# Cancer Forum

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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. Microarray 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.

| Control doublet | Paclitaxel 175mg/m² IV (3 hr) | D 1 x 8 cycles (q 21 days) | Carboplatin AUC 6 IV | D 1 |
| Gemcitabine triplet | Paclitaxel 175mg/m² IV (3 hr) | D 1 x 8 cycles (q 21 days) | Carboplatin AUC 5 IV | D 1 |
| Gemcitabine 800mg/m²/d IV | D 1, 3 |
| Modified Doxil triplet | Paclitaxel 175mg/m² IV (3 hr) | D 1 x 8 cycles (q 21 days) | Carboplatin AUC 5 IV | D 1 |
| Doxil 30 mg/m² IV (every other) | D 1 |
| Topotecan doublet (module A) | Paclitaxel 175mg/m² IV (3 hr) | D 3 |
| Carboplatin AUC 6 IV | D 1 |
| Topotecan 1.5mg/m²/d IV | D 1-3 |
| x 4 cycles (q 21 days) | D 1 |
| Gemcitabine doublet (module A) | Paclitaxel 175mg/m² IV (3 hr) | D 8 |
| Carboplatin AUC 6 IV | D 1 |
| Gemcitabine 1000mg/m²/d IV | D 1, 3 |
| x 4 cycles (q 21 days) | D 1 |

OVERVIEW

M Davy
Royal Adelaide Hospital
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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, focusing 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;
- Furthermore ensuring 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, age and presence of hormones. Ovarian cancer Pregnancy and oral contraceptive use are associated with a reduced risk of ovarian cancer. Prophylactic oophorectomy1, tubal sterilisation and hysterectomy2 have been shown to reduce a woman’s risk of ovarian cancer.

The five-year relative survival of women with ovarian cancer after diagnosis is about 42%.2 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 evidence that women with ovarian cancer who are treated by a gynaecological oncologist have improved survival rates4,5, 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 nationally distributed in 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 those with cancer who are informed about their treatment options6. 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.

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 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.

References

RISK FACTORS FOR EPITHELIAL OVARIAN CANCER

SI Jordan (pictured top), DM Purdie, DC Whiteman, PM Webb (pictured bottom) 
Queensland Institute of Medical Research 
Royal Brisbane Hospital, QLD

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. 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 focused on the 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 gonadotropins. 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. 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 stopping the pill. In one study of women in the Nurses’ Health Study, the different histological subtypes of ovarian cancer have been shown to differ with respect to some risk factors1 but it remains unclear whether this is the case for the effect of the contraceptive pill. Some have found a protective effect of pill use on all histological subtypes1 but one group reported an increased risk of mucinous EOC associated with ever-use of the OCP. Whether the oral contraceptive pill decreases the risk of EOC is still debated and a recent meta-analysis 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 carriers17 while a second study found significant reductions in risk in both ever-users and non-users with increasing duration of use among women with BRCA1 and BRCA2 mutations18. Further studies are required to clarify this important issue.

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 breastfeeding. A pooled analysis of 17 studies22 has suggested that the protective effect of breastfeeding may increase with increasing numbers of live births but this is limited and inconsistent so it is not possible to evaluate the effect of these interventions on ovarian cancer risk.

Breast feeding may increase risk of ovarian cancer21 but these data are less consistent.

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 EOC2 suggesting that both of these procedures confer a protective effect against this cancer. It has been suggested that the apparent protective effect 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 studies20, but the effects have been small 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 medications on the risk of EOC. It also has been suggested that some psycotropic medication may influence the risk of EOC by altering the release of gonadotrophins2. 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. 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)21. The significance of this association is clear from a follow-up study 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 EOC22. 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 diagnosis23. It has also been suggested that inflammatory conditions on or around the ovary may contribute to the development of EOC24. Some evidence suggests that pelvic infection may be associated with a modest increase in risk of EOC25 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 unlikely26. 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 cancer27. There is consistent evidence of a small but significant effect of high body-mass index on risk of EOC (OR 1.4, 95% CI 1.2-1.6)28. Some studies suggest this association is strongest in women diagnosed with EOC pre-menopausally29. 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 activity30 but others have found neither an association or a decrease in risk31. 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. 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 use32. 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 but subtype-specific analyses provide fairly consistent evidence that the risk of EOC is increased by cigarette smoking (OR ~3 for ≥25 pack-years)35. 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) but this finding was not replicated by a subsequent population-based case-control study. 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)36. 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 white women. 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. The weight of evidence suggest there may be a small positive association between coffee drinking and the risk of EOC; 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 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 stronger association between tea consumption and EOC. It is thus possible that any effect of tea may depend on the type of tea (green or black) that is consumed.

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 and, possibly, b-carotene 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. 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. There is less consistent evidence for an association between intake of dietary fat and EOC risk, but studies demonstrate higher consumption of dairy products and ovarian cancer, 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 have treated epithelial ovarian cancer as a single disease and it is now clear that the different histological subtypes differ with respect to key risk factors. 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.

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

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Association</th>
<th>Approximate relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral contraceptives</td>
<td></td>
<td>0.4-0.6 for 2 years use</td>
</tr>
<tr>
<td>Pregnancy</td>
<td></td>
<td>0.5-0.7 for ever vs never pregnant</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td></td>
<td>0.8 for ever having breastfed</td>
</tr>
<tr>
<td>At menarche / menopause</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRT (?) for oestrogen + /- sequential progesterone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infertility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hysterectomy / Tubal ligation</td>
<td></td>
<td>0.5 – 0.8</td>
</tr>
<tr>
<td>Analgesics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endometriosis</td>
<td></td>
<td>1.7-1.9</td>
</tr>
<tr>
<td>Polycystic ovary syndrome (?)</td>
<td>Obesity</td>
<td>1.2 – 1.5</td>
</tr>
<tr>
<td>Talc</td>
<td></td>
<td>1.3</td>
</tr>
<tr>
<td>Smoking</td>
<td>for mucinous tumours only ~3 for &gt; 25 pack-years</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coffee/Tea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet</td>
<td>Fat</td>
<td>2-3 for 2+ eggs per week</td>
</tr>
<tr>
<td>Eggs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetables</td>
<td></td>
<td></td>
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</tbody>
</table>

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

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10. 151
The management of these women at increased risk of ovarian cancer is difficult and presents many challenges. It should be remembered that, in addition to 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 penetrance of the specific germline mutations associated with ovarian cancer. 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. 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 history11,12. 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 risk13,14. However, the confidence intervals of these risk estimates are wide and studies such as the Canadian population study among others challenge these figures, which may be too simplistic. 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 or more relatives with ovarian cancer should be considered to be at potentially higher risk and be referred to a familial cancer clinic for further advice and counselling13,14.

Breast cancers and up to 90% of cancers in families with both first-degree relatives for the three common founder mutations. The lifetime risk of ovarian cancer in women with mutations in BRCA1 and BRCA2 varies considerably in different studies and within different families with the same mutations15,16. However, a recent large-scale study has estimated that in women who have a germline mutation in either BRCA1 or BRCA2 with a 10-60% chance of having a founder mutation identified in BRCA1 or BRCA2 and are particularly useful in families in which there is a tendency to develop ovarian cancer by age 70 while women with BRCA2 mutations have a lower risk of 11% (CI 2.4-19%)19. There are age-related differences in the penetrance of these genes. The mean age at presentation for women with BRCA1-related ovarian cancer 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 BRCA220,21. These data have important practical significance as it influences 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 to consider prophylactic surgery in younger women. It is our view that screening begins at age 25-30 and prophylactic surgery should be considered at completion of childbirth or at age 35 years22. While some may view our comments as hasty, 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 under 40 years of age and had been only observed in the late 50s or early 60s. Even women with mutations in BRCA1 rarely develop ovarian cancer under 40 years old23. This is in distinct contrast to BRCA1 and BRCA2-related prostate cancers which are usually seen at a younger age24,25.

Extracranial cancers occur in 69% of women with MS2 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 cancers other than ovarian cancer. Women with HNPCC-associated 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 20 to 74 years26. 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 cancers and are often confined to the ovaries27. 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 mutations in the general population is BRCA1 and BRCA2 has been estimated to be in 1 in 500 to 1 in 1000 although this is lower in certain populations1. 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 (Ashkenazi Jewish ancestry) where three specific mutations (185 delA and 382 insC in BRCA1 and 6174 delT in BRCA2) are present in approximately 1 in 40 of the population13,14. 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 they should therefore 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 25-38% of early onset breast cancers and up to 90% of cancers in families with both breast and ovarian cancers.

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 if so how. It is also likely that if the mutations are still confined to the ovaries and would therefore be expected to have a good prognosis. The majority of women with epithelial ovarian cancer diagnosis at a mean age of 53 years (range 29 to 74 years)23. It is beyond the scope of this paper to review all the relevant literature on this topic. It is clear that the genetic epidemiology of ovarian cancer screening will be useful in determining whether screening is associated with a reduction in mortality. There are three large population-based ovarian cancer screening studies in progress which will be used in determining whether regular ultrasound screening and estimation of serum CA125 will reduce mortality. Screening studies to date have largely focused on determining the sensitivity and specificity of various screening modalities. There are problems with specificity and positive predictive value of the screening tests and many women undergo unnecessary investigations because of a false positive result. It is beyond the scope of this paper to review this in detail, but it is clear that there is inherent problems associated with screening tools currently available and that we do not yet have a reliable method of detecting ovarian cancer. While it may sound counterintuitive we really don’t know if there is a stepwise progression from stage 1 to 2 and so on so, and if so, what the somatotype in each stage is. We have not been informed a clear progression of 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 cancer23,24.

As a result, endometrioid and mucinous cancers are usually confined to the ovaries at initial clinical presentation and have an excellent prognosis. In contrast, the majority of women with stage 1 ovarian cancer are at least 40% stage 2 and 25% stage 3 at diagnosis and only 20% are stage 125. Most of the stage 1 cancers are well differentiated and may have progressed from serous borderline tumours to invasive serous borderline tumours to invasive serous carcinomas 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.

**Table 1: Genes associated with hereditary ovarian cancer**

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Gene</th>
<th>Lifetime risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast/Ovarian syndrome</td>
<td>BRCA1</td>
<td>10-60%</td>
</tr>
<tr>
<td></td>
<td>BRCA2</td>
<td>30-50%</td>
</tr>
<tr>
<td>Hereditary non-polyposis</td>
<td>MLH1</td>
<td>10%</td>
</tr>
<tr>
<td>colorectal cancer</td>
<td>MSH2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MSH6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PM1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PM2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Colorectal, endometrial, gastric, urinary tract.</td>
<td></td>
</tr>
</tbody>
</table>

**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 age of 50), endometrial cancer, ovarian cancer, gastric cancer, and cancers involving the retinal tract.
at an “early” phase with our current technology 30. A good
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.

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
developing ovarian cancer has not been matched by good
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 serum markers. There is limited data
regarding reduction is seen in the studies of RRBSO, but
clearly this is not an attractive option to many women, and
temporary tubal ligation has been developed as a bridge
to 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 of genetic counselling and the interested reader is
directed to papers on this 42. The management guidelines and advice
on familial aspects of ovarian cancer recently have been
updated and will provide health professionals with a detailed
overview of familial ovarian cancer.

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characteristics relating to ovarian cancer risk: collaborative analysis of
their families face. This should not be interpreted as lack of
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on familial aspects of ovarian cancer recently have been
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Table 3: Ovarian cancer risk reduction strategies for BRCA1 and BRCA2 mutation carriers

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Risk reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubal ligation</td>
<td><strong>63%</strong></td>
</tr>
<tr>
<td>Oral contraceptive pill</td>
<td><strong>50%-55%</strong></td>
</tr>
<tr>
<td>Prophylactic salpingo-oophorectomy</td>
<td><strong>95%</strong></td>
</tr>
</tbody>
</table>

* Protective effect only seen in BRCA1 mutation carriers.

too prescriptive and the decision regarding timing of surgery
may be made only after detailed discussion with the individual
women. Women who have surgery in her family would need to be
told as well as the possibility of genetic anticipation as cancers in
subsequent generations tending to occur earlier. It is possible that
the use of prophylactic or risk-reducing bilateral salpingo-oophorectomy
(RRBSO) who will have the surgery performed following a strict
algorithm developed by Skates et al which takes into account
number of factors including careful pathological assessment
and New Zealand Gynecological Oncology Group (ANZGOG).

It is thought to improve the sensitivity and specificity of CA125
in case series unselected for family history: a combined analysis of 22
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characteristics of BRCA1 and BRCA2 mutations in ovarian cancer.”
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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 regimens. 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 of 47% in the USA. Therefore, the need for effective strategies aimed at improving treatment response and disease control is urgent.

Many biological factors have been described as predictor of response to chemotherapy, including tumour grade, stage, Ki67 and tumour ploidy. Combination chemotherapy is used commonly today, but the response of the tumour to chemotherapy remains a challenge. In parallel, with the pharmacological and genetic advances, there is growing interest in molecular correlates of chemotherapy resistance.

Studies have shown that the expression of genes involved in cell cycle regulation, DNA repair and apoptosis are associated with chemoresistance. Factors that upregulate proliferation and downregulate apoptosis, such as cyclins, receptor tyrosine kinases (RTKs), BCL2 family members, and p53, are overexpressed in chemoresistant tumours. These factors promote tumour progression by delaying cell cycle checkpoints, preventing DNA damage repair, and regulating cell survival.

In addition, the role of mitochondrial dysfunction and cell death mechanisms, such as necrosis and autophagy, have been investigated in the context of chemotherapy resistance. Mitochondrial dysfunction and increased autophagy are observed in chemoresistant tumours, which may contribute to the maintenance of tumour stem cells and drug resistance.

In conclusion, understanding the molecular mechanisms underlying chemotherapy resistance is crucial for the development of effective strategies to overcome resistance. Further research is needed to identify novel molecular targets and biomarkers to improve the prediction and management of chemotherapy resistance.

**Molecular Prognosis of Epithelial Ovarian Cancer: Observations from Current Literature**

D Bovetil

Research Division, Peter MacCallum Cancer Institute
Melbourne, VIC

Cancer of the ovary is both the most prevalent and lethal form of gynaecological cancer. 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 chemotherapeutic agents against ovarian cancer are cisplatin—also used for lung, head and neck, bladder and testicular cancers. Response rates to this drug vary from 40%-60% and it is often used in combination with other treatments (eg Paclitaxel) to achieve a subtle increase in the proportion of patients successfully treated.

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this study showed with the use of tissue arrays (120 cases in total) that expression of COLE6A3 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† (higher Human kallikrein 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 was significantly associated 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. This pathway is comprised of six genes associated with Fanconi anemia syndrome (FANCA, -C, -D2, -E, -F and -G) plus BRCA1 and BRCA2 and regulates cell proliferation 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 FANC6. 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† as shown in figure four. The power of microarray analysis to reveal important information about the variation in ovarian cancer patient survival rates is demonstrated by Lancaster et al.† 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 two years 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.† 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 overcome through an increased understanding and manipulation of the underlying molecular changes many lives may be saved from this aggressive and widespread disease.

References
Lysosphosphatic acid (LPA), a bioactive phospholipid, has been reported as a potential discriminating marker for ovarian cancer including rare forms of disease.

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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 spectrometry (surface-enhanced laser desorption and ionisation, SELDI) to define a profile associated with sera derived from patients with ovarian cancer. 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.

References


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 gynaecologist 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.

RAISING AWARENESS: OvCa Australia

S Lee
OvCa Australia
Fitzroy, VIC

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.
**ABSTRACT**

This paper reviews the evaluation of malignancy and prognostic parameters used in gastrointestinal stromal tumours (GIST). Incorporation of 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 question remains as to whether GIST represents a single entity, and the distinct entity, or 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. GIST have been estimated to comprise between 0.1% to 3% of all GI malignancies, 20% of small bowel malignancies and 0.1% of large bowel malignancies. 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%) or duodenum (6%). There may be a greater incidence in men while others note no sex difference. The effect of gender on tumour behaviour is uncertain; some suggest it does not influence tumour behaviour others associate male sex with markedly poorer prognosis and increased occurrence of metastases.

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

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. GANT should no longer be regarded as nerve tumours (GANT) are also GIST tumours, based on their KIT positivity and presence of essentially identical KIT activating mutations. GANT should no longer be regarded as nerve tumours (GANT) are also GIST tumours, based on their KIT positivity and presence of essentially identical KIT activating mutations. GANT should no longer be regarded as nerve tumours.

Whether these tumours arise from sympathetic or parasympathetic nerves is uncertain, 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, cytogenic aberrations and telomere length.

**Case report**

A 53-year-old male farmer presented with a three-day history of epigastric pain and melena, preceded by a syncopal episode. Two days later he was 88g/l and he was again transfused with two units of packed cells. Repeat gastroscopy enabled biopsy of the tumour and duodenal repair. Histological examination showed a spindle cell stromal tumour 13mm in diameter, with fewer than 1 mitoses per 50 HPFs. The patient underwent laparotomy with local complete excision of the tumour, which proved to be a gastrointestinal stromal tumour (GIST).

**Discussion**

GIST were most often classified, until recently, as leiomyomas and leiomyosarcomas, but are now known to represent a spectrum of tumours from benign to malignant. The term GIST, proposed by Mazur and Clark in 1983, was first used to classify all gastrointestinal mesenchymal neoplasms of the gastrointestinal tract, typically expressing KIT (a tyrosine kinase receptor). GIST arising in the muscularis propria and muscularis mucosae may expand towards the bowel lumen, the oesophagus or in both directions. 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. GIST have been estimated to comprise between 0.1% to 3% of all GI malignancies, 20% of small bowel malignancies and 0.1% of large bowel malignancies. 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%) or duodenum (6%). There may be a greater incidence in men while others note no sex difference. The effect of gender on tumour behaviour is uncertain; some suggest it does not influence tumour behaviour others associate male sex with markedly poorer prognosis and increased occurrence of metastases.

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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 supported by several immunohistochemical and ultrastructural similarities. Alternatively, GIST may originate from precursor stem cells that can differentiate towards either a smooth muscle or ICC phenotype, with KIT expression believed to be crucial in encouraging differentiation of these cells towards an ICC endpoint.

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. GANT should no longer be regarded as nerve tumours.

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). ICC are immunostained by antibodies against KIT (CD117). KIT encodes a transmembrane tyrosine kinase receptor, consistently expressed in GIST.

Structurally, the KIT receptor can be divided into four principal domains: an extracellular domain; a transmembrane domain; a juxtamembrane domain; and a kinase domain. The juxtamembrane domain is 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. The KIT gene sequence has 21 exons, and in sporadic GIST, the majority (50-70%) of KIT mutations have been found in exon 11, encoding the juxtamembrane domain of the receptor. A germline mutation identified in familial and multiple GIST has also been identified in the juxtamembrane domain. GIST with exon 11 mutations were originally reported to be of a higher grade, or associated with poorer outcomes. Subsequently, exon 11 mutations were reported to be associated with more aggressive behaviour. Further, mutations have been described in exons 9 (extracellular domain), 13 and 17 (the kinase domain) with the majority of exon 9 mutations associated with highly malignant GIST. The significance, if any, of exons 13 and 17 is overshadowed by their overall, the estimated frequency of KIT mutations is between 21% and 92%. 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. A number of GIST, although lacking KIT mutations demonstrate strong KIT activation. Presumably in these instances, have been detected by conventional screening methods, or, other non-mutation 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.

The majority of GIST are the result of somatic mutation. Rare familial cases have been described, however predisposing factors are unknown. A link to EBV infection, associated with acute myelogenous leukaemia and malignant lymphoma, and impaired lymphocyte apoptosis with gastric GIST and Von Recklinghausen’s syndrome have been reported. The pathogenetic link between NF1 and GIST may be purely causal.

Morphological parameters

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

Grading systems have been devised with different cut-off points for the number of mitoses per 10 HPF. Mitotic count per 50 HPF is now recommended. Tumours with 0-1 mitoses per 10-50 HPFs will not give rise to metastes, those with more than 5 mitoses per 50 HPFs are considered malignant. 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.

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

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. Predisposing factors independent of tumour size, mitotic rate and patient age are 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. Small bowel tumours have the worst prognosis and the outcome of patients with gastrointestinal stromal tumours is worse in patients with GIST and von Recklinghausen’s syndrome.

Histologically, GIST express a variety of cell types and growth patterns. Either of two cell types may predominate (spindle cells and epithelioid cells); however a mixed cell type may occur. Spindle cell-type form the majority comprising 70-80% of gastric tumours along with the majority of small intestinal GIST. Epithelioid lesions occur more often in the stomach. Lesions of mixed cell type exhibit an atypical transition between epithelioid and spindled cells, however there may be an intermediate cytologic appearance. There are some site-specific variations in morphology with spindle cell lesions of the small bowel having having
a tendency to contain skewid fibres. Skewid fibres formerly believed to correlate with neural differentiation, now appear to have no role in differentiation. Correlation of histologic pattern with prognosis is not established, nor is predominant cell type related to pattern of antigenic expression.

Rather than using distinct benign and malignant categories, GIST should be regarded as having some malignant potential, described in terms of risk assessment (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), SMA, protein, and neuron specific enolase (NSE).

GIST are usually positive for CD117 and CD34, variably positive for smooth muscle actin, and usually negative for desmin. Antibodies to CD34 can differentiate GIST from smooth muscle and other intestinal mesenchymal tumours.

CD34 reactivity is seen in a wide range of normal tissues and tumours. CD34 is expressed in 60-70% of GIST. Many of the larger series found CD34 positivity to have no prognostic significance. However, CD34 may aid in distinguishing gastrointestinal leiomyomas and schwannomas, which are negative for CD34.

Furthermore, CD34 in combination with CD117 and SMA can be used to differentiate GIST from most other mesenchymal tumours. It has also been shown to demonstrate a reciprocal relationship with SMA expression - CD34 positive tumours are often SMA negative. The variability of CD34 staining among GIST may be due to several phenomena of GIST precursor cells (ICC).

CD117 is now accepted as the most specific immunohistochemical marker for GIST. CD117 is expressed in 80-100% of GIST, including 24 benign, 36 malignant primary, and 35 metastatic tumours. The mean number of demonstrable chromosomal aberrations found was (2.6) benign GIST, (7.5) malignant GIST and (9) metastatic GIST. Deletions of chromosome arms 1p, 1q, 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. According to El-Rifai et al. 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.

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

Telomerase, an enzyme implicated in maintaining the de novo synthesis of the ends of eukaryotic chromosomes is expressed in 80-90% of carcinomas. Its activation is a hallmark of carcinogenesis, with continued renewal of the chromosomal ends by telomerase thought to be a mechanism favouring cell proliferation. Telomerase activity, a negative prognostic indicator, has been investigated in two studies (a total of 42 GIST cases). Unique to malignant GIST, telomerase activity was not detected in benign cases from either series, although not all malignant cases expressed telomerase. Guenther et al. 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. 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. Imatinib mesylate works by inhibiting tyrosine kinase activity 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. No benefit has been reported from obtaining wide margins. Failure to obtain histologically tumour-free margins is associated with adverse outcomes.

Regional lymph node dissection is of unproven value.

Metastases occur in more than 50% of patients diagnosed with malignant or high-risk tumours at the time of resection. Prognostic factors for local recurrence suggest a role for adjuvant therapy, however data is lacking in support of the use of radiation or chemotherapy. Pierre et al. found that patients receiving adjuvant therapy had worse outcomes. Radiotherapy is limited by potential toxicity to surrounding structures 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. Most recurrences occur within five years of primary treatment, but can appear more than 10 years after treatment, 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 cyto genetic studies, suggesting a possible correlation between clcopathologic behaviour and chromosomal aberrations, have significantly added the definition of new prognostic parameters. Cyto genetic 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 necessary, as no single 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.
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-empowerment of science and technology of which we know as the Renaissance, and among the finest exemplars of 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, cordon a ship, design a building, write a sonnet, balance accounts, build a wall, set a bone, read rhetoric – and烜 invading science – and perhaps the examples I have cited. Such collaborations can be sound, according to opportunity, according to your own interests, according to your own 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.

In many ways pride of place should go to Don Metcalf. Don’s work 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 his work at the National Cancer Institute, 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 this presentation I will review some of those collaborations, 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 continued 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 a consummate scientist, 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 computer, but was a 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. I had made a mistake. Just the right mistake. Where would that fit in to our overall understanding? After all, if it’s not right we’ll discard the idea quickly enough.

Sir Gustav Nossl was the director, and directly responsible for recruiting me to the Institute. Gus was also a regular at clinical meetings, and regularly brought a scientifc 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 diabetes had a prevalence of autoantibodies in the serum more typical of non-diabetes a decade older. The headline read "Insulin makes you age". Diabetic cows 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.

In 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 work 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 his work at the National Cancer Institute, 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.

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In my lifetime, I opted to continue an interest in cancer. In the mid 1970s there were no training programs in Australia. I was returned determined to apply some of the same principles to the research of the Eastern Cooperative Oncology Group, so that I could take up the next five years of my life." He was of course both right and wildly pessimistic.

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);
- 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.
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 into the FCCs, thereby providing a wonderful resource for cancer researchers with interests ranging from psychosocial medicine to the molecular biology of breast and ovarian cancer. With the support of the Kathleen Cunningham Foundation, KConFab rapidly emerged as a national consortium for research into familial breast cancer. Pivotal to its success was the rigorous collection of epidemiological 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 (held by KConFab, Australian Cancer Organisations Group, Suthers, Judy Kirk, Christobel Saunders, Donata Gertig, Nadia Trafacante and Heather Thorne). The program was expanded this year to include an important new initiative, the Australian Ovarian Cancer Information Service, 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. This meeting was also combined with the inaugural meeting of the Australian network that supported research into Familial 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 the media to improve clinical practice and to establish common national protocols. Topics covered included the organisational strategies in place for each FCC, imaging 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 150 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 research into familial and hereditary breast and ovarian cancer. There were plenty of opportunities for useful dialogue among this diverse group and the program itself provided interesting and useful sessions for the attendees.

There were four international plenary session speakers. Paul Melzer 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 therapeutic or diagnostic 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 proven 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.

Suniti Lakhotia (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 myoepithelial cells. The 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 Family Cancer Centre
and
VBCRC Laboratory

Australian Behavioural Research in Cancer

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

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 (CBRC) at the National Centre for Epidemiology and Population Health, the Centre for Cancer Control Research (CCCPR) of The Cancer Council South Australia, the Centre for Health Research and Psychosocial Oncology (CHEP) of the Centre Council New South Wales and the Cancer Prevention Centre (CRPC) of the University of Queensland.

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

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 Lipscombe 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. There was also a high level of public support for the most recent legislative amendments restricting smoking in Victorian alcohol licensed 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 (2003; 12 [Suppl III]) 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 available online at http://tc.bmjournals.com/content/vol12/suppl_3/.

The Centre for Behavioural Research in Cancer Control (CBRC), Victoria

Adverts for Philip Morris and Tobacco Industry 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 broadcasted in 38 countries. CBRC conducted adverts on three of the advertisements screened in cinemas in Australia to test their impact on young people in comparison to data gathered from the Younger Than We Appear 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 the other half non-smokers. 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, 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. 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 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

CBRC was commissioned by the Foundation of WA to compare the findings of the 2002 National Tobacco Campaign 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 during the nine years between 1993 and 1999. However suntan lotions 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 (CCCPR) and the Tobacco Control Research and Evaluation Program (TCRE), SA

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

Survival was analysed using the Kaplan-Meier product-limit estimate, and multivariable Cox proportional hazards regression, from the time of diagnosis (1 January 2000 to 31 March 2003, whichever came first. Numbers of confidants (with whom feelings were shared) as 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 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 diagnosis. At that time, shorter 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, tests and urological organs, was released in early October. As for previous monographs, its intended audience is medical practitioners, 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 of medical specialties: 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 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 and the 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 is the case.

Clare Johnson, a PhD candidate at the Centre for Health Research and Psycho-oncology undertook qualitative research to improve understanding of 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 Alf Gigns and Dr Chris Paul.

The study involved a semi-structured telephone interview with medical 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 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 with the concept of palliative care management with palliative care, particularly in the physical domain; and that doctors are cognisant in identifying physical symptoms as an appropriate reason for referral. Doctors appreciate that patients are more likely to be referred to be given 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 (‘print+phone’) who identified themselves as moderately active (18 men, 48 women) aged 45-78 years. Participants 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 motivational tailoring to 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 participants’ physical activity in both print and 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 0.7 miles/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 demonstrated 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 data to support development of health promotion 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. This includes considering a range of issues on content, sampling and funding. A recently developed survey research method that developed by Professor David Hill and colleagues in 1997 for monitoring sunburn and sun protection behaviours in Victoria. The survey was conducted on a total of eight Monday evenings from the end of November 2003 until January 2004, representing a representative sample of telephone interviews of 4,000 Australians aged 14 to 69 years. Contact Suzanne Dobrucki at CBRC for more details.

n The Gemini project

Self-identified women with breast and ovarian cancer have been included in a survey of 28 identical twins who were dissatisfied with 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 density index was designed to explore how the twins account for their behaviours and decisions around their discordant smoking status.

Nivo qualitative software package is being used to identify themes in the twins’ responses and a paper is being prepared for submission for publication.

n CBRC
Solaria study

CBRC 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 an interactive map of 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 southern 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 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. The national Sun Protection 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) 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 Alf Gigns from the Centre for Health Research & Psycho-oncology and Ms Louisa Thrush of the Cancer Council Research team in NSW, are conducting a population study to assess levels of compliance among solaria operators with these aspects of the standard. Investigation is being undertaken 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 vary in intensity 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 responses to ask the operator. Before the start 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 CBPC
Physical activity in population health

CBPC now provides a strong cancer prevention nexus for research networks and provides 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.

n CBRC
CBRC has recently launched its own website within The Cancer Council Victoria’s website. Visitors to www.cancervec.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 preventive medicine, 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 CBRC
CBRC 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.
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.

**TCR**

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”. Jacqui 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 New South Wales, 2000-2002.

**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.

**CPRC**


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 Cerni 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 & TCER), Narelle Mills (CHeRP) and Cathy Swart (CPRC) for their contributions.

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**LETTER**

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 breast 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. We are aware of the GP education seminar “On The Ball!” (www.ucr.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

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

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Bulletin name Bulletins appear in order of publication: issue 1-30
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 such as DNA. This is contrary to the 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 McLennett has been appointed Executive Officer of the Clinical Oncological Society of Australia (COSA). Ms McLennett also replaces Mr Laurene Wright as The Cancer Council Australia’s Administrator 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 women, 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.


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 Yamagawa-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://fellow.uicc.org/fellow3y.html

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://fellow.uicc.org/fellow11b.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 $90,000 for 12 months. Applications close 1 December 2003.

http://fellow.uicc.org/fellow11b.shtml

Wishlist Christmas hampers

Wishlist.com.au has developed a range of gourmet Christmas hampers as a fundraising initiative to support 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 Council Australia’s 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’ 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.

National Skin Cancer Action Week

It seems many Australians wrongly believe tanning without protective clothing will protect them from the dangers of tanning is a theme of The Cancer Council’s National Skin Cancer Action Week this year (16-22 November).

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

The Cancer Council believes 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 definitions, the Cancer Council believes 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.
CEO profiles

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

The Cancer Council ACT

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)
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 most 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 many articles that I would not have read otherwise.

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)
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 postgraduate 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. It is relatively expensive and is suitable for Australian users. This compact handbook is truly pocket-sized; yet it is packed with information not available 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 drugs that are not. 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 for breast therapies 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 (where 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 for a serious illness. Selected reading references are also provided.

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 and without 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 trains 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.

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 "worrying" breast. 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 covered, and 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 is clearly multidisciplinary, conditions. The non-surgeons amongst you however should not worry, 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 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 specialist research 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.

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CANCER INFORMATICS: ESSENTIAL TECHNOLOGIES FOR CLINICAL TRIALS
JS Silke et al
Published by Springer (2002)
RRP: $US179.95

People running clinical 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 use 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 up 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 are 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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The section on supportive care is incomplete. One of the most distilling 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 is not covered in this section. Similarly, the role of radiotherapy in pain management is not covered, although the overview of analgesia used is not unreasonable. The text provides a concise overview of the many agents that have potential uses in pain management. The chapter on pain management also provides a useful framework for clinical 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 addressed. 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.

The section on cancer rehabilitation remains a big challenge. It is currently involved in the care of cancer patients and their families. Accordingly, the appearance of a substantial book on the role of exercise in the recovery process is very welcome, and the format of this book allows it both to be used for consultation, 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 unrefereed assertion that all patients treated within the six-month intervention program at their institute report significant improvements in quality of life. This is of great concern to those who write of the impermanence of non-print citation. The book suffers from two significant limitations, in my view. First, the referencing is very patchy. Two papers by the book’s 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 imprudence of non-print citation.

Second, the book relies exclusively on the experience of the authors’ own centre, from an exercise physiologic viewpoint, in a large and wealthy country where cancer rehabilitation services have published 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 experiences of other disciplines working in the area of cancer rehabilitation.
Finally, the book is long (300 pages) and would have benefited from more rigorous editing and some illustrations. Despite 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)
165 pages plus index
RPP: US$243.50

In the history of biological research, and of medicine, a grand recurring theme is that the study of mutants can provide 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 potentially can 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 bears more than a passing resemblance to 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 a panel of 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 and 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.
are in receipt of technical mutation reports from specialised laboratories. Chapters nine to twelve are devoted to the cell cycle, apoptosis, and the molecular basis of cancer progression.

The third set of chapters (13-39) deal with the familial cancer syndrome 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 a real asset 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 and the key considerations in their management. Many of these chapters deal with accepted protocols and guidelines from a clinical management perspective.

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)
RPP: 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 the need for 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 toxicities relevant to this method of exposure. Mutagenesis tests, with the focus of detecting genotoxic agents, can be used with confidence in humans. Chronic exposure to genotoxic agents may result in genetic toxicity which is not necessarily reflected in a high frequency of cancer. This is due to the limitation of current genetic toxicology testing in detecting genotoxicity that results in a healthy cell, rather than a cancer cell. The relationship between cancer risk and exposure to genotoxic agents is a complex one and is not yet fully understood.

The book begins with a discussion of the importance of genetic toxicology testing and the role of genetic toxicology in the risk assessment process. It then goes on to describe the various methods of genetic toxicology testing and the principles underlying these methods. The book also includes a discussion of the current challenges and future directions in the field of genetic toxicology.

The book is divided into two main sections. The first section, “Principles of Cancer Risk Assessment,” covers the basic concepts of cancer risk assessment, including the definition of cancer risk, the types of cancer risk assessment, and the importance of genetic toxicology in cancer risk assessment. The second section, “Genetic Toxicology Tests,” describes the various methods of genetic toxicology testing, including in vitro and in vivo tests, and the principles underlying these methods. The book also includes a discussion of the current challenges and future directions in the field of genetic toxicology.

The book is an excellent resource for those involved in the field of cancer risk assessment and genetic toxicology testing. It is a comprehensive and up-to-date guide to the current state of knowledge in this field and is essential reading for anyone involved in the assessment of cancer risk.
other endogenous viruses that may be co-infecting the same attenuated viruses that may be useful for cancer therapy and host interactions receives ample consideration in the book, although the potential for harm through unwanted virus/theoretical framework that argues in favour of the cautious This book fails to place such efforts in the context of a theoretical framework that argues in favour of the cautious performance of genetic engineering in eukaryotic cells, a situation such studies has been slowed down by the limited ability to viruses with novel strategies for cancer cell killing. Progress in described, in parallel with efforts to endow such recombinant wild-type viruses to reduce their potential for harm are cancer therapy. Separate chapters review the use of herpes in the use of a number of replication-competent viruses for 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 in the context of damaged cells. Could the mechanisms of bacteriophage excision from the bacterial chromosome when the latter sustains double strand breaks have any relevance? 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. If this is correct, then these are 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 Drerup 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 viruses, adenovirus, reovirus, paroviruses, 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 currently changing. More and more large viruses are cloned as bacterial artificial chromosomal clones. Techniques recently developed for the precise genetic engineering of large genomic DNA viruses (adenovirus, poxviruses, paroviruses) 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 are applications of 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 of expression specificity of 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 exploit the natural defence mechanisms against cancer cells. P Ioannou Head, Cell & Gene Therapy (CAGT) Research Group The Murdoch Children’s Research Institute Royal Children’s Hospital Parkville, VIC 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 living and well-established experts in this field with additional contributions from both the US and Israel. There is a consistency of presentation throughout the text which is 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 infarction, 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 good quality bibliography. It is clear that 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 EGF, PTK-2 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. R Ozols Published by BC Decker (2003) ISBN: 1-550-90968-6. 237 pages plus index. RRP: $305.06 This book is part of the “Atlas of Clinical Oncology” series, edited by Dr Robert Ozols of Fox Chase Cancer Centre, with contributions from that centre or from the National Cancer Institute Sparre program. It is obvious from the start that the contributors are all at the cutting edge of their specialty. 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 sources. 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. M Quinn Royal Women’s Hospital Carlton, VIC PALLIATIVE CARE NURSING A GUIDE TO PRACTICE (2ND EDITION) M’Connor and S Aranda (eds) Published by Aumed 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 the 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 parameters. Inclusion of chapters about sexuality and body image, and psychological and existential distress, among others, adds 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 especially poignant. 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.

J Gibson
Clare Holland House
Canberra, ACT

PHYSICIANS’ CANCER
CHEMOTHERAPY DRUG
MANUAL 2003

E Chu and V DeVita
Published by Blackwell Publishing Asia (2002).
RPP: US$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 accessible and user-friendly book for any professional involved in the prescription or delivery of cytotoxics.

The book is presented in bullet form, except for 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 urine 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 format allowing quick access and drug information at a glance. 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.

R Sharma
Dept of Medical Oncology
Royal Prince Alfred Hospital
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PRACTICAL GUIDE TO INTENSITY MODULATED RADIATION THERAPY

S Hellman
Published by Medical Physics Publishing (2003).
RPP: 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 and basic principles. There is 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 practitioner 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, pancreatic, 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 feasibility 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 in 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.

M Penniment
Dept of Radiation Oncology
Royal Adelaide Hospital
Adelaide, SA

PRINCIPLES AND PRACTICE OF PALLIATIVE AND SUPPORTIVE ONCOLOGY

A Berger et al (eds)
Published by Lippincott Williams and Wilkins (2002).
ISBN: 0-7817-3234-3 1,140 pages plus index.
RPP: A$402.60

There are excellent texts available in anti-cancer therapies and 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 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 – this will be detailed in 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. Survivornship 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.

D Currow
Dept of Palliative and Supportive Services
Flinders University
Adelaide, SA

PRINCIPLES AND PRACTICE OF PEDIATRIC ONCOLOGY (4TH EDITION)

PA Pizzo and DG Poplack (eds)
Published by Lippincott Williams and Wilkins (2002).
RPP: A$605.00

For many years in the field of paediatric oncology there was a relative dearth of reference books containing what is 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 continue to strive to keep their patients and families informed of the latest advances in the treatment of cancer. The eagerly awaited fourth edition however has had major changes to the organisation of both the general sections and chapters. The editors and the contributing authors have succeeded in summarising the explosion in genomic knowledge of paediatric malignancies and in updating the information contained in the previous editions. The book now contains 38 chapters. The editors and the contributing authors have succeeded in summarising the explosion in genomic knowledge of paediatric malignancies and in updating the information contained in the previous editions.

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The book comprises 106 pages – but to curtail some of the discussions would seriously detract from the breadth and depth of information that the book serves as a timely reminder as to the import of further research. The book is commendable for being easy to read and for providing an adequate overview of each of the topic areas.

As in previous editions, the editors have retained the sections on tumour lysis syndrome, the use of urate oxidase is only briefly mentioned. However, these instances are few, and at worst seem to be simply reflections of differences in approach to particular problems. The book does not reference its material, however. Therefore, its pages will be flicked through on a daily basis. Although it is not possible to provide critiques on all chapters of the book, it is worth highlighting the different approaches by different chapters of the book, which makes it an interesting read. The role of the Rb tumor suppressor in cancer by Lili Yamakawa, begins with a short history of the discovery of the Rb gene, then summarizes 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 in discussing both the short- and long-term implications of this summary of mutations in ERα 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.
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 of the indications of rHuEPO 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 rHuEPO not sighted. Furthermore, other terms such as NESP (Novel Erythroid Stimulating Factor), rather than darbepoetin 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 rHuEPO and route of administration. Indeed, can we continue to administer rHuEPO 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.

H M Prince
Dept of Haematology
Peter MacCallum Cancer Centre
Melbourne, VIC

**VIRUSES AND LIVER CANCER**

E Tabor (ed)

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 pathology 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.

J Cobben
Ludwig Institute Oncology Unit
Heidelberg, VIC

**WORLD CANCER REPORT**

BW Stewart and P Kleihues (eds)

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), Noreille Lickiss (palliative care), Guy Maddern (surgical oncology), Bill McCarthy (melanoma), Murray Norris (minimal residual disease), Roger Riddell (telomere), Bernie Stewart (no less so) and Bill McCarthy (melanoma), Murray Norris (minimal residual disease), Roger Riddell (telomere), Bernie Stewart (no less so) and Murray Norris (minimal residual disease). Roger Riddell (telomere), Bernie Stewart (no less so) and Murray Norris (minimal residual disease). Roger Riddell (telomere), Bernie Stewart (no less so) and Murray Norris (minimal residual disease). Roger Riddell (telomere), Bernie Stewart (no less so) and Murray Norris (minimal residual disease). Roger Riddell (telomere), Bernie Stewart (no less so) and Murray Norris (minimal residual disease). Roger Riddell (telomere), Bernie Stewart (no less so) and Murray Norris (minimal residual disease). Roger Riddell (telomere), Bernie Stewart (no less so) and Murray Norris (minimal residual disease). Roger

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/IWCR. I commend it as excellent value.

A Coates
The Cancer Council Australia
Camperdown, NSW

**CALENDAR OF MEETINGS – AUSTRALIA AND NEW ZEALAND**

**CALANDER OF MEETINGS**

<table>
<thead>
<tr>
<th>Date</th>
<th>Name of Meeting</th>
<th>Place</th>
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<tr>
<td>2003</td>
<td>November 15-19</td>
<td>3rd International Symposium on Paediatric Pain: ‘Pain in Childhood The Big Questions’</td>
<td>Sydney NSW</td>
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<td>16-20</td>
<td>9th International Conference on Oral Cancer</td>
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<td>2003</td>
<td>3-28</td>
<td>30th COSA Annual Scientific Meeting</td>
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<td>2003</td>
<td>29-32</td>
<td>Sentinel Lymph Node Biopsy and Block Dissection</td>
<td>Perth WA</td>
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<td>2004</td>
<td>March 4-5</td>
<td>Research for Reality: the 6th National Breast Care Nurses Conference</td>
<td>Brisbane QLD</td>
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<td>2004</td>
<td>April 26-30</td>
<td>18th World Conference on Health Promotion and Education</td>
<td>Melbourne VIC</td>
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<td>May 18-21</td>
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<td>International Society for Nurses in Cancer Care 12th International Conference on Cancer Nursing</td>
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<td>Australia &amp; Asia Pacific Clinical Oncology Research Development (ACORD) Workshop</td>
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<td>Australian Health and Medical Research Congress</td>
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<td>24-26</td>
<td>31st COSA Annual Scientific Meeting</td>
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### CALENDAR OF MEETINGS – International

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<td>XVI FIGO World Congress on Gynecology and Obstetrics</td>
<td>Santiago de Chile, Chile</td>
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<td>9-14</td>
<td>Endocarcinoma Radiation Oncology: Methodological Basis and Clinical Application</td>
<td>Lisbon, Portugal</td>
<td>ESTRO Office Brussels, Belgium</td>
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<td>10th Hong Kong International Cancer Congress</td>
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<td>Department of Surgery University of Hong Kong Medical Centre</td>
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<td>Queen Mary Hospital Hong Kong</td>
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<td>3-6</td>
<td>36th Annual San Antonio Breast Cancer Symposium</td>
<td>San Antonio, Texas, USA</td>
<td>Cancer Therapy &amp; Research Center SACI, Rich Marlow</td>
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<td>15-16</td>
<td>New Insights in Molecular Diagnosis and Therapy</td>
<td>Paris, France</td>
<td>Institut Pasteur Euro-Conferences C15, 26, rue du Docteur-Houx 75724 Paris Cedex 15, France</td>
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<td>22-24</td>
<td>Gastrointestinal Cancers Symposium</td>
<td>San Francisco, California</td>
<td>USA ASCO 1900 Duke Street Suite 200 Alexandria, Virginia 22314 USA</td>
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<td>25-28</td>
<td>Multimodality Treatment in Malignancies Congress</td>
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<td>Tel: +30 210 94 08 750 Fax: +30 210 94 08 753</td>
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<tr>
<td>26-28</td>
<td>40th Annual Meeting of the Society of Thoracic Surgeons</td>
<td>San Antonio, Texas, USA</td>
<td>Society of Thoracic Surgeons Chicago, Illinois, USA</td>
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<td>Tel: +1 312 527 6635 Email: stsgba.com</td>
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<td>American Psychosocial Oncology Society 1st Conference Onco</td>
<td>Orlando, Florida, USA</td>
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<td>2265 Hunters Way Charlottesville, Virginia, USA</td>
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<td>15th International Congress on Anti-Cancer Treatment</td>
<td>Paris, France</td>
<td>Travel Congress Organisation 1 rue du Berni Paris - 75008 - France</td>
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<td>15-17</td>
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<td>7-11</td>
<td>3rd World Assembly on Tobacco Counters Health</td>
<td>New Delhi, India</td>
<td>Avnish Varma ICDAC M-3A, A. RAOUJI GARDEN NEW DELHI - 110027</td>
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<td>16-20</td>
<td>40th European Breast Cancer Conference</td>
<td>Hamburg, Germany</td>
<td>EBCC 2004 Secretariat Federation of European Cancer Societies Avenue E Mouner 83 Brussels, Belgium 1200</td>
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<tr>
<td>18-21</td>
<td>57th Annual Cancer Symposium of the Society of Surgical Oncology</td>
<td>New York City, New York</td>
<td>D.K. Rubin, MD 3725 Soudler, Illinois, USA Email: <a href="mailto:drubin@dakrubin.com">drubin@dakrubin.com</a> Website: <a href="http://www.surgery.org">www.surgery.org</a></td>
</tr>
<tr>
<td>27-31</td>
<td>15th Annual Meeting of the American Association for Cancer Research</td>
<td>Orlando, Florida, USA</td>
<td>American Association for Cancer Research Philadelphia, Pennsylvania, USA Email: <a href="mailto:aacr@aacr.org">aacr@aacr.org</a> Website: <a href="http://www.aacr.org">www.aacr.org</a></td>
</tr>
<tr>
<td>28-3 Apr</td>
<td>43rd Annual Meeting of the Society of Toxicology</td>
<td>Baltimore, USA</td>
<td>Society of Toxicology 1767 Business Center Boston, MA Tel: +1 703 438 3113</td>
</tr>
<tr>
<td>31 Mar-3 Apr</td>
<td>12th Congress of the European Society of Surgical Oncology</td>
<td>Budapest, Hungary</td>
<td>ESRO 2004 Secretariat Federation of European Cancer Societies Avenue E Mounier 83 Brussels, Belgium 1200 Tel: +32 0 2775 0201 Email: <a href="mailto:esso@fecs.be">esso@fecs.be</a> Website: <a href="http://www.fecs.be/conferences/ess04">www.fecs.be/conferences/ess04</a></td>
</tr>
<tr>
<td>April</td>
<td>Oncrology Nursing Society (ONS) 29th Annual Conference</td>
<td>Alexandria, USA, USA</td>
<td>DNS, Meeting Services Team Pittsburgh, Pennsylvania, USA Email: <a href="mailto:meetings@ons.org">meetings@ons.org</a> Website: <a href="http://www.ons.org">www.ons.org</a></td>
</tr>
<tr>
<td>8-13</td>
<td>95th Annual Meeting of the American Urological Association</td>
<td>San Francisco, California</td>
<td>Office of Education Association for Cancer Research 2425 West Loop South, Suite 333 Houston, Texas - 77027-4207 USA Email: <a href="mailto:info@aacr.org">info@aacr.org</a> Website: <a href="http://www.aacr.org">www.aacr.org</a></td>
</tr>
<tr>
<td>June</td>
<td>5-8 40th ASCO Annual Conference for the American Society of Clinical Oncology</td>
<td>New Orleans, LA, USA</td>
<td>ASCO 1900 Duke Street Suite 200 Alexandria, Virginia 22314 USA</td>
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<td>Tel: +1 703 2299 0101 Email: <a href="mailto:asco@asco.org">asco@asco.org</a></td>
</tr>
<tr>
<td>17-19</td>
<td>World Congress on Gastrointestinal Cancers</td>
<td>Barcelona, Spain</td>
<td>Headon Drew Impeax 70 Technology Drive Alpharetta - 75005 - Georgia</td>
</tr>
<tr>
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<td></td>
<td>Tel: +1 700 751 7332 Fax: +1 700 751 7334 Email:  <a href="mailto:asco@asco.org">asco@asco.org</a></td>
</tr>
<tr>
<td>24-27</td>
<td>16th MASCC/SGO International Symposium Supportive Care in Cancer</td>
<td>Miami Beach, Florida, USA</td>
<td>Amy Faber The Cleveland Clinic Center for Continuing Education C/O UTECH Communications 9500 Euclid Ave R 917 Cleveland, Ohio 44195 Tel: +1 216 444 8429 Fax: +1 216 444 8410 Email: <a href="mailto:mascc@fecs.be">mascc@fecs.be</a> Website: <a href="http://www.clevelandclinicmeded.com/mascc/index.htm">www.clevelandclinicmeded.com/mascc/index.htm</a></td>
</tr>
<tr>
<td>25-29</td>
<td>23rd International Congress of Radiology (ICR)</td>
<td>Montreal, Canada</td>
<td>International Congress of Radiology (ICR) 1740 Corte Vista Blvd Saint Laurent Quebec - H4L 2A4 Canada Email: <a href="mailto:info@icr.org">info@icr.org</a> Tel: +1 514 738 3111 Fax: +1 514 738 5199</td>
</tr>
<tr>
<td>July</td>
<td>3-6 18th Meeting of the European Association for Cancer Research</td>
<td>Innsbruck, Austria</td>
<td>EACR 18 Secretariat Federation of European Cancer Societies Avenue E Mounier 83 Brussels, Belgium 1200 Tel: +32 2 2775 0201 Email: <a href="mailto:eacr18@fecs.be">eacr18@fecs.be</a> Website: <a href="http://www.fecs.be/conferences/eacr18">www.fecs.be/conferences/eacr18</a></td>
</tr>
<tr>
<td>22-24</td>
<td>International Skin Cancer Congress</td>
<td>Zurich, Switzerland</td>
<td>Reinhard Dummer University Hospital of Zurich Department of Dermatology Glarnerstrasse 31 Zurich - 8091 Switzerland Tel: +41 1255 8837 Fax: +41 1255 8840 Email: <a href="mailto:diannekubis@acaai.org">diannekubis@acaai.org</a> Website: <a href="http://www.surgonc.org">www.surgonc.org</a></td>
</tr>
<tr>
<td>August</td>
<td>7-11 6th International Conference on Head and Neck Cancer</td>
<td>Washington, DC, USA</td>
<td>Rob Wagner Concepts in Meetings &amp; Events 1805 Andmore Blvd Pittsburgh, Pennsylvania, USA Tel: +1 412 243 5156 Fax: +1 412 243 5160 Email: headandneckcancer.org/</td>
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<tr>
<th>Date</th>
<th>Name of Meeting</th>
<th>Place</th>
<th>Secretariat</th>
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Carcinoma: Eastern and Western Experiences  
Hong Kong  

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<tr>
<th>Name of Meeting</th>
<th>Place</th>
<th>Secretariat</th>
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<tbody>
<tr>
<td>3-6 27th Annual Meeting of the American Society of Hematology</td>
<td>San Antonio, Texas, USA</td>
<td>American Society of Hematology</td>
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<tr>
<td>3-6 11th World Conference on Lung Cancer</td>
<td>Barcelona, Spain</td>
<td>Heather Drew</td>
</tr>
<tr>
<td>16-20 ASTR O: 47th Annual Meeting</td>
<td>Denver, Colorado USA</td>
<td>American Society for Therapeutic Radiology and Oncology (ASTRO)</td>
</tr>
<tr>
<td>17-19 1st International Conference for Oncologists and Other Health Care Leaders</td>
<td>New York USA</td>
<td>Barnes Cafissi</td>
</tr>
<tr>
<td>5-7 11th World Conference on Lung Cancer</td>
<td>Barcelona, Spain</td>
<td>Heatherr Drew</td>
</tr>
<tr>
<td>3-6 46th Annual Meeting of the American Society of Hematology</td>
<td>San Diego California USA</td>
<td>American Society of Hematology</td>
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<tr>
<td>14-18 44th Annual Meeting of the American Society of Hematology</td>
<td>San Francisco California USA</td>
<td>American Society of Hematology</td>
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<tr>
<td>26-29 Primary Therapy of Early Breast Cancer</td>
<td>St. Gallen Switzerland</td>
<td>Hans-Jorg Senn</td>
</tr>
<tr>
<td>23-25 9th Central European Lung Cancer Conference</td>
<td>Garda Italy</td>
<td>Departement of Oncology and Radiotherapy Medical University of Graz</td>
</tr>
<tr>
<td>3-6 58th Annual Cancer Symposium of the Society of Surgical Oncology</td>
<td>Atlanta Georgia USA</td>
<td>D.K. Rubinstein</td>
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<tr>
<td>10-14 10th American Society for Blood and Marrow Transplantation Annual Meeting</td>
<td>Keystone CO USA</td>
<td>American Society for Blood and Marrow Transplantation</td>
</tr>
<tr>
<td>24-28 23rd Annual Meeting of the American Society for Therapeutic Radiology and Oncology</td>
<td>Washington DC 20036 USA</td>
<td>American Society for Therapeutic Radiology and Oncology</td>
</tr>
<tr>
<td>5-7 5th Annual Conference of the World Federation of Neuro-Oncology</td>
<td>Lugano Switzerland</td>
<td>Olga Janseck</td>
</tr>
<tr>
<td>23-26 2nd Quadrennial Meeting of the World Federation of Neuro-Oncology</td>
<td>Edinburgh Scotland</td>
<td>EANZ 6 Secretariat</td>
</tr>
<tr>
<td>11-15 10th International Conference on Geriatric Oncology, Cancer in the Elderly</td>
<td>San Francisco California USA</td>
<td>Heather Drew Imexis</td>
</tr>
<tr>
<td>10-14 EHA 10th Annual Congress</td>
<td>Orlando Florida USA</td>
<td>Oncology Nursing Society</td>
</tr>
<tr>
<td>4-7 41st Annual Meeting of the American Society of Hematology</td>
<td>New Orleans LA USA</td>
<td>American Society of Hematology</td>
</tr>
<tr>
<td>17-19 Memorial Sloan Kettering Cancer Center</td>
<td>New York USA</td>
<td>Barrie Cafissi</td>
</tr>
<tr>
<td>3-6 2004 International Society of Paediatric Oncology</td>
<td>Oslo Norway</td>
<td>Congres Holland BV</td>
</tr>
<tr>
<td>1-4 12th International Society of Endocrinology Congress</td>
<td>Lisbon Portugal</td>
<td>International Society of Endocrinology (ISe)</td>
</tr>
<tr>
<td>30-31 December 2002</td>
<td>December 2002</td>
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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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Professor R Lowenthal MBBS, MD, FRCP, FRACP, FACP
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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.

EXECUTIVE COMMITTEE
President
Dr L Kenny MBBS, FRANZCR
President Elect
Dr S Ackland MBBS, FRACP
Council Nominees
Ms C Cameron RN, OncCent, GrDipN, MNSc
Dr D Goldstein MBBS, MRCP (UK), FRACP
Professor J Thompson BSc(Medi), MBBS, FRACS, FACR, 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