein

That's 21 skills. I'm not sure about you, but I barely pass. My career has, however, been one of change, and of interaction across boundaries.

In this presentation I will review some of those collaborations, give credit to at least some of those with whom I have worked, and suggest to you that, at least in terms of research, reaching out across the barriers of your own discipline can be creative and successful.

After completing the Membership, the first phase of my career was at the Walter and Eliza Hall Institute of Medical Research (WEHI), where I was immensely privileged to interact with a large number of extraordinarily talented people. The interface of relevance here was between clinical and laboratory medicine.

Sir Macfarlane Burnet – Mac – had won the Nobel Prize in 1960. By the time I was at WEHI he had retired as director but was a regular at seminars and at weekly case presentations in the Clinical Research Unit. He was sharp as a tack, and an inclusive thinker. I can best illustrate that by a conversation after a seminar – Mac lived near us in Kew and I sometimes used to drive him home. I was a young doctoral student, full of analytical reductionist zeal. I proceeded to describe the various potential flaws in the reasoning of the presenter – I have genuinely forgotten who it was or what it was about. Mac listened politely, then said "Wait a minute. Just suppose he's right. Where would that fit in to our overall understanding? After all, if he's not right we'll discard the idea quickly enough."

Sir Gustav Nossal was the director, and directly responsible for recruiting me to the Institute. Gus was also a regular at clinical meetings, and regularly brought a scientific angle to question any shaky clinical assumptions. He was an advocate for evidence-based medicine before the term was popular. Gus was also responsible for my interest in media relations. At the time there was no defined media contact policy at WEHI. One of our colleagues had discovered that insulin-dependent diabetics had a prevalence of autoantibodies in the serum more typical of non-diabetics a decade older. The headline read "Insulin makes you age". Diabetic comas increased dramatically. Gus came to me and said: "This must never happen again. From now on we have a media relations officer, and you're it". Gus is and was a consummate communicator, and I could not have asked for a better mentor.

Ian Mackay, head of the Clinical Research Unit, was my immediate boss. Ian was a rigorous and demanding bedside clinician, and carried both characteristics equally through into clinical and laboratory science. His own research and major contributions were in autoimmunity, but he fostered inter-disciplinary cooperation among his trainees and staff. Indeed this is the only phase of my career at which I was responsible for clinical patient care, laboratory experiments and simultaneously for reporting cardiographs and liver biopsies.

In many ways pride of place should go to Don Metcalf. Don's was the first laboratory I visited, in 1965. Typically, Don was at a microscope. Barely looking up, he said "Come here, Coates – have a look at this". This was a colony of haemopoietic cells growing in a dish of agar, a discovery he and Ray Bradley had made earlier in the year. "This will take up the next five years of my life." He was of course both right and wildly pessimistic.

My other contact from this period would probably be surprised to find himself listed. Through Ian Mackay I got to know Nigel Gray, then director of the Anti-Cancer Council of Victoria (ACCV), and to understand something of the possible contribution of a public health approach to disease control. It's perhaps a major reason for my latest career move.

The next major influence was the late Paul Carbone. I describe myself as a reformed immunologist. I had originally been attracted by the hope – common in the 1960s – that immunology would provide the answer to cancer. When it later appeared to me that such a hope was unlikely to be realised in my professional lifetime, I opted to continue an interest in cancer. In the mid 1970s there were no training programs in Australia. I was presenting some research on CEA at ACCV one day when Paul Carbone was visiting, and as I sat down he offered me a job. I knew of Paul's work at the National Cancer Institute, but he mentioned that he was about to move to Madison, Wisconsin. I accepted and went home to look up where exactly Madison was. Paul was a superb clinician, who revised my prejudices about American bedside medicine. He also provided training and leadership in what we now call translational research. He was generous in involving his Fellows in the clinical trials research of the Eastern Cooperative Oncology Group, so that I returned determined to apply some of the same principles to the conduct of clinical research in Australia.

While at WEHI I had developed an interest in melanoma – most immunologists with a cancer interest do – and in Wisconsin, I as an Australian, was the automatic choice to see melanoma patients. Returning to Sydney I had the opportunity to join Gerry Milton in the Sydney Melanoma Unit (SMU). I remain a member of that unit, under the successive leadership of Bill McCarthy and John Thompson. SMU has a long and successful record of collaboration both in international clinical trials, and with the immunologists, pathologists, psychologists, epidemiologists and even the medical oncologists who contribute to the management of melanoma. I was privileged to serve as its research director from 1985 to 1998.

My interest in clinical trials led me to join the relevant COSA committee, chaired by John Colebatch, one of the real pioneers of clinical trials in Australia. The experience of co-authoring a book with John (and Richard Fisher) was truly memorable. We put quotes at the head of each chapter. I can't be certain, but it seems very likely that John found this one.

> "Reading maketh a full man, conference a ready man and writing an exact man."
>
> Francis Bacon

Certainly exactitude in written expression was one of the disciplines to which he (and of necessity his co-authors) rigidly adhered.

In 1980 I joined the staff of the Sydney Branch of the Ludwig Institute for Cancer Research, under the direction of one of my distinguished predecessors in this award, Martin Tattersall. Martin has trained more medical oncologists than anyone else in Australia. It's a pleasure to acknowledge his selfless support and encouragement. Martin has many of the characteristics of modern Renaissance Man. I'm not sure how many of Heinlein's 21 abilities he can claim, but I'm sure he will be disappointed that his well-known ability to walk on water was not on Heinlein's list. Perhaps conning a sailboard counts.

I mentioned that I came back from the US keen to set up clinical trials in Australia. One of the first colleagues I visited was John Forbes, who had also been overseas – in Cardiff with Michael Baum – and had arrived back transformed from an HLA immunologist to a clinical trials researcher. The collaboration persists. I should also thank and give credit to my other fellow directors of the first Board of the Australian and New Zealand Breast Cancer Trials Group – John Collins, John Simes Vernon Harvey Michael Byrne and Ray Snyder.

Internationally, my work with the International Breast Cancer Study Group has been a real joy, especially because of my close working relationship with Aron Goldhirsch and Rich Gelber.

Another cross-disciplinary collaboration has been into psycho-oncology and quality of life research. Like many things, this arose by chance. On arriving at Ludwig I was presented with a mass of quality of life scores collected by a departed colleague and asked to apply my statistical skills make some sense of it. That led to the first of a series of papers christened (by Martin Tattersall) "On the receiving end". It also led to the inclusion of quality of life endpoints into the then new advanced breast cancer trial ANZ 8101, which I duly presented at ASCO in Los Angeles in 1985. While there I learned from Aron Goldhirsch that a couple of his Swiss colleagues were designing quality of life measures for the third generation adjuvant trials (IBCSG VI and VII). I was keen to incorporate our experience in the completed advanced trial, so I arranged to fly from Los Angeles to Switzerland to meet with Christoph Huerny and Juerg Bernhard. I suppose the reason it was easy to get a seat at short notice was that this was the weekend of the nuclear accident at Chernobyl, and practically no-one was flying east over the Atlantic. I'm happy to say that this collaboration too persists, and continues to be productive.

Clinical trials research requires the input and dedication of large numbers of colleagues – it's a pleasure to acknowledge the essential input of many colleagues in the International Breast Cancer Study Group and the Australian-New Zealand Breast Cancer Trials Group.

The final constructive collaboration I wish to acknowledge is with Lawrie Wright. Lawrie was appointed as executive director of the then Australian Cancer Society and the Clinical Oncological Society of Australia in 1978, just before I joined COSA. I count myself extremely fortunate to have become CEO of The Cancer Council Australia at a time when I could draw on his expertise, wisdom and guidance.

In summary, the lessons I would propose from this experience, which may be of value to younger colleagues are:

Master your own discipline (collaboration is not a substitute for competence); but
Specialisation need not be limiting (if you're not one of Heinlein's insects).

Look for interactions with other disciplines: pick them according to opportunity, according to your own interests, and perhaps the examples I have cited. Such collaborations can be constructive, productive, satisfying and fun.

* This is an edited version of the lecture presented in Canberra on 13 August 2003

REPORTS

Outclassing 'Kath and Kim': an Aussie kith and kin cancer conference

Meeting report on "Familial Cancer 2003 – Research and Practice", Couran Cove, Queensland, September 2003

In 1996, a small group of cancer researchers, under the guidance of Professor Joe Sambrook, developed an idea to create an Australian network that supported research into breast cancer. Their notion was to capitalise on a relatively new phenomenon in cancer medicine – Familial Cancer Clinics (FCCs) – which were being established throughout Australia. High-risk families were readily recruited from the FCCs, thereby providing a wonderful resource for cancer researchers with interests ranging from psychosocial medicine to the molecular biology of breast tumorigenesis. With the support of the Kathleen Cuningham Foundation, kConFab rapidly emerged as a national consortium for research into familial breast cancer. Pivotal to its success was the rigorous collection of epidemiologic data and biospecimens, as well as a philosophy of open membership and access to data.

The scientific meeting, held at Couran Cove on South Stradbroke Island in Queensland, was the sixth national meeting organised by kConFab (conference organisers Graeme Suthers, Judy Kirk, Christobel Saunders, Dorota Gertig, Nadia Traficante and Heather Thorne). The program was expanded this year to include an important new initiative, the Australian Ovarian Cancer Study (AOCS), directed by Professor David Bowtell. This national study, supported through a program grant from the US Department of Defense, is seeking to implement collaborative research into ovarian cancer. The meeting was also combined with the inaugural meeting of Family Cancer Clinics of Australia and New Zealand.

The first day and a half of the meeting was restricted to members of Family Cancer Clinics. This provided an invaluable opportunity for participants to discuss common areas of interest and need. Both pragmatic and esoteric issues were raised and discussed. One certain outcome will be enhanced dialogue among the Australian cancer genetics community as well as new measures to improve clinical practice and to establish common national protocols. Topics covered included the organisational strategies in place for each FCC, triaging protocols aimed at improving the selection of individuals for BRCA1 and BRCA2 and HNPCC gene mutation detection, disclosure of genetic information, and psychosocial issues in familial cancer.

The remaining two and a half day conference attracted more than 160 registrants from a variety of backgrounds (data managers, genetic counsellors, research nurses psychologists, patient advocates, epidemiologists, clinicians, surgeons, pathologists and laboratory scientists), all linked by a common interest in hereditary cancer and the Queensland sunshine. There were plenty of opportunities for useful dialogue among this diverse group and the program itself provided interesting and useful sessions for the vast majority of attendants.

There were four international plenary session speakers. Paul Meltzer from the Cancer Genetics Branch of the National Human Genome Research Institute at the US National Institutes for Health gave an excellent overview of the promises and some of the pitfalls of gene expression profiling. Examples from his group's pioneering work in the sarcoma, breast cancer and melanoma fields were presented, emphasising the value of gene expression profiling in probing cancer pathways, and identifying candidate genes that could serve as either prognostic markers or therapeutic targets.

Hanne Meijers (Erasmus Medical Centre, Rotterdam, Netherlands) provided a concise and distinctly European overview of clinical breast cancer genetics. Useful data and personal insights into risk management issues were presented. She discussed the unproven value of ovarian surveillance for high-risk women, despite its increasing use, in contrast to the clinical utility of prophylactic oophorectomy for mutation-positive women. MRI as a screening tool for breast cancer in high-risk women seems to be showing great promise in European studies. The role of prophylactic surgery for BRCA1 and BRCA2 mutation positive carriers was addressed in some detail, revealing quite marked differences in the mastectomy rate between the Netherlands and Australia. The notion of carrying out a BRCA1 or BRCA2 screen, where appropriate, to assist in planning a woman's breast cancer management was also canvassed.

Sue Hankinson (Brigham and Women's Hospital/Harvard Medical School, Boston, MA, USA) provided new data from the Nurses Health Study on dietary factors in breast and ovarian cancer. In their study, higher folate intake correlated with reduced risk, but only when associated with higher levels of alcohol consumption. This finding possibly reflects the antagonistic effect of alcohol on folate metabolism.

Sunil Lakhani (Institute of Cancer Research, Chester Beatty Laboratories, London, UK) presented important findings on genotype/phenotype correlations in BRCA1 breast tumours. It is now well established that BRCA1 tumours are often high grade and hormone receptor 'negative'. His group has recently observed that BRCA1 tumours often display a 'basal phenotype', expressing cytokeratins 5 and/or 14, markers found in myoepthelial cells. This finding could serve to facilitate more precise selection of patients for genetic testing and the clinical value of screening for a 'basal phenotype' clearly warrants further investigation, as does the basic biology.

Other overseas speakers included Yvonne Thorstenson (Stanford Genome Technology Center, Palo Alto, CA, USA) whose group is comprehensively screening cohorts of hereditary breast/ovarian cancer families (including kConFab) using the sensitive dHPLC method in order to identify candidate pathogenic sequence variants in the ATM gene. At this stage, however, the clinical utility of ATM testing remains unproven.

Australian speakers were well represented at the meeting, revealing the substantial breadth and depth of internationally competitive clinical and laboratory research that has developed in the hereditary breast/ovarian and colorectal cancer fields over the past few years. It was particularly gratifying to see that the resources being established by kConFab are being put to good use.

G Lindeman
Royal Melbourne Hospital Familial Cancer Centre and
VBCRC Laboratory

Australian Behavioural Research in Cancer

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

Australia has five behavioural research centres: the Centre for Behavioural Research in Cancer (CBRC) of The Cancer Council Victoria, the Centre for Behavioural Research in Cancer Control (CBRCC) at Curtin University of Technology Perth, the Centre for Cancer Control Research (CCCR) of The Cancer Council South Australia, the Centre for Health Research and Psycho-oncology (CHeRP) of The Cancer Council New South Wales and the Cancer Prevention Research Centre (CPRC) of the University of Queensland.

This report has been compiled by C Swart (CPRC).

New results

- The Centre for Behavioural Research in Cancer (CBRC), VIC

Findings from the Victorian Smoking and Health Population Survey 2002

Tessa Letcher, Carly Black, Irene Bobevski, John Lipscomb and Melanie Wakefield have been working on analysis and reporting of data from the Victorian Smoking and Health Population Survey 2002. A report on public opinion about smokefree policies in bars, nightclubs and gambling venues between 2000 and 2002 was released in July 2003. The data indicate strong support from the Victorian public for bans on smoking in bars, nightclubs and gambling venues, with approval for bans in bars increasing significantly over time among both smokers and non-smokers. There was a high level of public support for the most recent legislative amendments restricting smoking in Victorian alcohol licensed venues and gambling venues. Data from the population survey have also been used to generate reports on change in smoking prevalence and consumption among Victorian adults, as well as smoking behaviours and patronage of social venues associated with the introduction of smokefree policies. Visit the new CBRC website (www.cancervic.org.au/cbrc) to download copies of these reports.

Evaluation of the National Tobacco Campaign

CBRC has been very much involved with the evaluation of the National Tobacco Campaign since its inception. The September issue of Tobacco Control [Tobacco Control 2003; 12 (Suppl II)] contains a supplement devoted to the National Tobacco Campaign and features a number of papers by CBRC staff about various aspects of the campaign, including studies of the effects of the campaign on adult smokers and adolescents, and trends in Australian smoking prevalence. The supplement is online at http://tc.bmjjournals.com/content/vol12/suppl_2/.

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

Adtests for Philip Morris and Japan Tobacco MTV youth smoking prevention advertising

In 2001, British American Tobacco, Japan Tobacco International and Philip Morris International jointly funded an international advertising campaign featuring six advertisements broadcast in 38 countries. CBRCC conducted adtests on three of the advertisements screened in cinemas in Australia to test their impact on young people in comparison to data gathered from the Smarter Than Smoking campaign (Bus Stop and Fashion/Soaps) and an anti-smoking advertisement evoking the emotion of disgust (Disgust). A convenience sample of 257 youths aged 14 to 18 years was recruited with half being regular smokers and 40% being 14 or 15 years old. Among smokers aged 14 to 15 years, the tobacco industry advertisements performed better than the Fashion/Soaps advertisements for intentions in not wanting to smoke in the future and trying to quit, but not as well as the Disgust and Bus Stop advertisements. This under-performance of the tobacco industry advertisements compared with the Disgust and Bus Stop advertisements was consistent also among non-smokers aged 14 to 15 years. Among the 16 to 18 year age group, for both smokers and non-smokers, the Disgust advertisements performed far better than the tobacco industry advertisements in increasing intention in not wanting to smoke in the future. Similarly, current smokers who were shown the Disgust advertisements were far more likely to think about quitting than those shown the tobacco industry advertisements.

Secondary student survey: Sun behaviour results

CBRCC was commissioned by the Cancer Foundation of WA to compare the findings of a 2002 secondary student survey with those of similar surveys conducted in 1999, 1996 and 1993 that assessed attitudes and behavioural practices with respect to sun protection. The entire sample consisted of 3,545 students aged 12 to 17 years. Results indicate a high awareness that most skin cancers are caused by ultraviolet radiation from sun exposure (92%). However self-reported sunburn rates were high (77%) and most respondents did not spend the majority of their time inside on sunny days in summer between the hours of 10am and 2pm (76%). The data suggested that the adoption of a number of sun protective behaviours declined over the nine-year period and attitudes towards suntans remained highly favourable. The previously increasing trend in the proportion of respondents who do not like to get a tan appeared to have slowed, or, in the case of females aged 15 to 17 years, declined.

- The Centre for Cancer Control Research (CCCR) and the Tobacco Control Research and Evaluation Program (TCRE), SA

The relationship of emotional support and survival (further finding from the Canberra Cancer Quality of Life Project)

Survival was analysed using the Kaplan-Meier product-limit estimate, and multivariable Cox proportional hazards regression, from entry to the study in 1996 to date of death, or 31 March 2003, whichever came first. Numbers of confidants (with whom feelings were shared) at time of study entry were predictive of survival duration. The regression analysis indicated that compared with patients reporting 2-3 confidants, the relative risk of a shorter survival (95% confidence limits) was 0.44 (0.25, 0.79) for those with 0-1 confidants and 0.60 (0.40, 0.89) for those with four or more confidants. Shorter survivors shared their feelings more with family members than longer survivors. Conversely, longer survivors shared their feelings more with friends than shorter survivors. These relationships did not hold at 12 weeks from study entry. At that time, longer survivors were more likely to share their feelings with a doctor than shorter survivors. The relationship between emotional support and survival duration was not linear and appeared to be more complex than reported previously for people with heart disease and early breast cancer.

Monograph series

The Centre for Cancer Control Research has completed the seventh monograph in The Cancer Council Monograph series, South Australian Cancer Statistics. This one, entitled Cancers of

the prostate, testis and urological organs, was released in early October. As for previous monographs, its intended audience is senior secondary school students, science teachers, interested members of the public, and tertiary students enrolled in health and allied disciplines. The cancers addressed in this seventh monograph are an important group, accounting for about a fifth of all cancer deaths in South Australian males and about 50 deaths per annum in South Australian females. The monograph shows how these cancers affect the population, time trends in incidence, and survival outcomes. Local trends are placed in an international context. Risk factors are described, together with the opportunities that exist for cancer prevention through multiple avenues, including smoking cessation, adoption of diets rich in fruit and vegetables, weight control, and maintaining good industrial hygiene. Attention is given to the status of knowledge and debate about prostate specific antigen screening of asymptomatic men as a public health measure.

n The Centre for Health Research and Psycho-oncology (CHeRP), NSW

To refer or not to refer: Medical practitioners' perceptions of palliative care

While the use of palliative care services has been shown to improve outcomes including symptom control, care at site of choice, reduced costs and more needs of patients/family being met, recent data suggests that nearly 40% of advanced cancer patients in Australia are not referred to palliative care prior to death. There is little information available as to why this occurs.

Claire Johnson, a PhD candidate at the Centre for Health Research and Psycho-oncology undertook qualitative research to investigate medical practitioners' perceptions of palliative care and to gain an understanding of triggers used by medical practitioners to initiate the referral process, under the supervision of Associate Professor Afaf Girgis and Dr Chris Paul.

The study involved a semi-structured telephone interview with 40 general practitioners and medical specialists from around Australia. Information was sought regarding the medical practitioners' perceptions and understandings of palliative care and the referral of patients to specialist palliative care services. The perceptions and triggers were then compared with the identified principles of optimal palliative care practices, including the multidisciplinary approach to care and the provision of care across the physical, psychosocial, spiritual and cultural domains.

Results indicate that doctors in Australia are familiar with and comfortable in identifying symptom management with palliative care, particularly in the physical domain; and that doctors are cognisant in identifying physical symptoms as an appropriate reason for referral of patients. Less attention, however, appears to be given to psychosocial issues and even less to spiritual and cultural aspects of care. There is evidence to suggest that further education is needed to impart an understanding of the holistic nature and key principles of palliative care.

n The Cancer Prevention Research Centre (CPRC), QLD

Get mobile

This collaborative study with Stanford and Deakin Universities compared the effects on physical activity of a print-based intervention ('print'), and a print- plus telephone-mediated intervention. Sixty-five adults who identified themselves as physically inactive (18 men, 48 women) aged 45-78 years were recruited through advertisements and word-of-mouth at two sites (Melbourne and Brisbane), and randomised to the print or telephone intervention group. Participants in both groups attended an initial briefing session, and over the 12-week intervention period received an instructional newsletter, two motivational prize incentives, and the use of a pedometer. The telephone intervention group also received motivationally-tailored support via six telephone calls. Self-reported physical activity data were collected using the CHAMPS measure at baseline, 12 and 16 weeks. Results showed significant increases of approximately two hours/week in participation in moderate and higher-intensity physical activity, and in walking, in both intervention groups at 12 weeks, with increases maintained at 16 weeks. Participants in the telephone group maintained slightly higher levels of walking (by approximately 30 mins/week) than those in the print group at 16 weeks. Print and telephone-mediated interventions for promoting physical activity can reach large numbers of people at a relatively low cost. These interventions show potential for promoting initial increases in physical activity among older Australian adults, and should be evaluated across a more extended time period.

Research in the pipeline

n CBRC

The first national sun protection survey

Planning is well under way for the first national survey of Australian's sun-related activities on summer weekends; assessing people's sun protective behaviour, sunburn incidence, and related knowledge and attitudes. This collaborative project aims to provide national data to support evaluation of skin cancer control programs and campaigns at the state and national levels.

Research, evaluation and program staff from most states and territories have participated in a number of planning meetings to further develop the study protocol, considering a range of issues on content, sampling, and funding options. The proposed study method follows that developed by Professor David Hill and colleagues in 1987 for monitoring sunburn and sun protection behaviours in Victoria. The survey will be conducted on a total of eight Monday evenings from the end of November 2003 until January 2004, achieving a representative sample of telephone interviews of 4,000 Australians aged 14 to 69 years. Contact Suzanne Dobbinson in CBRC for more details.

The Gemini project

Semi-structured interviews have been undertaken with 28 identical twins who were discordant for smoking status during their teen and early adult years. The twin sets share the same genes, and lived in the same environment for much of this period. The interview questions were designed to explore the personal and environmental factors at play in one twin becoming a smoker, and the other, a non-smoker. A qualitative analysis is being undertaken to determine how the twins account for their decisions and behaviours around their discordant smoking status. Nvivo qualitative software package is being used to identify themes in the twins' responses and a paper is being prepared for submission for publication. The research team comprises Vicki White, Kim McLeod and Claire Davey.

n CBRCC

Solaria study

CBRCC has just begun a study involving solarium users to identify their characteristics. Participants will be interviewed via intercept surveys at solaria establishments and asked questions such as why they use solariums, how frequently they attend, how much time they spend in them, at what times of the year do they use them, and what is their awareness of any associated risks.

n CCCR & TCRE

Website modules

The Centre is collaborating with the Epidemiology Branch, Department of Human Services (DHS), in the development of website modules on cancer epidemiology in South Australia. The intended audience is the same as described for the monograph series. Two modules have been completed showing cancer trends in South Australia in an international context, plus trends in South Australia by country of birth. These are scheduled for placement on The Cancer Council SA and DHS websites in early October. A further module on cancer trends in South Australia by socio-economic status of residential area is nearing completion, and others are planned on time trends in incidence and mortality, geographic trends, and survival outcomes. Preventive and other cancer control messages are included in brief narrative descriptions that accompany the graphical presentations in these modules.

Cancer among indigenous South Australians

The Centre is collaborating with the DHS Population Health Division, the DHS Aboriginal Services Division, and the Aboriginal Health Council in South Australia in reviewing preventive opportunities for addressing the cancers risks demonstrated among indigenous residents.

Community support for smoking bans in bar and gaming venues over time

TCRE has investigated community support over time for smoking bans in hospitality venues in South Australia. Previous survey findings indicate that community support for hotels and bars has increased significantly over time. Support has remained high among all groups for smoking bans in gaming venues. Support for smoke-free venues among regular patrons is also high, with most patrons reporting that visiting these venues would become more enjoyable if smoking were banned altogether. The impact on smoking behaviour was also examined. TCRE is currently planning a survey for the coming months to investigate this issue further.

n CHeRP

Solaria compliance study

The association between exposure to ultraviolet radiation and skin cancer is well known. The number of establishments with artificial UV tanning equipment (ie solaria) has increased substantially over the past five years, with an associated increase in patronage. A new Australian standard has been developed for the operation of solaria emphasising the need for clients to be fully informed of the potential carcinogenic risks of using solaria, and recommends ways to make the practice of artificial tanning less dangerous.

Investigators Dr Chris Paul and Associate Professor Afaf Girgis from the Centre for Health Research & Psycho-oncology and Ms Irena Brozek and Ms Gill Batt from The Cancer Council NSW, are conducting a population study to assess levels of compliance among solaria operators with those aspects of the standard relating to minimising exposure among higher risk clients. This will be achieved through the use of simulated customer visits to a sample of solaria centres in Sydney, the Central Coast and Newcastle.

The simulated customers will use one of two scenarios which have been developed to determine the types of information given to customers and the policies of each solarium. Aspects covered in these scenarios include age, previous solaria use, tanning ability, skin cancer history and light reactions, medications, length of desired exposure and standard questions to ask the operators. At the conclusion of the study, the participating solaria will be informed of their overall assessment and will be offered assistance to improve compliance with the standard.

n CPRC

Physical activity in population health

CPRC now provides a strong cancer prevention nexus for research on physical activity. This is unique within the Australian network of cancer prevention research centers. Physical activity as a population health concern is now central to the cancer prevention agenda. Doing regular physical activity is very important for maintaining good health. It helps to prevent weight gain, type 2 diabetes, heart disease and breast and colon cancer. Unfortunately, most Australian adults are not active enough for health benefits. Rates of overweight and obesity are increasing rapidly; more than 50% of Australian adults are above the healthy weight range, and rates of type 2 diabetes have doubled in the past 20 years.

The Centre has been successful in obtaining substantial new research funding from NHMRC: a program grant on Understanding and influencing physical activity to improve population health outcomes ($4.38 million over five years) and a capacity building grant on Building capacity for physical activity research in population health ($2.12 million over five years). The research will develop better methods for measuring people's exercise habits and provide new insights into how personal, social and environmental circumstances can make people less active. It will also show how to design and deliver wide-reaching programs for different social groups and evaluated their effectiveness.

News

n CBRC

CBRC has recently launched its own website within The Cancer Council Victoria's website. Visitors to www.cancervic.org.au/cbrc can access information about CBRC, its staff, current research projects and previous publications. In addition, the new CBRC research paper series is a feature of the website and contains downloadable reports on specific CBRC research and evaluation studies.

CBRC has welcomed Dr Magdalena Lagerlund from the Karolinska Institute, Stockholm, Sweden, who has joined us for a one-year post-doctoral fellowship. Magdalena, whose background is in research in behavioural aspects of mammographic screening, will be working in the field of skin cancer prevention during her stay. CBRC also welcomes Sarah Durkin as the new Quit Research and Evaluation Manager, and John Lipscomb as a Data Analyst. Sarah is close to completing her PhD in psychology and took up her appointment in October. John is working both in skin cancer research and with the Quit evaluation team.

n CBRCC

CBRCC recently moved premises from the Bentley campus of Curtin University to its Shenton Park Health Research campus. We are now co-located with the National Drug Research Institute, the Centre for Developmental Health and the Australian Bio-Security CRC for Emerging Infectious Diseases. Staff contact numbers, email addresses and postal addresses remain the same. However the new address is:

Curtin Health Research Campus, 10 Selby Street, Shenton Park, WA 6008. The fax number has changed to (08) 9266 1642.

n CCCR

CCCR

Staff of the Centre co-authored reports that were accepted for publication in peer-reviewed journals. Topics included effects of hysterectomy status on estimated coverage of the population by cervical screening, mammographic detection as an independent prognostic indicator for female breast cancer, changing ratios of adenocarcinomas to squamous cell carcinomas of the oesophagus, and reasons for increases in survival from cutaneous melanoma. Preventive opportunities were discussed in these reports, both primary and secondary, together with changes in the prognostic messages conveyed by conventional prognostic indicators.

TCRE

Caroline Miller attended the 12th World Conference on Tobacco or Health in Helsinki, Finland in August. She presented two posters, entitled: Changes to smoking policies in private homes and cars after a restaurant smoking ban and the Impact of a quit smoking campaign for parents". Jacquie Hickling attended the annual conference of the Public Health Association of Australia, in Brisbane in October, and presented a paper entitled Public support for smoke-free hospitality venues in South Australia, 2000-2002.

n CHeRP

The Centre for Health Research & Psycho-oncology (CHeRP) recently celebrated its 15th birthday. The Cancer Council NSW initially established CHeRP in 1988 as the Cancer Education Research Program. CHeRP has grown from a few staff in 1988 to 25 staff members in 2003, including research personnel and postgraduate students.

Dr Chris Paul and A/Prof Afaf Girgis have been awarded $23,500 from the NSW Department of Health to undertake research into solaria operators' compliance with the Australian standard.

Dr Raoul Walsh also gave two presentations at the 12th World Conference on Tobacco or Health: Over-the-counter nicotine replacement therapy: Assessing evidence for its population impact and Qualitative studies of adolescent smoking: Review of methodologies and findings.

n CPRC

The Centre's website (http://sph.uq.edu.au/cprc/CPRC) has now been updated and includes our 2002/2003 annual report (http://sph.uq.edu.au/cprc/CPRC_Annual_Report_2003.pdf).

Neville Owen presented at the health promotion conference, "Promoting health: taking it to the streets", in August 2003, Innovative uses of websites for the delivery of health behaviour-change programs: promises, practicalities and opportunities.

Neville Owen and Liane McDermott presented at the PHAA Conference in Brisbane in October 2003. Their presentations were Measuring environmental attributes related to walking and The role of life-stage transitions in smoking behaviour among young women.

The Centre is pleased to welcome three new staff members: Dr Ester Cerin joined the Centre in September as a research fellow, and two new project officers, Lorinne de Toit and Phoebe Kearny, joined the Centre in October.

Thanks to Anne Gibbs (CBRC), Owen Carter (CBRCC), Kerri Beckmann (CCCR & TCRE), Narelle Mills (CHeRP) and Cathy Swart (CPRC) for their contributions.

LETTER

General Practitioners' focus on testicular cancer

In response to identification, by the National Cancer Control Initiative, of a need to keep GPs informed regarding cancer control, GPs in South Eastern Sydney have been provided with concise information on particular topics since October 1999. This end has been achieved through publication of Cancer Control Bulletins at a rate of about eight per year and their distribution with the active support of relevant GP divisions. In September 2000 the program expanded to the internet, where 32 Bulletins are currently available (www.sesahs.nsw.gov.au/publichealth/cancercontrol).

Being web-based, the bulletins are accessible to the wider community. However monitoring of the pattern of 'hits' following publicity in GP divisional newsletters has indicated that 'local' GPs are the foremost users. Thus, following such publicity, the number of hits to the website increased by 160%, remaining at this level for three months, and decreasing to pre-publicity numbers in the fourth month. The total number of 'hits' to the Bulletin website for the 15-month period was 32,612 (figure one).

Since monitoring of the website began, the Bulletin on testicular cancer has been, by far, the most downloaded file, being accessed up to five times more often than the average number of hits to any Bulletin. The testicular cancer Bulletin has been consistently the most frequently accessed Bulletin and has on numerous occasions been the most downloaded file from the whole South Eastern Sydney Area Health Service website. The 'hits' on the testicular cancer Bulletin are not explicable with reference to it being a recent publication, nor has this Bulletin been subject to any additional publicity.

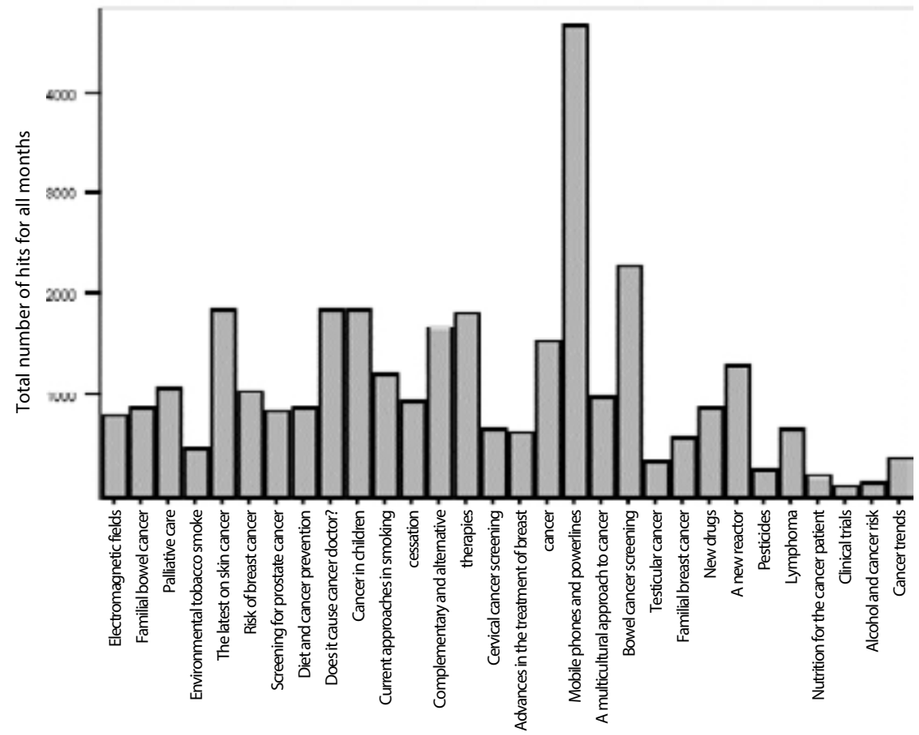
The second most commonly accessed Bulletin is the issue concerning new chemotherapy drugs, closely followed by the issue on the latest on skin cancer and cancer in children.

A simple explanation as to why testicular cancer should be consistently the focus of most enquiries is not apparent. It is evident, however, that there is a need for information on this subject by GPs. Such need does not appear to be correlated with enquiries from the general public, since analysis by The Cancer Council NSW of queries to the national helpline showed that testicular cancer was the 15th most called about cancer. Breast, skin, prostate, colon and lung were the most commonly asked about cancer sites[1]. We are aware of the GP education seminar "On The Ball" (www.uco.org.au) hosted by The Cancer Council NSW, this doesn't account for the pattern of enquiry.

K-A Ressler and BW Stewart
Cancer Control Program, South Eastern Sydney Public Health Unit, Randwick, NSW

1. The Cancer Council NSW. Helpline Report. Personal Communication, 2002.

Figure 1: Total number of hits to Cancer Control Bulletin website



NEWS & ANNOUNCEMENTS

Patenting human genes – Australian Law Reform Commission inquiry

Publicly-funded genetic testing and not-for-profit genetic research must be allowed to continue without penalty or undue restriction.

This is the key message of a submission by The Cancer Council Australia, on behalf of its member organisations, to the Australian Law Reform Commission's inquiry into Gene Patenting and Human Health.

The Cancer Council is concerned about a patenting system that allows exclusive rights to a naturally-occurring substance if such rights are to the detriment of public health, particularly by reducing access to or increasing the cost to the community of genetic testing; permitting testing without appropriate genetic counselling; and/or hindering research which would improve genetic testing methods and treatment.

The submission recommends several changes to the current patenting system to compensate for the unusual nature of gene patents and consequently the potential impact these patents may have on the wider healthcare system and health research.

Protecting the advocacy work of the Cancer Councils

The Cancer Council Australia has made a submission to the Board of Taxation, expressing concern about the potential impact of the draft Charities Bill 2003.

Cancer Councils believe they have a responsibility to advocate for improvements in government policy, programs or legislation to reduce the incidence and impact of cancer. Their goal is to ensure that issues related to cancer care and control get the attention, legislative action and funding they deserve.

While the draft bill broadens the legislative definition of a charity and resolves some ambiguities within current common law interpretations, the Cancer Councils believe that several provisions are badly drafted and may hinder rather than enhance the work of charities in Australia.

The submission seeks to ensure charities are expressly permitted to engage in advocacy in pursuit of charitable purposes and on behalf of those they seek to benefit.

The Cancer Council's submission can be read online at www.cancer.org.au.

National Skin Cancer Action Week

The dangers of tanning is a theme of The Cancer Council's National Skin Cancer Action Week this year (16-22 November).

Recent Cancer Council research shows that while around 50% of Australian women over the age of 18 say they aren't interested in being tanned, 25% still want a light tan, 21% a medium tan, and 4% a dark tan.

It seems many Australians wrongly believe tanning without burning and using a solarium is safe. The Cancer Council and the Australasian College of Dermatologists, a supporter of the Action Week, advise that any form of tanning which involves intentional exposure to ultraviolet radiation carries a risk of skin damage, including premature ageing and skin cancer.

Parliamentary briefing

"Cancer prevention: they key to reducing disease and health expenditure" was the topic of the latest meeting of The Cancer Council Australia's Parliamentary Cancer Information meeting.

Held at Parliament House in Canberra on 5 November, speakers included Professor Alan Lopez, head of the School of Population Health at the University of Queensland and former advisor to the WHO Director-General; Ms Christine Stone, Senior Epidemiologist – Cancer and Genetics at the Victorian Department of Human Services, and Ms Dorothy Reading, Chair of The Cancer Council's Public Health Committee.

The content of the presentation is outlined in the Cancer Update newsletter, which can be read online at www.cancer.org.au/publications.

Awards

Professor Alan Coates AM, CEO of The Cancer Council Australia, is this year's winner of the prestigious Medical Oncology Group of Australia/Pierre Fabre Cancer Achievement Award.

The Chairman of the MOGA Awards Committee, Dr Michael Jefford, said the award was in recognition of Professor Coates's outstanding contributions to cancer knowledge and control through his research, practice, teaching and service.

"He is internationally recognised as a leading expert in breast cancer, melanoma, cancer trials and quality of life research, and he has been a role model and mentor for many Australian oncologists," Dr Jefford said.

The prize was formally awarded to Professor Coates at the Annual Scientific Meeting of the Medical Oncology Group of Australia in Canberra on 13 August.

Professor Coates' address is published in this issue of Cancer Forum.

Professor Lester Peters AM has been awarded a prestigious Gold Medal by the American Society for Therapeutic Radiology and Oncology (ASTRO).

Professor Peters, a past president of ASTRO who is now Head of Radiation Oncology at the Peter MacCallum Cancer Institute in Melbourne, is one of only three to receive the Society's highest honour this year. He was formally presented with his Gold Medal at ASTRO's annual meeting at Salt Lake City in the US this week.

Professor Peters' award is in recognition of his excellence in pre-clinical and clinical research, his ability to translate research into clinical practice, and his many contributions to improve the standard of practice in radiation oncology.

He is a former chair, and continuing member, of The Cancer Council Australia's Medical and Scientific Committee.

Oncologists Forum

The first online medical forum for oncologists and haematologists in Australia and New Zealand will be held in February next year.

A faculty of leading oncology specialists has been established to help implement the new 20:20 Oncologist Forum.

The forum will include presentations from both international and Australian specialists and allow registrants to discuss the local implications of emerging issues and trends, via the Internet.

Dr Michael Green, Medical Oncologist at The Royal Melbourne Hospital and Chair of the 20:20 Oncologist Forum said the forum provides an innovative arena for the oncologists and haematologists to "debate, learn and share opinions on current issues and research".

A survey conducted with 25 Australian oncologists revealed the need for a unique, interesting setting that could facilitate scientific discussion rather than just provide an educational agenda.

"The Forum has been developed in response to these results, and it is the objective of the faculty to ensure the content and structure of the forum is not just educational but encourages debate," said Dr Green.

New COSA Executive Officer

Ms Margaret McJannett has been appointed Executive Officer of the Clinical Oncological Society of Australia (COSA). Ms McJannett also replaces Mr Lawrie Wright as The Cancer Council Australia's Administrative Officer.

Margaret has been involved in cancer care for the past 24 years. She was previously an oncology nurse consultant with the Sydney Melanoma Unit at the Royal Prince Alfred Hospital, and more recently working at the Sydney University's Medical Psychology Research Unit, where she was involved in developing treatment decision aids for cancer patients.

The first forum is to be held in late February 2004 and will be designed to fit into the RACP CME guidelines. For further information or to register interest, email oncology@virtuebroadcasting.com.au.

Cervical cancer screening conference

The Cancer Council Australia will be hosting a one-day conference on cervical cancer screening as part of an international meeting to be held in Melbourne next April.

The cervical cancer screening stream of the 18th World Conference on Health Promotion and Health Education will be held on Thursday, 29 April at the Melbourne Exhibition and Convention Centre.

The program will provide opportunities to share knowledge and showcase existing good practice in cervical screening programs, highlight future opportunities and new technologies, raise awareness of access and equity issues of disadvantaged woman, and allow for the development of networks to facilitate and maintain collaborative relationships.

It is expected that the focus of the cervical screening conference stream will offer the opportunity for presentations on current issues including new technologies in cervical screening, the human papilloma virus (including a vaccine and testing), and effective recruitment measures for reaching unscreened women.

For further information, including the registration form, go to http://www.Health2004.com.au/program2/cervical.asp.

The Cancer Council Australia gratefully acknowledges the Victorian and Australian governments for their assistance through funding support of the cervical cancer screening stream.

UICC grants and fellowships

The International Union Against Cancer (UICC) is offering research grants and international fellowships that provide opportunities for continuous professional education in a variety of disciplines through long, medium and short-term work and training periods abroad. They are intended for qualified investigators, clinicians and nurses who are actively engaged in cancer research, clinical oncology or oncology nursing or are educators in these fields.

UICC Yamagiwa-Yoshida Grants provide support for establishing or conducting three month long bilateral (between any two countries) cancer research projects to develop experimental research methods and techniques. Selection will take place in April 2004 and, if successful, projects can start within a month. There are six to eight grants available, valued at $10,000. Applications close 1 January 2004.
http://fellows.uicc.org/fell3yy.shtml

Beginning Investigators fellowships are funded by the American Cancer Society for beginning investigators and clinicians in the early stages of their career. There are six to eight fellowships available, valued at $40,000 for 12 months. Applications close 1 December 2003.
http://fellows.uicc.org/fel11abi.shtml

Translational Research fellowships are aimed at improving the translation of basic, experimental, and applied research insights. There are two to three fellowships available, valued at $55,500 for 12 months. Applications close 1 December 2003.
http://fellows.uicc.org/

Wishlist Christmas hampers

Wishlist.com.au has developed a range of gourmet Christmas hampers as a fundraising initiative to support The Cancer

Council Australia. Your purchase of a Blitzen Reindeer, Cupid Reindeer or Vixen Reindeer hamper includes a $5, $10 or $15 contribution to The Cancer Council Australia*. For further information or to order, visit Wishlist.com.au.

*Please note: Purchasing Blitzen, Cupid and Vixen hampers cannot be used as a tax deduction and tax invoices cannot be issued by The Cancer Council Australia.

CEO profiles

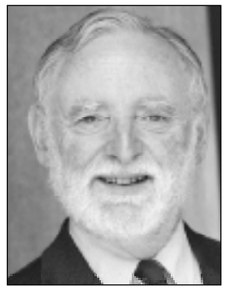
In each edition of Cancer Forum this year we have profiled the CEOs of The Cancer Councils.

The Cancer Council ACT
Joan Bartlett

Ms Joan Bartlett commenced as Executive Officer of The Cancer Council ACT in January 1999.

Ms Bartlett has worked in the not-for-profit sector since early 1991, working first for an organisation offering Employment Assistance Programs (EAPs), followed by four years as the Education Director of Family Planning ACT, and then three years as the Executive Director of Lifeline Canberra.

After arriving in Canberra from Queensland in June 1989, Ms Bartlett worked briefly in the training and development areas of three Commonwealth Government Departments: (the then) Department of Finance, (the then) Department of Health and the Department of Foreign Affairs.



At the beginning of her working life, Ms Bartlett had begun at Sydney Hospital as a student nurse in 1966, completing only one year before taking up teacher training. In 1971, after teaching in country NSW and Sydney she went overseas for four years working in hospitality (and occasionally crewing yachts) for a living.

After ten years working as a student and as a stay-at-home parent, Ms Bartlett returned to work in 1985 as a Special Education teacher at the Barrett Adolescent Centre, near Brisbane, working for two years with adolescents with psychiatric illnesses. Following this experience Ms Bartlett was employed as a guidance officer (counsellor) in high schools around Brisbane for three years.

Ms Bartlett is currently studying for an MBA majoring in Association Management from the University of New England. She holds a Masters of Educational Studies degree (Guidance and Counselling) and Bachelor of Educational Studies degree (both from the University of Queensland), a Graduate Diploma in Special Education from Charles Sturt University as well as a Diploma of Teaching and Teaching Certificate from (the now) University of Wollongong.

Her early attraction to things medical, plus training and experience in education and counselling and her current interest in governance and association management, have each contributed to her finding managing The Cancer Council ACT a most fulfilling experience.

The Cancer Council Tasmania
Lawson Ride

Mr Lawson Ride was appointed foundation Executive Director of The Cancer Council Tasmania in April 1995 and has been responsible for the growth and development of the Council and its programs to date.

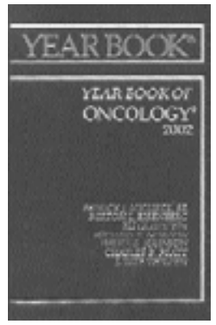
Prior to his appointment he enjoyed a long and varied career in a range of agencies within the Tasmanian public service. During eight years in the Department of Health Mr Ride held a range of senior management positions in health promotion, public affairs and the secretariat, before his final appointment as Senior Private Secretary to the Minister for Health and Community Services.

BOOK REVIEWS

2002 YEAR BOOK OF ONCOLOGY

PJ Loehrer et al (eds)

Published by Mosby (2002)
ISBN: 0-3230-1510-7. 396 pages plus index.
RRP: A$245.56



The Year Book of Oncology used to be one of my favourites. The 2002 edition is no exception, but it's losing its impact.

The book is 437 pages, divided into 19 sections ranging from epidemiology, ethics, the usual solid tumors and hematology to paediatric oncology. Seven reviewers/editors surveyed approximately 500 journals, and from these they selected what they felt were important articles from 74 separate journals – all English-speaking – to be abstracted in the 2002 edition. Each article is presented in abstract form. Some are extended with the inclusion of tables, graphs and radiology. Each article is put in perspective by one of the editors, and in some cases commented on by multiple editors. Some papers are grouped together in a theme and then a comment is made pertaining to all of them. The papers chosen vary from observational pieces to large randomised trials. I have to admit that some of the articles thought to be important by an editor would not attract my attention. All of the quoted papers have been published in 2000 or 2001, and herein lies the weakness of these books.

With oncology literature now so vast and the number of journals ever-increasing, even the best motivated and studious oncologist has difficulty in keeping up-to-date, if not in their sub-specialty, certainly in the area of general oncology. These year books are aimed at general oncologists who don't have the time to read articles that fall outside their area of expertise, published in more obscure, difficult-to-access journals, that don't make it to the high impact ones. They are very useful in filling gaps, and allow exposure to related work that may have bearing on their specialty.

The main limitation of the year books is that they are one to two years behind, and the reader is already aware of many of the quoted articles and, in some cases, the impact on their clinical practice. Alternate, faster information can be obtained through various electronic search engines that are making the usefulness of these series redundant. Nonetheless there were many articles that I would not have read otherwise.

How to improve these books? More timely publication, say within three months of the subsequent year, would make a year book more useful. This could occur by increasing the number of editors and sharing the workload.

The 2002 Year Book of Oncology is a good book to read from cover to cover to maintain a broad knowledge of recent literature in oncology, but not the source to go to, to look up a specific topic, to answer a clinical question, or to keep current in your interest. Oncology units and hospital libraries should have a copy. Some oncologists may enjoy having their own copy if they have $246 to spare; most won't.

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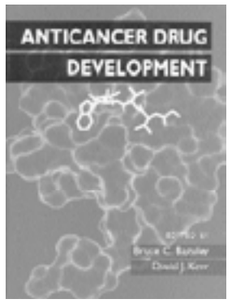
ANTICANCER DRUG DEVELOPMENT

B Baguley and D Kerr (eds)

Published by Academic Press (2002)
ISBN: 0-1207-2651-3. 384 pages plus index.
RRP: A$221.00



This ambitious text consists of 20 chapters with contributions from a total of 59 eminent scientists from seven countries and provides a well-structured and impressively broad overview of all aspects of anticancer drug development. Considering the breadth of topics covered, there is surprisingly little overlap of content. The editors, Professor Bruce Baguley (Co-director, Auckland Cancer Society Research Centre, University of Auckland, NZ) and Professor David Kerr (Head of Clinical Pharmacology, Institute for Cancer Medicine, University of Oxford, UK) have a wealth of experience in anticancer drug development and clinical trials respectively, and have collectively published well over 500 research articles in these fields of research.

The first nine chapters essentially deal with cellular targets for anticancer drugs. Chapters 10-14 deal with different approaches for anticancer drug development and chapters 15-20 deal with various aspects of pre-clinical drug development. Each chapter begins with a brief summary and most conclude with an outline of the progress that has been achieved to date in the relevant field, together with an indication of potential advances in the future.

The individual topics have been presented at an advanced scientific level, and there appears to have been a determined effort to ensure that as much current work as possible has been included, as indicated by the high proportion of relatively recent references cited.

Although most chapters provide useful diagrams, the text would have benefited from more "summary-type" figures. One unfortunate limitation was the restriction of most figures to black/white, where many would have benefited considerably from a good colour presentation. Some useful colour figures have been included, but are buried between chapters 19 and 20.

Overall, this text provides a magnificent resource for all those involved in any aspect of anticancer drug design or drug development. It is presented at an advanced scientific level and is ideally suited to those who are actively involved in anticancer drug discovery and/or drug development. However, it will also serve as a superb text for undergraduate and post-graduate students who require an overview of the status of current anti-cancer drug development strategies and approaches, and also to those who require some perspective of individual aspects of anti-cancer drug development. This is a relatively expensive text (unavoidable for this type of specialised topic), but well worth it! It is a must for every university and research institute library and for all laboratories involved in anticancer drug research. It is more research-oriented and more comprehensive than the only other similar text on this topic by Beverley Teicher (Anticancer Drug Development Guide, Humana Press, 1997).

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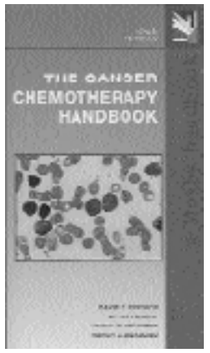
The cancer chemotherapy handbook (6th edition)

DS Fischer et al

Published by Mosby (2003)
Distributed in Australia by Elsevier.
ISBN: 0-3230-1890-4. 519 pages plus index.
RRP: A$97.90



This is the 6th edition of a chemotherapy handbook that started life in 1979 as an in-house handbook for fellows and nurses at Yale New Haven Hospital, USA.

Although designed for oncology professionals in the US, the use of generic drug names throughout, as well as American tradenames, makes it suitable for Australian users. This compact handbook is truly pocket-sized; yet it is packed with information not always included in this type of book. Traditional drug monographs, listed in alphabetical order, fill about half its pages and include cytotoxic and associated drugs that are commercially available in the US as well as many investigational agents. Individual monographs are not referenced, but many have one or more references listed under selected reading at the end of the monograph. There is a similar section on biotherapies which has a short overview of this topic followed by alphabetical listing of the individual products. A comprehensive chapter on cancer chemotherapy and biotherapy lists in alphabetical order the different cancer types. For each type there is a paragraph about the disease state and a number of protocols that have been used for treatment. These are from published research articles in the main, with a few from abstracts only (the limitations of using abstracts as a treatment resource are acknowledged). Selected reading references are also provided. In the introductory pages of this chapter the authors explain this section is a quick reference for those who use combination chemotherapy, not a "cookbook" for the inexperienced.

In addition there is a range of chapters on other topics related to cancer and its treatment. These start with standard chapters such as basic pharmacology including drug interactions, and administration of chemotherapy including dosing, administration methods and devices, complications of administration, and occupational exposure issues. Further chapters cover assessing and managing organ toxicity, managing cancer pain, and high dose chemotherapy with stem cell support. The very topical area of medication safety with chemotherapy is covered for the first time in this edition of the handbook. Other interesting chapters include principles and applications of clinical trials, and ethical considerations in cancer patients.

I am often asked what textbooks I recommend, and find it difficult to answer, as they can become dated quite quickly. However, I think oncology nurses, pharmacists and medical trainees would find this small, relatively inexpensive handbook a useful information resource. In this era of portable computer technology it would be great if it were available in a downloadable form to a personal digital assistant such as a Palm or Pocket PC.

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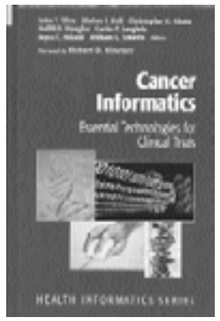
Cancer informatics: essential technologies for clinical trials

JS Silva et al

Published by Springer (2002)
ISBN: 0-3879-5328-0. 367 pages plus index.
RRP: US$79.95



People running cancer trials should read this book. It is about the US National Cancer Institute's plans to "liberate cancer trials from paper".

The authors' thesis is that "advanced information technologies and concurrent process enhancements will transform clinical trials, just as they have transformed businesses". The aim is to get better treatments into practice faster.

Richard Klausner championed the need for a cancer informatics infrastructure to enable clinical research and to link it to the delivery of cancer care. He took this on as a task for the US National Cancer Institute (NCI).

Although the issues needed to be addressed for all aspect of the National Cancer Research Program, the US NCI decided to make clinical trials the centrepiece and starting point. The book's editors were part of a team that met to assist the early formulation and implementation of the principles of the cancer informatics infrastructure.

The sections describe lessons from e-commerce – development of standards, common data elements, forms and terminology; integration with public health informatics and research; clinical trials information systems; and consumer education and support. The chapters were written by leading US experts. The content is detailed, technical, and surprisingly well-written. They give a clear vision of how cancer trials are likely to develop over the next 20 years.

This book is informative, interesting, and (I'm embarrassed to admit) enjoyable.

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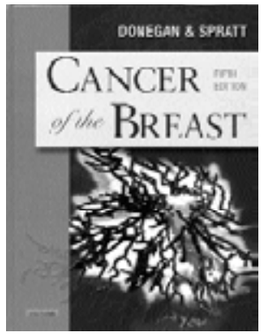
Cancer of the breast (5th edition)

WL Donegan and JS Spratt

Published by Saunders (2002)
Distributed in Australia by Elsevier
ISBN: 0-7216-8951-5. 1025 pages plus index.
RRP: A$390.50



This book is an update from the last edition in 1995 and is therefore a considerable advance on the previous text. Previous editions have been an excellent resource, but as always with textbooks, like computers, they quickly become outdated. With the speed of advancement in breast cancer research and treatment, this is especially so for reference texts on the topic of breast cancer.

This book, nevertheless, comprehensively covers just about all aspects of breast cancer and also has an excellent chapter on common benign conditions of the breast. A preceding chapter by one of the few non-American authors unifies the concept of benign breast disorders, which is pertinent to anyone dealing with the "worried well".

History never changes, but there is an excellent introductory chapter on the history of breast cancer with following chapters dealing with microscopic and gross anatomy of the breast and physiology. All the usual necessities of a breast cancer textbook are covered, which include clinical aspects around medical, radiation and surgery. Molecular biology, genetics and prevention are also dealt with well in separate chapters and a whole chapter is devoted to growth rates before leading into staging and prognosis. I found the chapter on nutrition and breast diseases quite interesting and informative. The editors of this textbook are surgeons and some of the key chapters eg In situ carcinoma of the breast, Stage IV carcinoma and Local and regional recurrence are authored by surgeons. This leads to a slight surgical bias for what are clearly multidisciplinary conditions. The non-surgeons amongst you however should not be perturbed as the chapters are still quite comprehensive and well-referenced. A large number of contributing authors provide a good coverage of many other aspects of breast cancer research and management not necessarily covered by other smaller textbooks. There are quite a few chapters that deal with aspects of metastatic disease and chapters devoted to some difficult management problems such as pregnancy and occult primary breast cancer. The final chapters deal with statistical methods and a critical analysis of clinical trials. A whole chapter is devoted to liability issues related to breast cancer, a North American issue of equal significance in Australia.

Overall I would highly recommend this reference textbook for the generalist with a breast interest or even the highly specialised researcher or clinician. No one knows it all and there will certainly be chapters that will educate, others that will serve as a quick ready reference and others, which the informed will wish to critically evaluate and perhaps even reach alternative conclusions. There are only a few textbooks on the management of breast cancer that are as encyclopedic as this one and this is the most current. It is highly recommended.

OA Ung
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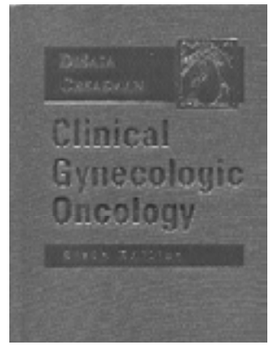
Clinical gynecologic oncology (6th edition) including clinical gynecologic oncology review (3rd edition)

PJ DiSaia and WT Creasman

Published by Mosby (2003)
Distributed in Australia by Elsevier
ISBN: 0-3230-2372-X. 656 pages plus index.
RRP: A$313.50



DiSaia and Creasman have recently released the sixth edition of their textbook Clinical Gynecologic Oncology. This American textbook is aimed at the "resident, fellow or student of gynecologic oncology" and represents a comprehensive text on the subject. The book was first published in 1981 and has been revised in line with progress in the field. In this regard it gives a clear historical perspective on many of the advances in the management of women with gynaecological malignancies.

The book has a broad clinical bias giving a detailed account of the epidemiology and clinical presentation and management of women with gynaecological cancers. It also includes comment on affiliated areas such as breast and colon cancer screening and guidelines for the management of the dying patient. Compared to previous editions the chapter on the genetics of cancer has been expanded. Also this new edition has a small colour atlas at the beginning of the book.

The text is quite expansive in character however important key statements are highlighted in red, and this is helpful when using the book as a reference. There is also a very useful chapter on cancer in pregnancy, an important topic, and one that is not addressed in such detail by other commonly used text books.

My main criticism of this textbook relates to the limited appreciation and acknowledgement of key research arising outside of America and the lack of comment in such regard. It is obviously challenging to the authors to have to continually update such a comprehensive text on the subject and this also is evident on occasion.

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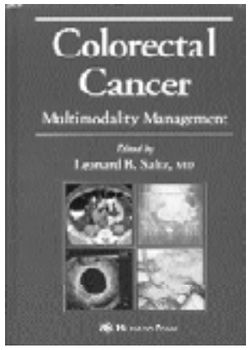
Colorectal cancer: multimodality management

LB Saltz (ed)

Published by Humana Press (2002)
ISBN: 0-8690-3935-8. 835 pages plus index.
RRP: A$195.00

This book is extensive in scope, aiming to provide a "well-balanced, authoritative, evidence-based review of the current approaches to the prevention, diagnosis and treatment of

colorectal cancer" and is divided into six segments. These are epidemiology and prevention, diagnostic and therapeutic radiology, surgery, medical oncology, supportive management and new agents in colorectal cancer.



Each section has significant strengths. In the first section on epidemiology and prevention there is an excellent overview on the chemoprevention of colorectal cancer. The chapter on screening and surveillance is reasonable, but does not adequately address the role of the Bethesda criteria in identifying families who may require investigation for hereditary non-polyposis colorectal cancer.

The section on diagnostic and therapeutic radiology provides excellent chapters on the role of virtual colonoscopy, nuclear medicine and preoperative staging of rectal cancer. Within the section on surgery, the chapter examining the role of laparoscopy in colorectal cancer is balanced by cautious concluding remarks, which rightly place the technique in the setting of research trials rather than routine clinical practice until long term outcomes and cost efficacies are known. The chapters on cryosurgical and radiofrequency ablation of hepatic metastases suffer from enthusiasm being weighted over evidence. Both techniques require better trials before their role can truly be assessed. The chapter on the surgical management of peritoneal surface spread is written by an obvious enthusiast, and is thinly referenced. Balancing this are solid chapters on surgery of the colon and rectum. Furthermore the chapter on management of cancer in a polyp is concise and helpful to any budding colonoscopist.

The section on medical oncology provides an excellent, detailed overview to an area that is experiencing rapid change. As with any text in an evolving area, the chapters inevitably are unable to be completely up-to-date, and hence this reduces its utility to established oncologists in the field. However, for non-oncologists involved in the management of colorectal cancer and trainees to the field all the chapters are valuable. Similar comments apply to the section on new agents in colorectal cancer.

The section on supportive care is incomplete. One of the most distressing aspects of advanced colorectal cancer can be bowel obstruction due to recurrent disease and/or peritoneal spread. The medical management role of venting percutaneous gastrostomy and surgery is not covered in this section. Similarly, the role of radiotherapy in pain management is not covered, although the overview of analgesics used is not unreasonable.

This text would be useful for any health professional working in the area of colorectal cancer who wishes to have an accessible text covering other disciplines beyond his or hers in this field. It is relatively weak with respect to palliative management, but the sections on medical oncology and epidemiology and prevention are its greatest strengths.

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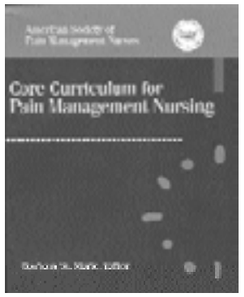
Core curriculum for pain management nursing: American Society of Pain Management Nurses

B St Marie

Published by WB Saunders (2002)
ISBN: 0-7216-9089-0. 564 pages plus index.
RRP: A$144.65



Despite the availability of a number of effective pharmacological and non-pharmacologic pain therapies, pain continues to be a major problem for a significant proportion of people with cancer. Many organisational, patient and health care provider factors have been identified as contributing to this problem. Education of health care professionals is, therefore, an important strategy in efforts to improve pain management.

Core Curriculum for Pain Management Nursing has been developed to help nurses improve their knowledge about assessment and management of acute, chronic and cancer pain throughout the life span. The scope of the text is broad, covering pain management issues in various clinical and sociocultural contexts. Section one covers curriculum content relating to foundational concepts of pain management nursing, including philosophical, epidemiological, cultural, legal, ethical and theoretical perspectives of pain. Section two addresses various clinical issues in pain management, while section three includes chapters addressing nursing roles and models for delivering pain management services.

Each chapter presents a list of topics for inclusion in pain curricula, with a brief description of content areas to be addressed. Many of the chapters provide extensive references lists, as well as useful tools for clinical practice. For example, the chapter on cultural perspectives includes numeric pain rating scales translated into various languages. Similarly, the chapter on pharmacological agents provides a useful overview of adult drug doses including routes, average does ranges and intervals and other special considerations for drugs, including antidepressants, anxiolytics, hypnotics, NSAIDS, opioids and steroids. While the chapter does not elaborate on how such dosage guidelines may be applied or modified in more complex and rapidly changing pain management situations, such as in palliative care, the information presented does provide a concise overview of the many agents that have potential uses in pain management. The chapter on pain assessment also provides a useful framework for nursing practice, although it does not cover in any depth the importance of assessment data obtained from clinical investigations that may help to determine various pain mechanisms and appropriately tailored management strategies.

The strength of the text is its broad perspective and its clear definitions and descriptions of complex pain management concepts. Attention to the specific needs of special populations, such as older persons, children and chemically- dependent persons is also a useful addition. The text is targeted primarily to the US audience, and as such epidemiological data, legal and regulatory references and some drugs are not applicable to the Australian setting.

Moreover, as a core curriculum, the text focuses solely on content and areas of knowledge, rather than on practice or competency outcomes, or on teaching and learning processes that will help to achieve desired learning outcomes. Nonetheless, the text does provide a valuable resource not only for those involved in designing educational programs for nurses, but also for nurses in practice who are looking for a guide to assist their own learning in this field.

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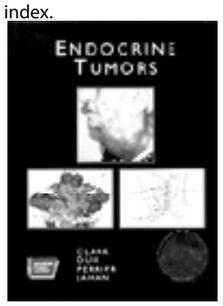
Endocrine tumors

OH Clark et al (eds)

Published by BC Decker (2003)
Distributed in Australia by Elsevier.
ISBN: 1-5500-9134-4. 239 pages plus index.
RRP: A$333.30



This book on endocrine tumours is part of the Atlas of Clinical Oncology series (G D Steele Jr et al) from the American Cancer Society. It also contains a CD with full text and illustrations as searchable PDFs. The book is structured by endocrine organ systems, dealing sequentially with the thyroid, parathyroid, adrenal glands, endocrine pancreas and "other", which includes a chapter each on the multiple endocrine neoplasia type 1 and 2 syndromes (MEN 1 and MEN 2). Two to five chapters are devoted to each organ, being specific for a particular tumour type, eg phaeochromocytoma/paraganglioma and adrenocortical carcinoma, constitute two of the five chapters under the adrenal glands.

Chapter authors are largely writing from the perspective of updating the reader on options for clinical management of patients with endocrine and neuroendocrine tumours, including surgery, medical treatment, and in the case of MEN 2, the availability of genetic testing. Chapters are rich in figures, including photographs of resected surgical specimens, physical manifestations of diseases such as Graves's disease and Cushing's syndrome, imaging including computed tomographic and sestamibi scans, as well as detailed histopathology and line illustrations. Chapters are, in general, well referenced.

This book would be an excellent text for students interested in endocrinological tumours/syndromes or endocrine surgery, or for the more established clinician looking for a quick reference text or teaching tool. It is not written with the molecular biologist in mind, although a scientific researcher wishing to learn more about the endocrine diseases would benefit from reading relevant chapters. Some genetics is presented in the chapters on differentiated thyroid carcinomas, including information on the RET receptor mutated in medullary thyroid cancer and the RET/PTC rearrangements seen in papillary thyroid carcinoma. A screening, diagnostic and treatment algorithm for genetic testing in patients with medullary thyroid cancer is presented that would be helpful for those involved in the clinical management of this condition.

In sum, this text should constitute a useful reference that is well placed in the Atlas of Clinical Oncology series.

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Exercise & cancer recovery

C Schneider et al

Published by Human Kinetics Australia (2003)
ISBN: 0-7360-3645-8. 205 pages plus index.
RRP: A$129.80

Cancer survivor rehabilitation remains a big challenge. It should concern all involved with the care of cancer patients and their families. Accordingly, the appearance of a substantial book on the role of exercise in this recovery process is very welcome, and the format of this book allows it both to be read for information, and to be used as a teaching and service development resource, with recognition of its limitations.

The early chapters of the book present a very brief and basic overview of cancer pathology and the effects of cancer treatment and toxicity on physiological systems. At the very end of the second chapter, the authors make the unreferenced assertion that all patients treated within the six-month intervention program at their institute report significant improvements in quality of life. The authors thus exhort those of us who care for our patients to go and likewise incorporate exercise into our treatment regimes. In the following chapters, basic principles of exercise prescription are developed, and clearly illustrated from the experience of the treatment centre where the authors are the principal therapists. Indeed, the name or logo of the centre is clearly visible on the T-shirts worn by both therapists and models, throughout the book. It gave me the impression of product placement advertising.

The book suffers from two significant limitations, in my view. First, the referencing is very patchy. Two papers by the books' authors, quoted in each of the five central chapters of the book, are described as being manuscripts in preparation, not yet submitted, let alone accepted, and much of the rationale for what they describe in the later chapters rests on the content of these papers. In other places electronic references are cited which, on going to the cited web pages, are not now available to this reviewer. It is of historical interest that the authors were able to access these pages on a given past date, but it is of no intellectual use to the reader in the present, and should warn those who write of the impermanence of non-print citation.

Second, the book relies exclusively on the experience of the authors' own centre, from an exercise physiology viewpoint, in a large and wealthy country where other cancer rehabilitation services have publicised their work and practice. These two factors limit the use of the book as a teaching aid, which is a pity.

To sum up, there is a lot of useful content, in an important area of cancer practice. The book has its place in the library of cancer rehabilitation. To balance its limitations, read it in comparison with the published experience from other disciplines working in the area of cancer rehabilitation.

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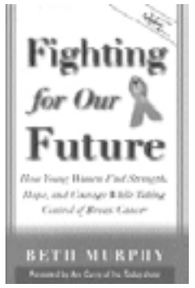
Kensington, NSW

Fighting for our future: how young women find strength, hope and courage while taking control of breast cancer

B Murphy

Published by McGraw-Hill Australia (2003)
ISBN: 0-0714-0925-4. 314 pages plus index.
RRP: A$39.95



While there is a plethora of breast cancer information resources for women and their families, some gaps remain. Fighting for our future, based on an earlier US Lifetime Television documentary, aims to fill one such gap. In writing this book for young women with breast cancer, the author is supported by an expert medical advisory board.

Given their relative youth and earlier life stage, breast cancer presents young women with particular physical, medical and emotional challenges. This book addresses many of these challenges. In particular it helps to address the isolation that many young women with breast cancer experience. Throughout the book, the voices of young women carry the central message: you are not alone.

The book addresses an extensive range of topics including: screening and diagnosis, treatment options, alternative and complementary methods of healing, support issues, body image, sexuality, fertility; workplace issues, recurrence, and breast cancer advocacy.

Each chapter provides significant details on a range of issues, drawing on both medical expertise and women's experience. The books emphasis is to provide information from varying and sometimes opposing perspectives, and aims to give women the information that they can use when talking with their practitioner. Key features of each chapter are the highlighted checklist of questions, useful tips and women's stories.

The chapters on psychosocial support, body image, relationships and sexuality, and fertility and pregnancy stand out. They address critical issues for young women that remain with them long after treatment has been completed. The chapter on reconstruction deals well with the issue of implants, the silicone controversy and different types of flap surgery. However some of the flap techniques discussed are not used regularly in Australia and may lead to confusion.

In its conversational style, the book relies on the views given by individual eminent medical experts. At times I would have preferred stronger articulation on the level of evidence underpinning their views, rather than just the expert's stated academic qualifications and/or professional roles. Given the increasing focus on evidence-based medicine, some general discussion on levels of evidence also would have been useful for readers.

While this book provides very relevant information for young Australian women with breast cancer, an obvious limitation is its focus on the US health system. While containing some useful generic information, the workplace chapters strong focus on US workplace legislative and appeal processes also makes it less relevant to the Australian reader.

Finally, the book is long (300 pages) and would have benefited from more rigorous editing and some illustrations.

Inspite of these limitations, this book is a useful addition to the resources for young women with breast cancer and others. While relevant at any time, it may be particularly helpful when early treatment is completed and women have time to make sense of their experiences and to explore the implications of breast cancer and its treatment on their future lives.

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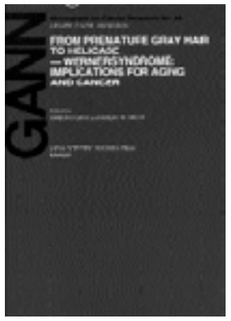
From premature gray hair to helicase – Werner syndrome: implications for aging and cancer

Gann Monograph on Cancer Research No 49

M Goto and RW Miller (eds)

Published by by Japan Scientific Societies Press and S Karger AG, Basel (2001)
ISBN: 3-8055-7158-5. 165 pages plus index.
RRP: US$243.50



In the history of biological research, and of medicine, a grand recurring theme is that the study of mutants has provided many major insights. The ramifications of mutations in the WRN gene, which are responsible for most cases of Werner syndrome, include the early onset of age-related diseases such as atherosclerosis, osteoporosis, cataracts, type II diabetes mellitus and cancers. Therefore many diseases that have a major impact in Western countries can potentially be illuminated by a study of this uncommon autosomal recessive condition.

Werner syndrome itself has an interesting history. It was described in 1904 by a German medical student, Otto Werner. The disease occurs most frequently in Japan, where two WRN mutations account for the majority of cases. The most common of these is thought to have arisen in a member of a Samurai clan. Japanese clinicians have assembled large and informative case series. A landmark paper on the clinical features, co-authored by George Martin who is a contributor to this book, was published in 1966. The WRN gene was identified by a group led by Gerry Schellenberg in Seattle in 1996. From the viewpoint of understanding the molecular details of Werner syndrome, however, this was just the beginning of the story.

The gene was found entirely on the basis of the knowledge of its approximate position on the long arm of chromosome 8 (ie by positional cloning), without any knowledge of its function. When the gene was identified, the function did not suddenly become clear. Some features of the encoded protein provided a clue, however, that it is almost certainly involved in normal processing of DNA, which underscores the importance of DNA damage in ageing and in cancer.

At 165 pages, this is not an excessively thick book, but it is a fairly comprehensive summary of knowledge about Werner syndrome. The 16 chapters of this book on Werner syndrome have a broad scope. There are two main sections, the first of which contains a brief history of research on this syndrome, and chapters on epidemiology, pathology, and clinical manifestations, with particular emphasis on features of premature ageing, dermatological features, atherosclerosis, nervous system disorders, and cancer (especially thyroid carcinoma and osteosarcoma). There is not a separate chapter on the ocular manifestations, although Werner discovered the syndrome while on rotation in an ophthalmology clinic. The second section contains chapters on cellular and molecular studies of Werner syndrome.

Appropriately, the chapters on epidemiology, clinical features and pathology mostly have Japanese authors. In addition to his contributions to other chapters, Makoto Goto, a Tokyo rheumatologist who has worked extensively on case collection and clinical studies, has written a chapter that puts Werner syndrome in the context of other premature ageing syndromes. The link between the clinical section of the book and the section on cellular and molecular changes is provided by Ray Monnat's thoughtful chapter which speculates on possible ways in which the WRN mutation may lead to the clinical manifestations, especially cancer. There are chapters on the chromosomal changes, the cellular phenotype, and on the function of the WRN protein. There is a chapter on WRN homologues in nonhuman systems, including yeast and even bacteria. The class of proteins to which WRN belongs is in fact named after a bacterial enzyme, RecQ, that is involved in unwinding helical DNA. As an aside, it is pertinent to note here that Werner made the remarkably insightful observation that the syndrome he described was most similar to one published by Rothmund in 1868, the features of which include proneness to osteosarcoma. Ninety-five years later, Yasuhiro Furuichi and colleagues found that a subset of Rothmund-Thomson cases have a mutation in another RecQ helicase gene.

The chapters have been thoroughly edited, so that they have a fairly uniform style and are all easy to read. This has not stymied the appropriate expression of various viewpoints by different authors. The reader will readily pick up differences of opinion, for example, regarding the extent to which this syndrome can be used as a model for normal ageing.

I must confess to a partiality to the WRN gene. My laboratory group was involved very peripherally in the race to clone it, and we have an ongoing interest in investigating its functions. The reader may therefore wish to discount some of my enthusiasm for this book, but I think that there is something for everyone here. The richness of its progression from clinical features to emerging molecular details makes it easy to agree with the first sentence of the preface: "If you love the diversity of medicine you should enjoy this book".

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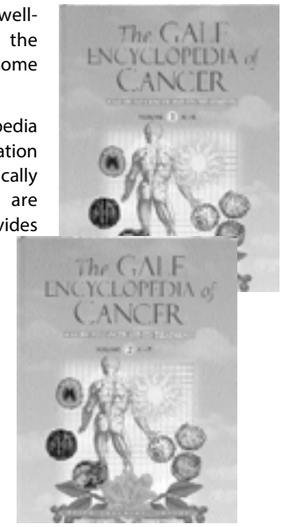
The Gale encyclopedia of cancer: a guide to cancer and its treatments (volumes 1 and 2)

E Thackery

Published by The Gale Group (2002)
ISBN: 0-7876-5609-7. 1,163 pages plus index
RRP: US$285.00

Upon first glancing through the encyclopedia, I presumed that the target audience was nursing or medical students. However, on reading it more closely I notice that it states that it is "for use by anyone touched by cancer". I would think that the reader would have to be well-educated to comprehend the content and be able to face some of the graphic photographs.



Having said that, the encyclopedia is well laid out with information able to be accessed alphabetically by topic. The diagrams are extremely well done. It provides an excellent in-depth coverage of specific cancer types, diagnostic procedures, treatments, cancer side effects and cancer drugs. A comprehensive general index and cross-referencing enables ease of use. I especially liked the "key terms" box and the "questions to ask your doctor". The information about drugs is especially useful as I know that patients often call to enquire about the drugs they are being treated with.

Once the shock of diagnoses has been absorbed, people affected by cancer and their families often have a terrific need for information. The encyclopedia would give the person affected by cancer a good background resource of information to take along to their doctor to discuss their specific type of cancer and treatment.

I think this would be an excellent resource for cancer information services and hospital drop-in centers and I am sure that it would be regularly checked out of libraries. The resources listed are all North American, but the information about cancer and all related clinical treatment issues is excellent.

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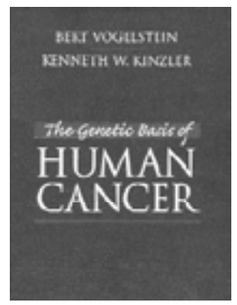
The genetic basis of human cancer

B Vogelstein and KW Kinzler (eds)

Published by McGraw Hill
ISBN: 0-0713- 7050-0. 802 pages plus index.
RRP: US$125.00



This book represents a comprehensive resource text on the genes that cause cancer. It was originally designed as an addition to the textbook Metabolic and molecular bases of inherited disease and in fact 42 of the 52 chapters have been adapted from the 8th edition of that text.

The Vogelstein book is organised into four distinct sections. The first eight chapters provide a detailed explanation of the basic concepts of cancer genetics. Included in these chapters are sections on the nomenclature of gene mutations and chromosomal alterations. This information would be of particular value to clinicians and counsellors who

are in receipt of technical mutation reports from specialised laboratories. Chapters nine to 12 are devoted to the cell cycle, apoptosis, oncogenes and tumour suppressor genes.

The third set of chapters (13-39) deal with the familial cancer syndromes under the subsections of defects in caretakers and gatekeepers. These chapters are a delight to read. They cover the clinical and pathological manifestations of each familial cancer syndrome as well as the genetic basis of the disease. The real strength of these chapters lies in the succinct descriptions of the gene discovery process, the key sites of mutations and the link between mutation and disease. These chapters would be an ideal resource for those individuals seeking to gain a deeper insight into the genetic basis of a particular disease. They are not designed to provide comprehensive or practical clinical management guidelines.

The final chapters (40-52) discuss a number of common malignancies in which predisposing mutations may have a role. The focus here is naturally on somatic mutations however the information is once again of the highest quality. My only criticism of this book is that many of the diagrams and photographs have been poorly reproduced and there are no colour illustrations. It is, however, a beautiful resource book and should be in the library of all clinical and research cancer departments.

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Genetic toxicology and cancer risk assessment

WN Choy (ed)

Published by Marcel Dekker (2001)
ISBN: 0-8247-0294-8. 371 pages plus index.
RRP: US$150.00

This short and concise text offers the reader an authoritative, practical insight to the status of genetic toxicology testing in industry. It deals with accepted protocols and controversial issues. Both these aspects are discussed in the context of current basic research, allowing the reader to surmise the potential resolution of some of these controversies.

The introductory paragraphs summarise the molecular events underpinning human cancer genetics, the major types of genetic toxicity tests in use at this time and provide a broad classification of mechanisms of carcinogenesis. The historical classification of carcinogenic mechanisms is rapidly becoming outdated: genotoxic mechanisms (the initial perturbation results in a genetic change or mutation) versus nongenotoxic mechanisms (the first change affects an epigenetic mechanism, altering gene expression which may lead to secondary genetic changes and effects such as increased cell growth – there is no DNA sequence change as the first step). For example, the epigenetic process of DNA methylation (hypo- and perhaps hypermethylation), previously considered to be a nongenotoxic process, has direct effects on genetic events such as imprinting and mismatch repair of point mutations. This is of practical relevance because to date, chemicals considered to be nongenotoxic are assumed to have a threshold effect (that is, for there potentially to be a "safe" lower dose) compared with genotoxic carcinogens, for which no safe dose is assumed (ie a linear dose-response curve, although accurate data is not available in most contexts).

A detailed explanation of structure-activity relationship is provided, as this process (computer-assisted) is required for prioritisation of new or existing chemicals when their use in industry is being considered, prior to the initiation of in vitro tests or expensive, time-consuming rodent models. This is followed by a discussion of the way in which the genetic toxicology tests are utilised: bacterial mutagenicity tests and mammalian tests, such as the in vitro mouse lymphoma cell assay for genetic mutation, in vitro or in vivo chromosome aberration (a required test, performed by metaphase spread) and newer in vivo tests such as the micronucleus test (for example, performed on peripheral blood of rodents which have undergone the relevant exposure). The latter test is an interesting recent advance for analysis of dividing cells as it directly demonstrates the loss of chromatin: a small separate nucleus from the main nucleus forms during telophase when the nuclear envelope is reconstituted (structural damage to a chromosome will lead to an acentric chromosomal fragment(s) or damage to the spindle apparatus will lead to loss of a whole chromosome(s)). By definition, the changes observed have been passed on through a cell division, ie inherited by the daughter cell (in contrast to information from metaphase spreads from cells which have not yet undergone a cell division). This is a simple process that requires only a small amount of biological material and can be automated.

The guidelines from the relevant international bodies are clarified in terms of context and process. A recent move away from requiring in vivo animal testing for chemicals identified as being produced in high volume and for which there is likely significant human exposure is discussed. The in vitro micronucleus test may well become established in this context, presumably leading the way for other areas of genotoxicity assessment to adopt a similar approach.

The difficulties of discerning the basis of a carcinogen dose-response curve and its dependency on both chronicity of exposure and individual susceptibility is detailed. Molecular biomarkers and epidemiological evaluation of individual susceptibility are discussed and these presumably will become of increasing importance as genomic tools such as SNPs and HAPMAPs allow us to better understand the genetic basis of individual susceptibility and the identification of specific at-risk groups.

This book provides an excellent generic understanding of the relevant issues involved in genetic toxicology and subsequent cancer risk assessment using specific examples in an illustrative way, rather than also being a source of information regarding individual chemicals. It has a lot to teach us, both in terms of critical analysis of research data and extrapolation of that data into our daily thinking about the basis of cancer risk assessment.

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Health communication: cancer communication and aging (Vol 15, No 2)

L Sparks (ed)

Published by Lawrence Erlbaum Associates Publishers (2003)
ISSN: 1041-0236. 253 pages.
RRP: US$25.00

The preface to this issue of Health Communication sets the scene well: Cancer communication and ageing is an important area of health care that is generally under-researched. The articles in this book encompass a variety of aspects of communication in the context of cancer and ageing, from diagnosis and treatment to palliation. In this context, the articles focus on different aspects of communication research including models of communication and change, the relationship between communication and culture, social relationships, identity, technology, and importantly, communication with healthcare professionals.

The articles in this book vary in their approach, some focus on theoretical models that have utility as explanatory frameworks, others present quantitative research into aspects of communication in the cancer/ageing context, some utilise a qualitative orientation to explore the experiential nature of cancer across the care continuum. An important theme is the effect of communication issues in cancer on the intrapersonal, social, cultural, systemic and organisational health-related outcomes.

This book contains a collection of articles that is interesting, in part, because of the diversity of perspectives. On the whole these articles are well written and presented. Overall the reader may find a useful collection of articles, which are intended to provide a resource for those interested in increasing their knowledge or pursuing research in this field.

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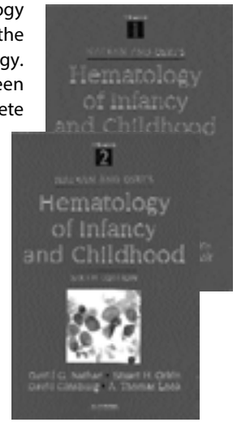
Hematology of infancy and childhood (6th edition)

DG Nathan, SH Orkin et al

Published by Saunders (2003)
Distributed in Australia by Elsevier
ISBN: 0-7216-9317-2. 1,864 pages plus index.
RRP: A$708.40



This is the sixth edition of Hematology of infancy and childhood – to most, the key text in paediatric haematology. The previous editions have been heavy in weight, but very complete in context, and have presented conditions/diseases based around current biological information and pathophysiology. This approach has been maintained in the sixth edition.

The textbook is divided into two volumes, making handling easier. The first volume focuses on neonatal haematology, bone marrow failure syndromes, disorders of red cell production, haemolytic anaemia, disorders of haemoglobin and the phagocyte system. The first chapter on the historical perspective of paediatric haematology is an excellent means of introducing the text.

For the purpose of this review, I have been asked to focus on the oncology component of the text, which has changed markedly from the previous editions. Previous editions have included specific chapters on the epidemiology, molecular biology and chromosomal abnormalities in childhood cancer. Additionally principles of paediatric radiation therapy and management of malignant solid tumours were included. The editors of the sixth edition, in particular Thomas Look, have "totally reconstructed" the section on oncology. As this is essentially a textbook on haematological conditions, the chapters specific to solid tumours, radiation therapy have been omitted. The section on oncology, now appropriately, is devoted to haematological malignances. The authors comprehensively cover epidemiology including prenatal origins of ALL and current controversies, chromosomal abnormalities with discussion on newer methods for identification; and the leukaemias and approaches to treatment, incorporating a chapter on the pharmacology of antineoplastic agents and multidrug resistance. Lymphoma, lymphadenopathy and lymphohistiocytic disorders also are covered. Importantly the molecular basis of haematological malignancy is covered in a chapter which clearly describes, with the use of excellent figures, the complicated intracellular signaling and transduction pathways. This chapter also describes current technological approaches, which is very useful for the clinician. Assessment of MRD also is described clearly by the author. Also of relevance to the oncologist is the complete chapter on acquired disorders of haemostasis.

In summary, this text is the key reference for paediatric haematologists. The information is clearly and very comprehensively presented and is current. The figures, diagrams, illustrations and photomicrographs are excellent. The loss of chapters on solid tumours and management mean that those training in paediatric haematology will need to source other texts for reference, but the information on haematological malignancy is very complete. This text remains an essential for the library of the paediatric haematologist/oncologist.

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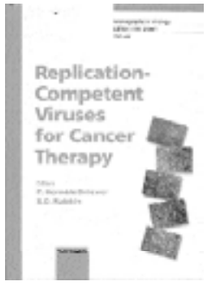
Monographs in virology: replication-competent viruses for cancer therapy (volume 22)

P Hernaiz Driever and SD Rabkin (eds)

Published by Karger (2001)
ISBN: 3-8055-7248-4. 182 pages plus index.
RRP: US$148.00

Cancer is primarily a disease arising from random damage to the genes of some somatic cells that confers to them a growth advantage over other cells in the body. In this context, one of the major challenges in the evolution of higher organisms from unicellular bacteria is the need to rapidly distinguish from the healthy cells those cells in a multicellular organism that sustain somatic DNA changes that radically alter the growth properties of the cells. Such cells must then be eliminated in a timely fashion, so as not to endanger the existence of

the whole organism. The increasing understanding of the mechanisms of apoptosis is indeed gradually revealing the intricate mechanisms that link the process of apoptosis to DNA damage and the mechanisms of DNA replication, DNA repair and cellular growth. Conversely, each case of cancer testifies on how often these mechanisms of molecular surveillance fail, with disastrous consequences for the individual patient.



An interesting question to consider in this process is how viruses of higher organisms may modify the mechanisms of DNA replication, DNA repair and apoptosis and to what extent the evolution of these viruses could have been shaped by the needs of the host to eliminate damaged cells. Could the mechanisms of bacteriophage excision from the bacterial chromosome when the latter sustains double strand breaks have a correlate in eukaryotic cells? Could the rapid production of many linear molecules of viral DNA in a eukaryotic cell serve a role in testing the ability of the cell to repair double strand breaks in its chromosomal DNA? Or conversely, could some of the common human viruses serve a positive role in the identification and killing of those cells in the body whose DNA repair mechanisms fail and become permissive for uncontrolled viral replication?

Viewed in this context, it seems quite likely that natural selection may have already endowed some human viruses with properties that may be useful for the identification and killing of damaged cells in various tissues before they can give rise to cancer. Furthermore, a specific type of cancer that may escape the endogenous molecular surveillance mechanisms that may exist in a certain cell type still may be susceptible to killing with some viruses. However, the balance between good and harm with many wild-type viruses may often be too close to allow useful clinical application. Genetic engineering of such viruses may be necessary before they can be employed usefully for cancer therapy.

The book by Driever and Rabkin reviews practical progress in the use of a number of replication-competent viruses for cancer therapy. Separate chapters review the use of herpes simplex virus, adenovirus, reovirus, parvoviruses, vaccinia virus and Newcastle disease virus. Efforts to genetically engineer wild-type viruses to reduce their potential for harm are described, in parallel with efforts to endow such recombinant viruses with novel strategies for cancer cell killing. Progress in such studies has been slowed down by the limited ability to perform genetic engineering in eukaryotic cells, a situation that is rapidly changing as more and more large viruses are cloned as bacterial artificial chromosomes. Techniques recently developed for the precise genetic engineering of large genomic DNA fragments in bacterial artificial chromosomes are being used to remove undesirable genes from the genomes of large human viruses, while endowing them with new genes targeted to limit tumour growth.

This book fails to place such efforts in the context of a theoretical framework that argues in favour of the cautious use of common viruses for cancer therapy. Similarly, although the potential for harm through unwanted virus/host interactions receives ample consideration in the book, there is no consideration of any possible interactions between attenuated viruses that may be useful for cancer therapy and other endogenous viruses that may be co-infecting the same cells. This is indeed a serious omission in the midst of the HIV pandemic, given the high propensity of this virus to integrate and the low sequence specificity of its integration mechanism. The last thing anybody would want to do in the struggle against cancer is to provide HIV with a novel mechanism of transmission by integration of its genome into a large human virus of reduced pathogenicity.

Although this book is restricted in scope, it should be useful not only to the specialists that may be interested in the field of cancer therapy with replication-competent viruses, but for all those seeking novel approaches to cancer therapy by exploiting the natural defence mechanisms against cancer cells.

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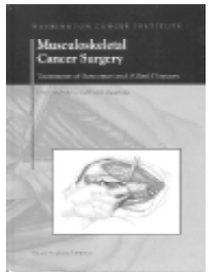
Musculoskeletal cancer surgery: treatment of sarcomas and allied diseases

MM Malawer and PH Sugarbaker

Published by Kluwer (2001)
ISBN: 0-7923-6394-9. 608 pages plus index.
RRP: US$199.00

This surgical text is a delight to the eye and difficult to put down. It is authored by two leading and well-established experts in this field with additional contributors from both the US and Israel.



There is a consistency of presentation throughout this text which is well laid out and certainly easy to read. The illustrations by Joyce Hurwitz are a highlight. The reproductions of both the imaging, and clinical and operative photographs, are also of the highest quality.

The first section covers the more routine fundamentals regarding sarcomas, and stresses particularly the increasing role of chemotherapy and radiation therapy in the management of these problems. It goes further however by discussing isolated limb perfusion (as opposed to limb infusion, more often practised in Australia) as well as an entire chapter devoted to the correct approach to the biopsy of these tumours. There is a very succinct and appropriate chapter on the surgical management of metastatic bone disease.

The majority of the book is then given over to various aspects of surgery, divided into three sections: muscle group resections, limb-sparing surgery and amputations. In each instance the various chapters are opened with an overview, reference to the unique anatomic considerations of the region or site, a discussion of the relevant preoperative imaging and then a set of surgical guidelines with discussion of the various surgical manoeuvres. The text is supported by, and indeed at times is secondary to, the beautiful illustrations and clinical photography used to highlight the author's objectives. The information, particularly regarding the history, development, availability and applications of prostheses in this type of surgery, is certainly the most complete account that I have seen. This section also includes excellent chapters on phantom limb pain, anaesthetics and pain management for such large resection cases and also a discussion of the principles of rehabilitation without excessive detail.

This text is an excellent and perfect reference for any surgical department but in particular for those where oncology has a high profile. It would make excellent reading for any general or orthopaedic registrar and similarly would be an appropriate addition to the library of any individual orthopaedic surgeon or surgical oncologist.

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Novel anticancer drug protocols

JK Buolamwini and AA Adjei (eds)

Published by Humana Press (2003)
ISBN: 0-8690-3963-3. 342 pages plus index.
RRP: A$125.00

I thought this book was full of new chemotherapy recipes, but it contains recipes of another kind. It is an eclectic collection of methods for the laboratory assessment of anticancer drugs: protocols for measurement (mostly) of intermediate endpoints of drug effects or "biomarkers". It covers a broad gamut: antiangiogenesis; pharmacogenetics; signal transuction; microarrays; PET scanning; and flow cytometry among others. It is not clear why some methods were chosen, for example measurement of tumour DNA in plasma, and not others. A good method is certainly worth its weight in gold. A practical setting out of instructions (in "recipe" format) often contains information, that cannot be extracted from the methods section. The utility of this book is limited by the impossibility of a comprehensive coverage (all novel protocols), and the availability of standard protocols via other medium, especially the internet. What this book needs is a Jamie Oliver or a Nigella Lawson (depending on your sexual preference) to add some excitement and perspective. The introductory chapter outlining the range of possible targets and some inhibitors attempted to explain a large number of complex pathways and didn't even have any pictures!

One useful thing a book like this could do is to provide a perspective about the use of competing techniques in preclinical models. This was done well in the chapter on single nucleotide polymorphisms and quite poorly in most others. Despite the uneven chapters and the criticisms above, I quite enjoyed this book. It is fun to flip through recipes you are never going to cook, and it does give you an idea of what is possible. This is perhaps the only real usefulness of a book like this. If you are really interested in angiogenesis methods, you will want a more focused volume. If you are interested in drug-development more generally, you will probably want more perspective. The field of biomarkers for drug effects faces enormous challenges. No doubt there are lessons to be learned from methods, which are technically possible, but turn out to be unhelpful. There are also lessons from drugs that have "failed" clinically despite effective biomarkers or because of lack of them. Inhibition of EGFR, PKC-a and matrix metalloproteinases spring to mind in this regard. This book doesn't take on board any of these lessons (with the chapter on PET a possible exception). I would pocket the $125 and eat out at a good restaurant instead.

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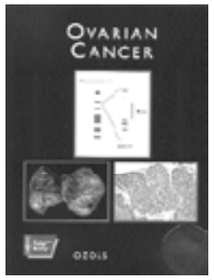
Ovarian cancer

R Ozols

Published by BC Decker (2003)
ISBN: 1-5500-9096-8. 237 pages plus index.
RRP: A$306.06

This book is part of the "Atlas of Clinical Oncology" series, edited by Dr Robert Ozols of Fox Chase Cancer Centre, with contributors mainly from that centre or from the National Cancer Institute Spore program. It is obvious from the start that the contributors are all at the cutting edge of their speciality. The book covers every facet of ovarian malignancy including germ cell tumours and ovarian sex cord stromal tumours, has magnificent illustrations, is sequentially and logically laid out and is accompanied by a CD, which is especially useful for those of us who like to use illustrations from state-of-the-art publications.



Perhaps the strength of this book lies in its basic biological contributions, and in particular the chapters on biology, genetics, developmental chemotherapy and advances in biological therapy and high-dose chemotherapy are all extremely interesting and contain information not readily accessible from other sources.

This is a book for the post-graduate. It will be of use particularly for the gynaecological oncologist and the medical oncologist caring for women with this malignancy and for those working in family cancer clinics, given the excellent chapters on genetics and genetic counselling.

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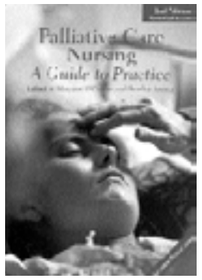
Palliative care nursing: a guide to practice (2nd edition)

M O'Connor and S Aranda (eds)

Published by Ausmed Publications (2003)
ISBN: 0-9577-9884-9. 377 pages plus index.
RRP: A$65.95

The goal of the first edition of this book, according to the editors, was to make palliative care accessible to nurses in all health care settings. This second edition has been completely revised and rewritten and achieves continuing relevance to nurses, in all settings, who require information about palliative care. The book presents palliative care as a "continuum of practice from a generalised approach to a specialist discipline". The editors and the authors of other chapters in the book write with acknowledged expertise in the subject areas.

The book is divided into 24 chapters and the content centres



on contemporary practice issues in palliative care nursing. There is a focus on clinical issues faced by nurses caring for dying people. The topics covered provide the capacity for nurses and other readers of the book to think about the depth and breadth of issues that are involved in palliative care that is described as "holistic, expert and interdisciplinary". The scope of the contents of this book ranges from evidence-based practice in palliative care, psychological and existential distress, sexuality and body image to nutrition and hydration, occupational stress, frameworks for detailed and continuous assessment, and palliative care for people other than those with malignancy. The book chapters are clearly set out and are discrete, making it easy to access relevant chapters.

So often issues around staff stress for those working with people who are dying are positioned at the end of publications or education sessions. It is interesting to note that in this book the chapter about occupational stress is in the first section. Similarly, knowledge related to care of the spirit is often relegated to less prominent positions than information about other symptom management. Again, the positioning of the chapter on spirituality at the beginning of this book is noteworthy.

The problems that often cause the most discomfort for the people experiencing them, such as breathlessness, fatigue and constipation, are important inclusions in the book. The psychosocial aspects of palliative care often present challenges for health care providers, particularly those working in areas where the dominant culture is framed by technical and biomedical paradigms. Inclusion of chapters about sexuality and body image, and psychological and existential distress, among others, add a vital dimension.

This is a book that will enhance readers' understanding of care and support for people (and their families, friends and carers) at the end of life. It provides accessible comprehensive evidence-based guidelines for practitioners. The dedication at the start of the book to the memory of a daughter by a mother is essential. This dedication ensures the voice of the patient and the people who mean most to them is at the forefront. This is the essence of excellent palliative care.

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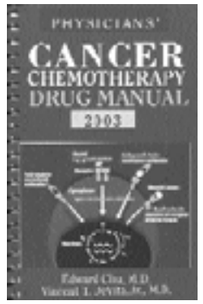
Physicians' Cancer Chemotherapy Drug Manual 2003

E Chu and V DeVita

Published by Blackwell Publishing Asia (2002).
ISBN: 0-7637-2131-X. 506 pages plus index.
RRP: A$151.80

Vincent DeVita and Edward Chu are two well-known US oncologists with distinguished academic and research records. In writing this handbook they have successfully created an invaluable resource for any professional involved in the prescription or delivery of cytotoxics.

The book is presented in bullet form, except the first chapter, which is a brief overview on the principles of chemotherapy, which is very similar to their larger publication, Principles and Practice of Oncology.



The drugs are listed in alphabetical order and are described using a number of subheadings including the mechanism of action and resistance, basic pharmacokinetic information, indications, interactions and toxicity. Although this information is presented in note form, it is still extremely comprehensive, particularly information with regards to drug interactions.

The following chapter is really a collection of tables. The first few tables cover basic formulas like creatinine clearance, area under the curve and body surface area. What follows though are some invaluable tables on dosing according to impaired renal or hepatic function. There is also a table that evaluates whether certain cytotoxics are cleared by either peritoneal or haemodialysis.

There is then a section entirely devoted to lists of tumour types and the currently used treatment regimens, which may be useful to those unfamiliar with standard treatments. These regimens are all appropriately referenced and serve mainly as a guide to treatment. Finally there are lists of antiemetic agents presented in a similar manner to the information on cytotoxics.

The book itself is well-presented in a ring binder form allowing quick access to drug information. It also comes with a free CD-ROM. What would have been useful are links to a website so that articles referenced could be studied in more detail. Furthermore, there is no link to a website where more up-to-date information could be accessed. So while this book is easy to use and comprehensive, like all books of this kind, certain information such as current chemotherapy regimens used will become less up-to-date with time.

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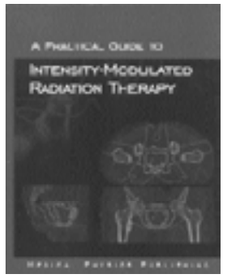
Royal Prince Alfred Hospital
Camperdown, NSW

Practical Guide to Intensity Modulated Radiation Therapy

S Hellman

Published by Medical Physics Publishing (2003)
ISBN: 1-9305-2413-7. 406 pages plus index.
RRP: US$125.00



This textbook is a comprehensive guide to all aspects of intensity modulated radiation therapy (IMRT). The initial chapters deal with medical physics aspects after an initial chapter on imaging, including image fusion and an overview of the IMRT process. During the chapters on optimisation, delivery, computer algorithms and treatment planning, there is significant detail that is beyond the need for a clinician but would provide a very useful departmental primer. In the second half of the book there are clinical chapters in the areas of IMRT for prostate cancer, head and neck cancer, paediatric, breast and non-small cell lung cancers..

In pouring through the first 190 pages, I was waiting for information that would help me to make a decision regarding the clinical applicability of IMRT and the process involved from seeing a patient to delivery of an optimised plan. It is in these later chapters that this is dealt with very well.

There is an excellent reference chapter on normal tissue complication probability (NTCP) and tumour control probability (TCP). The book closes with two chapters on advanced treatments addressing areas of future development, including the integration of respiratory gating and stereotactic immobilisation with IMRT.

The staff of the Memorial Sloan-Kettering Cancer Centre's, Department of Medical Physics wrote this book. This emphasises that although the book is a valuable departmental resource, it would only suit individual radiation oncologists and registrars wishing to extend their current knowledge.

I would thoroughly recommend departments purchase a copy for their library. Clinicians, however, should take caution over the first 190 pages if seeking relaxing reading prior to bedtime.

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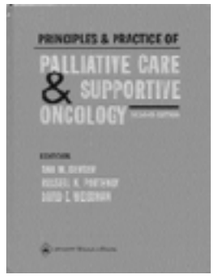
Principles and Practice of Palliative and Supportive Oncology

A Berger et al (eds)

Published by Lippincott Williams and Wilkins (2002)
ISBN: 0-7817-3324-3. 1,140 pages plus index.
RRP: A$402.60



There are excellent texts available in anti-cancer therapies and in palliative care. For the oncology patient, this text by Berger and her colleagues provides an important contribution to bridge the two. A book that deals with such a broad remit – people with cancer who will be cured, live with the disease over extended periods of time or die as a result of the disease – will always pose a challenge for the editors. This team has balanced this well.

As supportive care gains evidence and a defined role in practice, the need for a definitive text in the area is obvious. This book is such a text. Beyond oncology, there are some chapters on HIV/AIDS, paediatrics and intensive care. Although interesting, they are brief and not oncology-focused.

The list of contributors is strong and includes many people whose research expertise is reflected in their chapters. There is a good mix of people working in acute oncology, supportive care and palliation. However, contributions are almost entirely from the US and, in an area where the clinical encounter so often needs to be interdisciplinary, mostly from medical practitioners. One unfortunate consequence of this is the recurring theme of affordable access to health care. Sections on models of health service delivery are not be easily generalised to the Australian context.

There is the continuing challenge of how to reflect the best evidence base for practice. The text does not easily identify high-quality evidence for interventions from anecdote or case series in the body of the work. Although the references help in this process, this omission detracts from the wealth of evidence presented.

Although areas such as the impact of cancer and its treatment on sexuality and intimacy are generating new and important evidence, this area is presented in a very biomedical paradigm. Survivorship and its consequences are well presented. Issues of effective communication between patients and health professionals are dealt with in a very practical chapter.

If there were one new reference text for your bookshelf this year, would this be it? It should be. It complements rather than competes with texts such as the Oxford Textbook of Palliative Care and standard oncology texts. Certainly, your library should have a copy.

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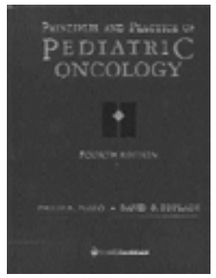
Principles and Practice of Pediatric Oncology (4th Edition)

PA Pizzo and DG Poplack (eds)

Published by Lippincott Williams and Wilkins (2002)
ISBN: 0-7817-2658-1. 1,628 pages plus index.
RRP: A$605.00



For many years in the field of paediatric oncology there was a relative dearth of reference books compared with that available to our adult medical oncology colleagues. In the late 1980s the first edition of Principles and Practice of Pediatric Oncology was published and it quickly became the pre-eminent paediatric oncology resource text. A multidisciplinary team approach has become standard practice for managing paediatric cancer patients and all those involved in this field could turn to this text for detailed information on the majority of disease processes that occur in this patient group. Subsequent editions during the 1990s only served to enhance the reputation of this tome, though the third edition did suffer from several chapters only having minor 'cosmetic' changes to the text.

The eagerly awaited fourth edition however has had major changes to the organisation of both the general sections and chapters. The editors have made the inclusion of up-to-date data on the molecular biology of paediatric malignancies their primary stated goal for this edition. While new advances and discoveries will quickly overtake the information provided, the editors and the contributing authors have succeeded in summarising the explosion in genomic knowledge of paediatric malignancies that has occurred over the past five to 10 years. In particular the basic issues section provides a solid foundation of understanding of core aspects of childhood cancer.

The majority of contributing authors are North American in origin, but the individual disease chapters have in-depth discussions reflecting the global experience of previous

treatment protocols. There are still idiosyncrasies that are simply reflections of differences in approach to particular problems. For example, in the discussion on the management of tumour lysis syndrome, the use of urate oxidase is only briefly mentioned. However, these instances are few, and at worst serve as instigators for debate and consideration.

As in previous editions, the editors have retained the sections and chapters on supportive care, late effects, clinical trials, and psychosocial issues. This reflects the fundamental philosophy of the multidisciplinary team approach to paediatric cancer. It is no longer a question of simply surgery, chemotherapy and radiotherapy. The focus on other inter-related issues has contributed to improving both the quantity and quality of life of our patients. The emphasis on clinical trials throughout the text serves as a timely reminder as to the import of further collaborative work (including multinational studies) to the advancement of our knowledge and understanding.

This text has therefore maintained its status as the most significant single resource in paediatric oncology. There will be criticisms that it is now too large (58 chapters with 1,692 pages) – but to curtail some of the discussions would seriously impact on its ability to provide an overall picture of where we are (and probably just as important – how we got there) with the various diseases. This is a text that should be held in every paediatric oncology unit. It may rarely be read cover to cover but its pages will be flicked through on a daily basis.

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Prostate cancer: a comprehensive guide for patients

J Smith et al

Published by TFM Publishing (2002)
ISBN: 1-9033-7810-9. 106 pages plus index.
RRP: GBP£9.99

This book is written for patients by three urologists and a medical writer. The book comprises 106 pages and consists of 12 chapters. Four appendices conclude the book. The first appendix helpfully summarises the different types of treatment, including the potential for each to cure the disease, side-effects and the positive and negative aspects. As such, the appendix serves as a useful stand-alone item of information.

The book is commendable for being easy to read and for providing an adequate overview of each of the topic areas. Information on test procedures and treatments as well as advice on self-care immediately after treatment would be particularly welcome for patients about to undergo these procedures. The information about tests, treatment, and pain control is especially helpful in demystifying a subject area that can be very confronting and threatening.

The book does not reference its material, however. Therefore, it is unclear upon what evidence the authors base the information (for example, the likelihood of cure and side-effects associated with treatment). Notably, the book does not conform to the standards developed by the Ottawa Health Decision Centre, a centre that specialises in developing patient information and decision-aids. Therefore, my concern is whether the information is based upon the best available evidence and is able to facilitate informed decision-making. Another concern is that the book may be seen to persuade and influence patients' decisions. For example, this statement: "although the final decision about whether or not to undergo surgery is yours, do bear in mind that your doctor probably feels this offers the best chance of curing your prostate cancer and that its benefits are outweighed by the risk of impotence". Such statements may counter the tenet of patient autonomy by suggesting that doctors, and not patients, are better able to make trade-offs between the benefits and risks of treatment.

The diagrams and layout of the book are somewhat bland, giving the appearance of a textbook. While the language is simple to understand, information seeking to reassure men about the effect of prostate cancer on quality of life, psychological aspects and relationships may have been more vividly conveyed by the use of patient testimonials.

Nonetheless, the book represents a good attempt at covering the range of issues about prostate cancer, including its prevention, early detection, diagnosis and treatment. All chapters, except the final chapter on hospice care in the UK are relevant to an international audience. The book would best serve the interests of patients who have already made their decisions; the practical advice on dealing with immediate and long-term effects of treatment and explanations of procedures are especially valuable. However, the book may be less relevant to those men struggling to make treatment decisions after diagnosis.

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Prostate cancer: science and clinical practice

JH Mydlo and CJ Godec (eds)

Published by Academic Press (2003)
Distributed in Australia by Elsevier
ISBN: 0-1228-6981-8. 554 plus index.
RRP: A$300.30

This is an excellent text covering a wide range of topics related to prostate cancer written by experts in their respective fields. It will have broad appeal both to clinicians and researchers while some sections will be suitable for informed consumers wishing to understand some of the controversies such as the screening debate or alternative strategies for the management of the disease. Many chapters have general introductions to a field of study as background before providing more specific information relating to prostate cancer.

There are chapters on tumour biology, aetiological factors, both hereditary and environmental, and epidemiology. The whole spectrum from prevention, which examines aspects of diet and lifestyle as well as medication, and screening through to treatment is covered. Where there are contentious issues, for example population screening, both viewpoints are provided along with accompanying data. The chapters on surgical and radiotherapeutic treatment not only focus on the specific techniques available but compare the merits of each where choices can be made. Hormonal therapy is well-covered as expected, but in addition the section on hormone independent disease and the use of chemotherapy is a comprehensive summary. Several chapters speculate on future systemic treatments from angiogenesis inhibitors to vaccines. A rather novel chapter for this type of text reviews the information on prostate cancer which is available on the internet and although this is a rapidly expanding area, provides a guide to useful resources. Other interesting topics selected for inclusion in the book explore artificial neural networks for prostate cancer modeling, compare breast with prostate cancer and look at prostate cancer when it occurs in conjunction with other cancers. Chapters on the patient experience allow for the exploration of quality of life and sexual aspects of prostate cancer treatment. The only area not covered in any detail is the newer modalities for imaging the prostate.

A feature of many of the chapters is well-drawn illustrations, graphs and photographs that complement the text, and there are several pages of colour prints. The references at the end of each chapter focus on key recent publications.

With the increasing spotlight on men's health and specifically prostate cancer this will be an invaluable source of background information for the many discussions that arise in the diagnosis and management of this disease.

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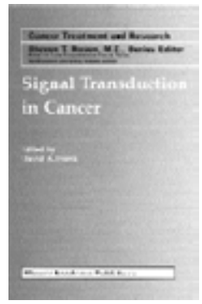
Signal transduction in cancer

DA Frank (ed)

Published by Kluwer Academic Publishers (2002)
ISBN: 1-4020-7340-2. 354 pages plus index.
RRP: US$125.00



This compact volume of short reviews is divided into themes of receptors, intracellular pathways and transcription factors, with two short final chapters covering cell death pathways. The timeframe required to publish books such as this means that most chapters do not include references beyond 2001, although a couple do include 2002 manuscripts. Perhaps acknowledging the rapid pace of change of this field, the book's cost has not been burdened by expensive colour plates and the large number of cartoon diagrams of signalling pathways are all black and white.

The chapters of the book, written by experts and by younger researchers in the field, are not interlinked, therefore the short index where major tumour types and signalling molecules can be cross-referenced is a useful addition. As readers such as the reviewer are likely to be familiar with only a proportion of the subject areas, the number of typographical errors that affect the accuracy of the text is important. In screening the chapter on the steroid hormone receptors, by Shinta Cheng and Steven Balk (Harvard Medical School), several errors where ERb was written as ERa or ER_ were noted. The number of errors identified in this and in other chapters should serve as a caution to students or researchers using the textbook as a principle source for lectures or research.

Although it is not possible to provide critiques on all chapters of the book, it is worth highlighting the different approaches by authors of each of the chapters, which make the book an interesting read. The role of the Rb tumor suppressor in cancer by Lili Yamasaki, begins with a short history of the discovery of the Rb gene, then summarises the basic structure of pRb family members and the upstream regulators and downstream effectors of Rb. A most useful part of the chapter as a resource for scientific learning, is the summary of mutant mouse phenotypes that either involve or have shed light on the function of this pathway.

In contrast, the chapter on the steroid hormone receptors summarises the oestrogen receptor (ER) in breast cancers and the androgen receptor (AR) in prostate cancers as illustrations of the subject area. The chapter briefly covers ER and AR expression in normal and malignant breast and prostate (respectively), receptor structure, transcriptional modulators (activators and repressors) of the receptors and other proteins and pathways that can regulate steroid hormone receptor activation. This in particular ties in well with other chapters of the book that describe these pathways. The chapter ends with short summaries of mutations in ERa and AR in breast and prostate cancers.

While the chapters in this book are necessarily brief, all are extensively referenced and most authors have included historical as well as more recent references. Thus this book is an excellent summary of important signalling pathways in cancer that will be useful for students and researchers. It will serve as a resource for general and specialised knowledge regarding these pathways as well as a platform for more detailed research.

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Recombinant Human Erythropoietin (rhEPO) in clinical Oncology

MR Nowrousian

Published by Springer Medicine (2002)
ISBN: 3-2118-3661-6. 492 pages plus index.
RRP: EUR98

This comprehensive text is an excellent resource and examines the biology of erythropoietin, causes, prevalence and management of cancer-related anaemia with rhEPO. It is well-referenced and has helpful "conclusions/summary" sections at the end of each chapter. It is well-balanced, highlighting areas where rhEPO is currently appropriate while exploring areas where further investigation is required. Unfortunately there is a lack of tables summarising the data and some of the methodological deficiencies of referenced publications are not discussed.

The initial chapters discuss the biology of endogenous erythropoietin. A basic level of erythropoietin pathophysiology is assumed with lack of discussion about mechanisms of renal responses to tissue hypoxia and how that translates to renal erythropoietin production. It would be difficult for those not

familiar with the area as there is a lack of simple diagrams explaining feedback loops, yet there are numerous more advanced illustrations of cell signalling.

Subsequent chapters discuss the mechanisms of anaemia of chronic disease and cancer-related anaemia. A somewhat excessive three chapters are dedicated to radiation therapy and tumour hypoxia. The chapters dedicated to anaemia and its impact on end-organ function and fatigue are valuable and the important inter-relationship between anaemia, fatigue and quality of life (QOL) is appropriately discussed. The text provides an excellent review on the indications of rhEPO for solid tumours and haematological malignancies, although the section on myelodysplasia is a bit thin.

Unfortunately, the text is already somewhat out-of-date with a number of recent publications on QOL and rhEPO not sighted. Furthermore, outdated terms such as NESP (Novel Erythroid Stimulating Factor), rather than darbepoietin are used. This text also was published prior to recent release of the American Society of Haematology/American Society of Clinical Oncology Guidelines on erythropoietin therapy. The text also predates the report of erythropoietin antibodies and consequent pure red cell aplasia (N Engl J Med 2002; 346:469-75), which has had major ramifications as to the risks of rhEPO and route of administration. Indeed, can we continue to administer rhEPO subcutaneously in cancer patients as recommended by the text? The answer is probably yes, but it is a pity that a text such as this does not explore this issue.

Thus, this book is a useful reference text for treating oncologists, haematologists and transfusion medicine specialists, but purchase it soon before it goes any further out-of-date.

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Viruses and liver cancer

E Tabor (ed)

Published by Elsevier (2002)
ISBN: 0-4445-0580-6. 176 pages.
RRP: A$198.27

This book is a relatively slim volume priced at $198.27. It is one of a series entitled Perspectives in Medical Virology.

In 13 chapters this volume covers viral hepatitis and the relationship with liver cancer. In particular there are chapters on hepatitis B, hepatitis C and other viruses as well as discussion about the role of oncagenes and growth factors, tumour suppressor genes and the molecular biology of viral-associated hepatocellular carcinoma. One chapter is devoted to animal hepadnaviruses and their host species. These serve as models for human hepatocarcinogenesis. The final chapters cover prevention with immunisation, the use of interferon and the treatment of hepatocellular carcinoma.

This is a useful book for medical oncologists, gastroenterologists and liver surgeons. The most valuable content relates to the underlying molecular mechanisms and recent insights into the molecular biology and pathogenesis of the disease. The sections on treatment cover little more than 20 pages, so do not provide an exhaustive review of management. There is little more here than can be found in standard oncology textbooks. Consequently this book cannot really be recommended as a useful resource for readers who are seeking detailed information about the management of HCC. Nonetheless, it should prove to be a helpful resource to readers who are interested in understanding the molecular basis of HCC at a more detailed level and for this niche audience, it comes recommended.

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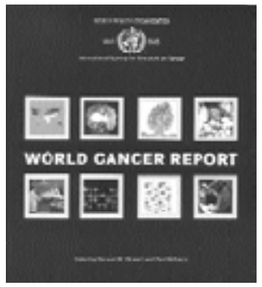
World cancer report

BW Stewart and P Kleihues (eds)

Published by IARC Press (2003)
ISBN: 9-2832-0411-5. 351 pages plus index.
RRP: US$25.00



This is an excellent book. It provides a concise and up-to-date global view of cancer burden, epidemiology, carcinogenesis, prevention, screening, management and cancer control. Seventeen separate chapters detail specific cancer sites.

This formidable collection is the work of 77 contributors, including 26 from IARC or WHO, and no less than 10 Australians. This no doubt reflects the locally persuasive powers of the editors. The contributors were aided by 11 reviewers, so the unity of style and format in a volume of such diverse origins is commendable. The Australian contributors are Frank Alvaro (childhood cancers), Peter Hersey (immunotherapy), Norelle Lickiss (palliative care), Guy Maddern (surgical oncology), Bill McCarthy (melanoma), Murray Norris (minimal residual disease), Roger Reddel (telomerase), Bernie Stewart (no less than three topics: reduction of UV radiation, apoptosis and multi-stage carcinogenesis), Martin Tattersall (cancer education in medical schools) and Graham Young (lymphoma).

The standard of the more than 500 illustrations is extremely high – indeed an electronic version would provide a formidable resource for cancer education. It is to be hoped that WHO will eventually make such a collection available.

Meanwhile the book itself can be purchased through IARC Press at http://www.iarc.fr/WCR/. I commend it as excellent value.

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Calendar of meetings

Calendar of meetings – Australia and New Zealand

Date	Name of Meeting	Place	Secretariat
2003			
November			
15-19	6th International Symposium on Paediatric Pain: "Pain in Childhood: The Big Questions"	Sydney NSW	Dianna Crebbin DC Conferences Pty Ltd PO Box 571 St Leonards NSW 2065 Tel: +61 2 9439 6744 Fax: +61 2 9439 2504 Email: mail@dcconferences.com.au
16-20	9th International Conference on Oral Cancer	Melbourne VIC	ICMS 84 Queensbridge Street Southbank VIC 3006 Tel: +61 3 9682 0244 Fax: +61 3 9682 0288
26-28	30th COSA Annual Scientific Meeting	Perth WA	Ruth Lilian Pharma Events PO Box 265 Annandale NSW 2038 Tel: +61 2 9280 0577 Fax: +61 2 9280 0533 Email: conferences@pharmaevents.com.au
28-29	Sentinel Lymph Node Biopsy and Block Dissection	Perth WA	Dr Robert Davies CTEC University of Western Australia Email: rjdavies@cyllene.uwa.edu.au Web: www.ctec.uwa.edu.au
2004			
March			
4-5	Research to Reality: The 6th National Breast Care Nurses Conference	Brisbane QLD	6th National Breast Care Nurses Conference Conference Manager OzAccom Conference Services PO Box 164 Fortitude Valley QLD 4006 Tel: + 61 7 3854 1611 Fax: +61 7 3854 1507 Email: breast2004@ozaccom.com.au Web: www.breastcarenurses2004.com
April			
26-30	18th World Conference on Health Promotion and Health Education	Melbourne VIC	Conference Manager 15 Pelham Street Carlton VIC 3053 Tel: + 61 3 9667 1313 Fax: +61 3 9667 1375 Email: enquiries@Health2004.com.au Web: www.Health2004.com.au
May			
18-21	Australasian College of Dermatologists Annual Scientific Meeting	Brisbane QLD	Australasian College of Dermatologists 136 Pittwater Road Gladesville NSW 2111 Fax: +61 2 9816 1174
August			
4-7	Medical Oncology Group Australia Faculty Radiation Oncology	Cairns QLD	MOGA/FRO Pharma Events Email: conferences@pharmaevents.com.au
8-12	International Society for Nurses in Cancer Care 13th International Conference on Cancer Nursing	Sydney NSW	MP Events Tel: +61 3 9418 3930 Email: kirsten@mpevents.com.au www.isncc.org
8-14	Australia & Asia Pacific Clinical Oncology Research Development (ACORD) Workshop	Palm Cove QLD	Medical Oncology Group of Australia Level 6, 52 Phillip Street Sydney NSW 2000 Tel: +61 2 8247 6207 Email: fmarine@bigpond.com or mog@racp.edu.au
November			
10-14	Leura V International Breast Cancer Conference	Sydney NSW	Leura V Conference Managers Tour Hosts Conference & Exhibition Organisers Level 4, 66 King Street Sydney NSW 2000 Tel: +61 2 9248 0800 Fax: +61 2 9248 0894 Web: www.bci.org.au/leura
21-26	Australian Health and Medical Research Congress	Sydney NSW	The Australian Society for Medical Research 145 Macquarie Street Sydney NSW 2000 Tel: +61 2 9256 5450 Fax: +61 2 9252 0294 Email: asmr@world.net Web: www.asmr.org.au
24-26	31st COSA Annual Scientific Meeting	Canberra ACT	Clinical Oncological Society of Australia GPO Box 4708 Sydney NSW 2001 Ph: +61 2 9036 3100 Fax: +61 2 9036 3101 Email: cosa@cancer.org.au

CALENDAR Of MEETINGS – International

Date	Name of Meeting	Place	Secretariat
2003			
November			
2-7	XVI FIGO World Congress of Gynecology and Obstetrics	Santiago de Chile Chile	International Federation of Gynecological Oncologists London, United Kingdom Fax: +44(0) 207 935 0736 Email: figo@figo.org Website: www.figo.org/figo2003.asp
9-14	Evidence-Based Radiation Oncology: Methodological Basis and Clinical Application	Lisbon Portugal	ESTRO Office Brussels, Belgium Fax: +322 779 5494 Email: info@estro.be Website: www.estro.be
19-21	10th Hong Kong International Cancer Congress	Pokfulam Hong Kong	10th HKICC Congress Secretariat Department of Surgery University of Hong Kong Medical Centre Queen Mary Hospital Hong Kong Tel: +852 2818 0232 Fax: +852 2818 1186 Email: mededcon@hku.hk Website: www.hkicc.org
December			
3-6	26th Annual San Antonio Breast Cancer Symposium	San Antonio Texas USA	Cancer Therapy & Research Center SACI, Rich Markow San Antonio, Texas, USA Fax: +1210 949 5009 Email: Rmarkow@saci.org Website: www.sabcs.org
2004			
January			
15-16	New Insights in Molecular Diagnosis and Therapy	Paris France	Institue Pasteur Euro-Conferences C.I.S. 28, rue du Docteur Roux 75724 Paris Cedex 15, France Fax: +33 1 40 61 30 25 Email: euroconf@pasteur.fr
22-24	Gastrointestinal Cancers Symposium	San Francisco California	USA ASCO 1900 Duke Street Suite 200 Alexandria, Virginia 22314 USA Tel: +17 0 3299 0150 Web: www.asco.org
25-28	Multimodality Treatment in Malignancies Congress	Thessaloniki Greece	Nectaria Passarivakis Hazlis and Rivas 24 Raedestou Street GR 171 22 Nea Smyrni Athens, Greece Tel: +30 210 94 08 750 Fax: +30 210 94 08 753
26-28	40th Annual Meeting of the Society of Thoracic Surgeons	San Antonio Texas USA	Society of Thoracic Surgeons Chicago, Illinois, USA Fax: +1312 527 6635 Email: sts@sba.com
29 Jan- 1 Feb	American Psychosocial Oncology Society 1st Annual Conference Orlando	Florida USA	Alison Holcomb American Psychosocial Oncology Society 2365 Hunters Way Charlottesville - Virginia Tel: +1 434 293 5350 Fax: +1 434 977 0899 Web: www.apos-society.org/
February			
9-12	15th International Congress on Anti-Cancer Treatment	Paris France	Travel Congress Organisation 1 rue de Berri Paris - 75008 - France Tel: +33 (0)1 42 94 8732 Fax: +33 (0)1 42 94 8733 Web: www.icact.com/
15-17	2nd Multidisciplinary Colorectal Cancer Congress	Noordwijk Netherlands	Congress Care PO Box 440 5201 AK's-Hertogenbosh Netherlands Tel: +31 7 3683 1238 Email: info@congresscare.com Web: www.colorectal2004.org
March			
7-11	3rd World Assembly on Tobacco Counters Health	New Delhi India	Avnish Varma ICOOC M-38-A RAJOURI GARDEN NEW DELHI - 110027 India Tel: +91 11 2510 9397 Fax: +91 11 2544 7395 Web: www.watch-2000.org/
16-20	4th European Breast Cancer Conference	Hamburg Germany	EBCC 2004 Secretariat Federation of European Cancer Societies Avenue E Mounier 83 Brussels, Belgium 1200 Tel: +32 0 2775 0201 Email: ebcc4@fecs.be Web: www.fecs.be/conferences/ebcc4
18-21	57th Annual Cancer Symposium of the Society of Surgical Oncology	New York City New York USA	D K Kubis, SSO Arlington Heights, Illinois, USA Fax: +1847 427 9656 Email: diannekubis@acaai.org Website: www.surgonc.org
27-31	95th Annual Meeting of the American Association for Cancer Research (AACR)	Orlando Florida USA	American Association for Cancer Research Philadelphia, Pennsylvania, USA Fax: +1 215 351 9165 Email: meetings@aacr.org Website: www.aacr.org
28 Mar- 3 Apr	43rd Annual Meeting of the Society of Toxicology	Baltimore USA	Society of Toxicology 1767 Business Center Reston, VA - 22090 Fax: +1 703 438 3113
31 Mar- 3 Apr	12th Congress of the European Society of Surgical Oncology	Budapest Hungary	ESSO 2004 Secretariat Federation of European Cancer Societies Avenue E Mounier 83 Brussels, Belgium 1200 Tel: +32 0 2775 0201 Email: esso4@fecs.be Web: www.fecs.be/conferences/esso4
April			
29 Apr- 2 May	Oncology Nursing Society (ONS) 29th Annual Congress	Anaheim California USA	ONS, Meeting Services Team Pittsburg, Pennsylvania, USA Fax: +1412 921 6565 Email: meetings@ons.org Website: ww.ons.org
May			
8-13	99th Annual Meeting of the American Urological Association	San Francisco California USA	Office of Education American Urological Association 2425 West Loop South, Suite 333 Houston, Texas - 77027-4207 USA Tel: +1 713 622 2700 Fax: +1 713 622 2898 Web: www.auanet.org/
June			
5-8	40th ASCO: Annual Conference for the American Society of Clinical Oncology	New Orleans LA USA	ASCO 1900 Duke Street Suite 200 Alexandria, Virginia 22314 USA Tel: +17 0 3299 0150 Email: asco@asco.org
17-19	World Congress on Gastrointestinal Cancers	Barcelona Spain	Heather Drew Imedex 70 Technology Drive Alpharetta - 30005 - Georgia Tel: +1 770 751 7332 Fax: +1 770 751 7334 Web: www.imedex.com/calendars/oncology.htm
24-27	16th MASCC/ISOO International Symposium Supportive Care in Cancer	Miami Beach Florida USA	Amy Faber The Cleveland Clinic Center for Continuing Education C/O UNITECH Communications 9500 Euclid Ave. P17 Cleveland - 44195 - Ohio Tel: +1 216 444 8420 Fax: +1 216 444 8410 Web: www.clevelandclinicmeded.com/mascc/index.htm
25-29	23rd International Congress of Radiology (ICR)	Montreal Canada	International Congress of Radiology (ICR) 1740 Cote-Vertu Blvd Saint-Laurent Quebec - H4L 2A4 Canada Tel: +1 514 738 3111 Fax: +1 514 738 5199
July			
3-6	18th Meeting of the European Association for Cancer Research	Innsbruck Austria	EACR 18 Secretariat Federation of European Cancer Societies Avenue E Mounier 83 Brussels, Belgium 1200 Tel: +32 0 2775 0201 Email: eacr18@fecs.be Web: www.fecs.be/conferences/eacr18
22-24	International Skin Cancer Congress	Zurich Switzerland	Reinhard Dummer University Hospital of Zürich Department of Dermatology Gloriastrasse 31 Zurich - 8091 Switzerland Tel: +41 1255 8837 Fax: +41 1255 4403 Web: www.skincancer.ch/
August			
7-11	6th International Conference on Head and Neck Cancer	Washington DC USA	Robin Wagner Concepts in Meetings & Events 1805 Ardmore Blvd Pittsburgh - 15221 - Pennsylvania Tel: +1 412 243 5156 Fax: +1 412 243 5160 Web: www.headandneckcancer.org/

Date	Name of Meeting	Place	Secretariat

CALENDAR OF meetings

25-28	7th World Congress of Psycho-Oncology	Copenhagen Denmark	The Danish Cancer Society Strandboulevarden 49 Copenhagen - 2100 Denmark Web: www.ipos2004.dk/
September			
1-4	12th International Society of Endocrinology Congress	Lisbon Portugal	International Society of Endocrinology (ISE) 51-53 Bartholomew Close London - EC1A 7BE United Kingdom Fax: +44 171 796 4676
16-19	SIOP 2004: International Society of Paediatric Oncology	Oslo Norway	Congrex Holland BV PO Box 302 Amsterdam, Netherlands 1000 AH Tel: +31 2 0504 0200 Email: siop@congrex.nl Web: www.siop.nl
23-25	9th Central European Lung Cancer Conference	Gdansk Poland	Department of Oncology and Radiotherapy Medical University of Gdansk ul Debinski 7 Gdansk - 80-211 - Poland Tel: + 48 58 349 2270 Fax: + 48 58 349 2270 Web: www.lungcancer.pl/
October			
3-7	ASTRO: 46th Annual Meeting	Atlanta USA	American Society for Therapeutic Radiology and Oncology 12500 Fair Lakes Circle Suite 375 Fairfax, Virginia 22033 USA Tel: +17 0 3227 0170 Email: meetings@astro.org
3-8	10th Biennial Meeting of the International Gynecologic Cancer Society	Edinburgh Scotland	International Gynecologic Cancer Society PO Box 6387 Louisville, Kentucky, USA Tel: +1 50 2891 4460 Web: www.igcs.org
10-14	6th Congress of the European Association of Neuro-Oncology	Jerusalem Israel	Ortra 1 Nirim St PO Box 9352, Tel Aviv – 61092 - Israel Fax: +972 3 638 4455
15-16	The 9th International Conference on Geriatric Oncology: Cancer in the Elderly	San Francisco California USA	Heather Drew Imedex, Inc 70 Technology Drive Alpharetta - 30005 - Georgia United States of America Tel: +1 770 751 7332 Fax: +1 770 751 7334 Web: www.imedex.com/calendars/oncology.htm
24-28	23rd Annual European Society for Therapeutic Radiology and Oncology Meeting (ESTRO 23)	Amsterdam Netherlands	ESTRO 23 Secretariat Avenue E Mounier 83 Brussels, Belgium 1200 Tel: +32 2775 9340 Email: info@estro.be Web: www.estro.be
29 Oct- 2 Nov	29th European Society for Medical Oncology Annual Meeting	Vienna Austria	ESMO Secretariat via la Santa 7 CH-6962 Viganello-Lugano, Switzerland Tel: +41 9 1973 1919 Web: www.esmo.org/congress2004
November			
5-7	Oncology Nursing Society Institute of Learning	Nashville Tennessee USA	Oncology Nursing Society 125 Enterprise Drive Pittsburgh, Pennsylvania 15275-1214 USA Tel: + 1 86 6257 4667 Email: meetings@ons.org Web: www.ons.org
17-19	1st International Conference for Oncologists and Other Health Care Leaders	New York USA	Barrie Cassileth Memorial Sloan-Kettering Cancer Center 1275 York Ave New York - 10021 - New York Tel: +1 212 639 2000
December			
3-7	46th Annual Meeting of the American Society of Hematology	San Diego California USA	American Society of Haematology 1900 M street NW Suite 200 Washington DC 20036 USA Tel: +1 20 2776 0544 Email: meetings@hematology.org Web: www.hematology.org
3-6	27th Annual San Antonio Breast Cancer Symposium	San Antonio Texas USA	Cancer Therapy & Research Center SACI, Rich Markow San Antonio, Texas, USA Fax: +1210 949 5009 Email: Rmarkow@saci.org Web: www.sabcs.org

Date	Name of Meeting	Place	Secretariat
15-16	4th International Meeting of Hepatocellular Carcinoma: Eastern and Western Experiences	Hong Kong	Congress Secretariat Department of Surgery, University of HongKong Medical Centre Queen Mary Hospital, Pokfulam Tel: + 85 2 2818 0232 Fax: + 85 2 2818 1186 Email: hccewe04@hku.hk Web: www.hcc-ewe.org

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January			
26-29	Primary Therapy of Early Breast Cancer	St Gallen Switzerland	Hans-Jörg Senn St. Gallen Oncology Conferences Rorschacherstr. 150 St. Gallen - 9006 Switzerland Tel: +41 71 243 0032 Fax: +41 71 245 6805 Web: www.oncoconferences.ch/index.html
February			
10-14	American Society for Blood and Marrow Transplantation Annual Meeting	Keystone CO USA	American Society for Blood and Marrow Transplantation 85 West Algonquin Road Suite 550 Arlington Heights, Illanois 60005 USA Tel: +1 84 7427 0224 Email: mail@asbmt.org
March			
3-6	58th Annual Cancer Symposium of the Society of Surgical Oncology	Atlanta Georgia USA	D.K. Kubis - Society of Surgical Oncology 85 W Algonquin Rd, Suite 55 Arlinghton Heights IL - 60005 Tel: +1 847 427 1400 Fax: +1 847 427 9656 Web: www.surgonc.org/
April			
16-20	96th Annual Meeting of the American Association for Cancer Research	Anaheim California USA	AACR 615 Chestnut Street 17th Floor Philadelphia, PA USA 19106-4404 Tel: + 1 21 5440 9300 Email: meetings@aacr.org
28 Apr- 1 May	Oncology Nursing Society's 30th Annual Congress	Orlando Florida USA	Oncology Nursing Society 125 Enterprise Drive Pittsburgh, Pennsylvania 15275-1214 USA Tel: +1 86 6257 4667 Email: meetings@ons.org Web: www.ons.org
June			
2-5	EHA-10: 10th Annual Meeting of the European Haematology Association	Stockholm Sweden	Eurocongres Conference Management Jan van Goyenkade 11 Amsterdam, Netherlands NL-1075 HP Tel +31 20 679 3411 Eha2005@eurocongres.com www.ehaweb.org
8-11	9th International Conference on Malignant Lymphoma	Lugano Switzerland	Olga Jackson Lymphoma Conference Secretary viale Cattaneo 23 Lugano - 6900 Tel: +41 91 921 4561 Fax: +41 91 921 4563 Web: http://www.lymphcon.ch/
23-26	2nd Quadrennial Meeting of the World Federation of NeuroOncology	Edinburgh Scotland	EANO 6 Secretariat Federation of European Cancer Societies Avenue E Mounier 83 Brussels, Belgium 1200 Tel: +32 0 2775 0201 Email: eano6@fecs.be
July			
3-6	11th World Conference on Lung Cancer	Barcelona Spain	Heather Drew Imedex 70 Technology Drive Alpharetta - 30005 - Georgia Tel: +1 770 751 7332 Fax: +1 770 751 7334 Web: www.2005worldlungcancer.com/2005WLC/
October			
16-20	ASTRO: 47th Annual Meeting	Denver Colorado USA	American Society for Therapeutic Radiology and Oncology (ASTRO) 12500 Fair Lakes Circle Suite 375 Fairfax Virginia 22033 USA Tel: +1 70 3227 0170 Email: meetings@astro.org
December			
2-6	47th Annual Meeting of the American Society of Hematology	San Diego California USA	American Society of Haematology 1900 M street NW Suite 200 Washington DC 20036 USA Tel: +1 20 2776 0544 Email: meetings@hematology.org Web: www.hematology.org

CALENDAR OF meetings

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

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Professor A Coates AM, MD, FRACP, AStat

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Dr S Hart FRACS
Professor D Hill AM, PhD
Dr L Kenny MBBS, FRANZCR
Hon S Lenehan BA, DipMan, MBA, FAICD
Mr R McGowan
Assoc Professor S Smiles RN, RM, ICC, BHA, GradDipPSEM
Professor J Ward MBBS, MHPEd, FAFPHM, PhD
Dr K White PHD

THE CLINICAL ONCOLOGICAL SOCIETY OF AUSTRALIA INC

The Clinical Oncological Society of Australia (COSA) is a multidisciplinary 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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Council Nominees
Ms C Cameron RN, OncCent, GrDipN, MNSc
Dr D Goldstein MBBS, MRCP (UK), FRACP
Professor J Thompson BSc(Med), MBBS, FRACS, FACS, MD

MEMBERSHIP

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

Membership fees for 2003

Ordinary Members: $140
Associate Members: $80
(includes GST)

INTEREST GROUPS

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