O&G Magazine

Vol 14 No 1 Autumn 2012

Cancer

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists

O&G Magazine

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O&G Magazine authorised by Dr Peter White The submission of articles, news items and letters is encouraged.

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ISSN 1442-5319

Cover image 40888609 ©Shutterstock Optimarc

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Women's health

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From the President

Dr Rupert Sherwood
President

Welcome to the Autumn issue of *O&G Magazine*. Mindful of the extensive reach of this publication among women's health professionals, I want to touch on a range of topics relevant to our College today. First, the theme of this issue, Cancer, exemplifies the focus of the Editorial Advisory Committee on subjects of critical importance to promoting our College motto 'Excellence in Women's Health'.

An excellent list of experts in this field has been recruited to bring a series of articles that cover most aspects of cancer in women's health, in a format that will inform and educate both the specialist and generalist who needs to be continually alert for early presentations of malignancy and aware of the options to allow timely referral to those specialising in this area.

The revised Integrated Training Program (ITP) structure was approved by Council in November, and will apply to those entering the program in 2013. The College regulations that underpin the program are being revised to take into account the new program structure. In addition to the changes being implemented from December 2012, the Board is overseeing two other changes to training:

1. Development of an Academic Stream that will allow those Trainees whose intent is to pursue an academic career to complete a PhD in a field relevant to women's health during, rather than after, the core training. The completed doctorate will be credited as Advanced (post-ITP) Training. The intent of this change is to identify early in training those candidates with aptitude and talent for much-needed research in O and G, who may then progress to become the future leaders of University O and G faculties.
2. An evaluation of flexibility within the training program with respect to managing issues such as part-time training, parental leave and continuity within the program for individuals who take extended leave. Reconciling the two separate, but inevitably linked, roles of RANZCOG as a provider of a structured training program with set objectives based on a curriculum, and the health jurisdictions as employers with an ever-expanding service commitment that has to be met within constrained budgets is a challenge that taxes both Regional and College Training Committees. Currently, 80 per cent of Trainees entering the program are female and the College has a responsibility to ensure equity is maintained for all parties.

Integral to training is assessment, and a significant part of the current work of RANZCOG is developing assessment tools that are both valid and reliable, meeting the criteria that make them 'fit for purpose' in ensuring those who graduate from both our Diploma and Fellowship programs meet the standards set by the College and expected by the community. Several of the subspecialty groups are currently trialling new assessment tools that, it is envisaged, could enhance this process.

After training and qualification, the graduate embarks on a chosen career that includes a commitment to continued learning, practice improvement and further development of professional skills that is the hallmark of the specialist medical practitioner. RANZCOG's Continuing Professional Development (CPD) program will soon be available online, accessed through the individual member's web portal myRANZCOG, with an indivualised self-directed plan encompassing the three curriculum elements of clinical skills, academic and teaching activities, and professionalism. Supported by a growing number of excellent online learning tools, it is envisaged that the College will play an increased role in not only recording CPD points and suggesting projects to enable Fellows to meet the mandatory requirements, but also provide some of the educational resources required to do so.

The annual Activities Report for RANZCOG has been recently produced and will be available online soon. This very valuable summary of the 'output' from the College is both interesting reading and also a very useful resource for members who require facts and figures about the College for jurisdictional interactions.

Intercollegiate collaboration with our colleagues involved in maternity care remains a key aspect of continuing to deliver the highest standard of care. The Joint Committee of Maternity Services (JCMS) was reconvened in December, after several years, and is a meeting of the Presidents and CEOs of the four colleges directly involved in maternity care: Australian College of Midwives (ACM), Australian College of Rural and Remote Medicine (ACRRM), Royal Australian College of General Practitioners (RACGP) and RANZCOG. The Terms of Reference promote a high-level 'think-tank' to promote collaboration, best practice and ensure reforms in maternity care are always in the best interests of woman-centred care.

In addition, an expert group with representatives from ACM and RANZCOG met in December to draft a common Referral Guidelines for guidance of midwives and obstetricians with respect to indications for referral during collaborative care arrangements. This was a very successful meeting, and we await a draft document that will be put to both ACM and RANZCOG executives. Our College is also looking at further avenues for resource sharing with the primary care colleges by making the online resources that underpin the Certificate of Women's Health and Diploma programs available to members of RACGP and ACRRM.

Taking another perspective of collaborative involvement by RANZCOG, I want to bring to the attention of members an organisation of which the College is a founding sponsor: Send Hope, Not Flowers (SHNF). With the very simple, but daunting, aim of making an impact on the frighteningly high maternal death rate in our near neighbours PNG and Indonesia, SHNF was founded by RANZCOG Fellow and board member A/Prof Stephen Robson. The website http://www.sendhope.org tells in few words and pictures why this is a Millennium Goal, and how simple small acts of charity by those of us fortunate enough to have been born in two of the safest maternity environments in the world can and will make a difference.

Important meetings in 2012 include our own ASM in Canberra in September, the International Urogynaecological meeting in Brisbane (IUGA), chaired by Prof Chris Maher, Provincial Fellows meeting in Mackay (April) and other regional meetings, all of which involve substantial time and effort to stage, for which the

Board and I are always grateful. On a similar note, I should like to congratulate Andrew Ngu on his appointment as the President-Elect of the International Society of Ultrasound in Obstetrics and Gynaecology (see page 64). The College website has a detailed calendar of both local and international meetings. RANZCOG is also participating in the biennial Breathing New Life conference to be held in Melbourne in May, which brings together midwives, obstetricians and other maternity health professionals to discuss and debate a range of issues.

RANZCOG participation in a range of external committees and working groups relevant to women's health forms an important part of the contribution Fellows make to maintaining a voice in groups dealing with, among other things, perinatal and maternal data collection, delineating and defining models of maternity care, monitoring sentinel high-morbidity obstetric outcomes (via the Australasian Maternity Outcomes Surveillance System), e-Health and the development of the personally controlled electronic health record, and ongoing negotiations over the ultrasound reaccreditation private practices using mainly self-referred MBS item numbers.

> 'I look to both Fellows and College staff for their continued support and contributions to ensure the organisation maintains its pre-eminent position as a leader in women's health care in both Australia and New Zealand.'

In my last eight months as President, I will be involved in a wide range of meetings and activities at which I hope to actively promote the College and our RANZCOG 'brand'. As well as attending the always enjoyable New Zealand Annual Scientific Meeting (Rotorua) and Provincial Fellows Meeting (Mackay), I will attend a meeting of the South African Academy of Medicine, at which leaders from O and G colleges from several nations including the USA, UK and Canada will be present to discuss issues relevant to education and training in our specialty. In May, I will represent RANZCOG at the American College meeting in San Diego and, in June, present a plenary paper on RANZCOG's role in training and capacity building in the Oceania Pacific region at the RCOG international meeting in Malaysia.

RANZCOG is hosting a meeting of the Asia Oceania Federation of O and G (AOFOG) in Fiji during June, along with some workshops that aim to provide onsite training for Fiji School of Medicine O and G Trainees, using the expertise of the AOFOG faculty attending the Council. Dr Ngan Kee and I will be leading a working party to review the governance of the AOFOG organisation.

In March, the Council will elect the incoming President to lead the eighth RANZCOG Council from November of this year. Before handing over the wheel of what my predecessor, Dr Weaver, referred to as the 'good ship RANZCOG' there is much work to be done and, as always, I look to both Fellows and College staff for their continued support and contributions to ensure the organisation maintains its pre-eminent position as a leader in women's health care in both Australia and New Zealand.

From the CEO

Dr Peter White
CEO

It is with great pleasure that I write 'From the CEO' for this Autumn issue of *O&G Magazine*. I was fortunate enough to be able to take a period of leave in the second half of 2011 – during which there was an alteration to what had become a seasonal routine that had run for almost six years, with Valerie Jenkins writing the column for the Summer 2012 edition – as my family and I adjusted to a different seasonal routine in the northern hemisphere.

My thanks go to Valerie for sitting in the CEO's chair during the time that I was away; an act that surely reinforced the adage that 'no-one is indispensable'. Having spent a period of time in a French provincial town off the regular tourist trail, where we slowly adjusted to the pace of life that governs activities there, including my two children experiencing a term of school in a foreign-speaking system with noticeably different pedagogy and routines, the return to Melbourne reminded me very quickly of the pace of life in a modern city and a job of the kind that I am fortunate to occupy.

November saw the RANZCOG Annual Scientific Meeting (ASM) in Melbourne. As is now standard for such meetings, the program incorporated days dedicated to College Diplomates, as well as workshops addressing specific needs of Fellows in both the clinical and non-clinical aspects of practice. As was the case in Adelaide in 2010, newly elevated Fellows were welcomed to the meeting, with complementary registration for the main meeting, and it was encouraging to note the attendance of 70 recipients and their families to receive their Fellowship or subspecialty certification from the President at the opening ceremony. Based on feedback received from attendees, sponsors and exhibitors, the meeting can clearly be categorised as successful and my thanks go to Prof Michael Permezel, Chair of the Organising Committee, and Prof Euan Wallace, Chair of the Scientific Committee, and their teams, for their efforts.

The meetings are, in my view, one of the showcase examples of the partnership approach between College members and College staff, and the College staff involved in the ASM, led by Kylie Grose, Val Spark and Lee-Anne Harris, also deserve congratulations for the role they played in making the meeting a success. Even before all is finalised in regard to the Melbourne meeting, work is well underway in regard to this year's meeting in Canberra (9 to 12 September), and meetings of the organising Committee responsible for the 2013 meeting to be held in Sydney

have already taken place. It is hoped that the 2015 meeting in Brisbane will be held in concert with the 12th International Scientific Meeting of the RCOG and we keenly await definite advice from the RCOG in regard to the success of our bid to host that meeting.

> 'Through the generous support of the Victorian Managed Insurance Authority (VMIA), the College has been fortunate to secure the exclusive rights to conduct PROMPT training services throughout Australia and New Zealand.'

Along with regional scientific meetings and other offerings, the ASM is an example of the College's desire to deliver worthwhile professional development activities that represent value for members. As Fellows are aware from information previously published in *O&G Magazine*, during 2010 the College conducted a trial of a revised Continuing Professional Development (CPD) program, which uses a framework modelled on the Profile of an O and G Specialist contained in the RANZCOG Curriculum.

The framework enables a wide range of activities to be recognised for the purposes of College CPD and Fellows to tailor CPD activities to reflect their practice profile and education needs as their scope of practice and/or areas of interest alter over time. It is anticipated that the revised program will be introduced on a staged basis to Fellows from late this year, with a highly functional online capacity to complement the revised program currently under development. Future editions of *O&G Magazine* will keep readers appraised of information in relation to this, as well as other initiatives currently being progressed in the College, including the revised training program due for introduction with the next intake of trainees (from December 2012 in New Zealand).

In the Spring 2011 edition of *O&G Magazine* I wrote of the pending retirements of Valerie Jenkins, manager, fellowship services, and Bob Kelly, finance manager. While winding down her College commitments, Valerie has elected to stay on to assist the College with the implementation of the PRactical Obstetric MultiProfessional Training (PROMPT) Course. Through the generous support of the Victorian Managed Insurance Authority (VMIA), the College has been fortunate to secure the exclusive rights to conduct PROMPT training services throughout Australia and New Zealand. This is an exciting initiative for the College, which will no doubt benefit many involved in the delivery of maternity services in Australia and New Zealand, and I welcome Valerie's willingness to continue at RANZCOG to ensure the successful implementation of PROMPT.

Bob Kelly retired from the College in January after more than a decade of service. Bob contributed much to the College in his time as Finance Manager and was formally farewelled by me and the President at a staff function in December. On behalf of all members of Council, with whom Bob worked over time, I thank him for his contributions.

Partly as a consequence of the scaling back of Valerie's commitments and Bob's retirement, I have taken the opportunity to make some changes to the College organisational structure. Bob's replacement is Damian Waters. Qualified as a CPA and possessing an MBA in strategy and planning, as director of finance and infrastructure, Damian will have responsibility for the College's financial matters, as well as the strategic and operational aspects of College ICT and day-to-day oversight of risk management. Penelope Griffiths continues as director of corporate services and has assumed the role of deputy CEO. Lyn Johnston continues as director of education and training, while Anne Robertson is the director of women's health.

Having four senior college staff leading four recognised organisational subunits that link directly to the designated areas of responsibility of the three College Vice Presidents and Treasurer, enables a more efficient reporting process.

> 'I urge any College member not currently involved in College business to become so...the rewards can be satisfying and long-lasting on both a professional and personal level.'

As always, members of College staff are aware that the overriding priority is to work with the College Board, Council and membership to deliver the services that constitute the core business of the College and continually improve the organisation. As CEO, I never lose sight of that objective and the range of activities currently being progressed are testament to the endeavours of all involved.

The first meeting of the College Board for 2012, recently held in Wellington – following a meeting of the New Zealand Committee the day before, as well as a satellite meeting between representatives of the College and representatives of the Medical Council of New Zealand – reinforced an awareness of the range of tasks with which the College is required to deal. Three days later the written examinations for the first half of the year were held, two days after that the Presidents and CEOs of the member Colleges of the Committee of Presidents of Medical Colleges (CPMC) held the first of four meetings scheduled for the year, and Council and associated Committee meetings, along with the second meeting of the College Board for the year, are only four weeks away.

As ever, I urge any College member not currently involved in College business to become so. While perhaps not tangible, nor even readily apparent in advance, the rewards can be satisfying and long-lasting on both a professional and personal level.

Cancer

A/Prof Stephen Robson
FRANZCOG

My mother's death from cancer, a couple of years ago now, was the worst experience of my own life. It played out over almost exactly six months (the median survival for her condition), during which time she was devitalised to a husk I barely recognised. The experience had profound effects on my immediate family, ripples of which lap at our lives still.

The drama of slow and inevitable death that cancer may bring will be familiar to many reading these words. Shock and disbelief, with plenty of anger at times. Denial. The trials of radiotherapy and chemotherapy. The clutching at straws.

I recently read the ambitious and sweeping 'biography' of cancer, The Emperor of All Maladies, by oncologist Siddartha Mukherjee. Every doctor who has any contact with patients affected by cancers should consider reading it. Through its pages, Dr Mukherjee traces the impact of cancer and its treatment from antiquity to the present day. It is a book of hope. I thoroughly recommend it.

Gynaecological cancers will reveal themselves in our clinical practice with some regularity, but unless our work is closely allied to oncology it can be difficult to keep pace with changes in their management. In this issue of *O&G Magazine*, we have asked a group of experienced cancer specialists to share their insights with us. You will find reviews of most of the important cancers relevant to our specialty, with overviews of how we should approach and deal with them. This should provide an invaluable guide to managing the women whose care is entrusted to us. As always, the team here at *O&G Magazine* has striven to provide our readers with access to the best advice our colleagues in Australia and New Zealand can provide. In these pages you will find information on every aspect of gynaecological cancer care and, perhaps most importantly, optimism.

My own impressions of cancer are indelible. So many of those who read this will have had experiences similar to mine. My colleagues and I hope that you find this issue of *O&G Magazine* valuable in your practice. As always, we welcome and look forward to your thoughts and comments.

The way we live now

Prof Jonathan Berek
FACOG, FACS
Chair, Department of O and G
Stanford University School of Medicine
Director, Stanford Women's Cancer Center
Stanford Cancer Institute

Prof Neville Hacker
FRANZCOG, CGO
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It is now over 30 years since we were gynaecological oncology Fellows together in the late 1970s at the University of California in Los Angeles. Since that time, there have been enormous improvements in the way women with gynaecological cancers have been managed in most parts of the world.

Undoubtedly, the biggest single improvement has been the progressive subspecialisation in gynaecological oncology in many centres in Europe and Asia, following the lead of the USA in 1973. Australia was an early adopter of this important change, with the then RACOG officially recognising gynaecological oncology as a subspeciality in 1985. This soon led to accreditation of grandfathers and establishment of approved training centres. Gynaecological oncologists cannot work in isolation, so the next step was the establishment of gynaecological cancer centres in all major cities and the development of multidisciplinary teams of medical specialists, oncology nurses and paramedical personnel with a particular interest and expertise in gynaecological cancer. With the concentration of expertise in major centres, all modalities of treatment can be used optimally as each new case is discussed at multidisciplinary tumour board meetings. In addition, patients can be offered the psychosocial support, which is so important in the patient's journey.

The founding of the International Gynaecologic Cancer Society, in 1987, brought together clinicians, scientists and paramedical personnel from around the world, bound by a common interest in gynaecological malignancies. This society has done much to improve the standard of gynaecological cancer care and to facilitate dialogue between professionals internationally.

Thirty years ago, surgery was all performed by open laparotomy and teaching was done as a master-and-apprentice model. In the past 20 years, minimally invasive surgery has been progressively introduced, initially with the laparoscope and, more recently, with the daVinci robot. Use of these devices has led to longer operating times, but faster postoperative recoveries. Indications for these approaches have been progressively expanded, but it will be some time before properly controlled trials determine their exact role. Learning curves are certainly longer than for open surgery, and it is no longer acceptable to 'practise' these skills on patients. The necessary surgical skills should be acquired outside the operating room on various inanimate and animal practice models.

The incidence of cervical cancer has fallen in developed countries, with better cervical screening, and will continue to fall further with the introduction of the HPV vaccine. The incidence of ovarian and endometrial cancers continues to rise as the population ages as well as with the obesity epidemic sweeping Western countries.

As cure rates improve for most cancers, quality-of-life issues have become increasingly important. Conservative vulvar resections have been progressively introduced for invasive vulvar cancer and these have been shown to decrease morbidity, without compromising survival. The possibility of using sentinel node biopsies rather than full lymphadenectomy has been investigated for early vulvar, cervical and endometrial cancers to decrease the incidence of lower limb lymphoedema. Although theoretically attractive, these procedures carry a definite false negative rate and most patients, properly informed, are not prepared to risk death from recurrent disease.

With women now delaying childbearing until well into their 30s, there is an increasing demand for fertility-sparing surgery, which was not a major issue 30 years ago. The introduction of the radical trachelectomy for early cervical cancers and accumulating data on uterine and ovarian conservation for unilateral ovarian and early endometrial cancers has enabled selected women to maintain their childbearing capability, while being treated effectively for their malignancy.

Ovarian cancer remains a major diagnostic and therapeutic problem. A successful screening test has remained elusive. Although median survival times have been prolonged and survival rates for all stages have improved somewhat over the past 30 years, overall five-year survival remains below 50 per cent. Cisplatin was introduced into routine clinical practice in the late 1970s, and proved to be a major therapeutic advance. It was replaced by the equally effective, but less toxic, carboplatin in most regimens. The introduction of the taxanes, in the 1990s, incrementally improved survival rates. Efforts are underway to find new cytotoxic drugs that are well tolerated and agents that aim to control growth through blocking other targets, such as the vascular endothelial growth factor, tyrosine kinase receptors and other molecular pathways.

The major hope for the future is the explosion in genetic and molecular research, particularly since the completion of the Human Genome Project in 2003. The discovery in the mid-1990s of germline mutations BRCA1 and BRCA2 defined those women at substantially higher risk of developing ovarian cancer. For these women, prophylactic removal of fallopian tubes and ovaries is presently the best course of action. The elucidation of other germline mutations – such as the recent discovery of ARID1, which predisposes to clear cell and endometrioid tumours – will hopefully lead to targeted therapies for women with those tumours. Although many relevant cellular pathways have been elucidated and therapies that specifically target those pathways are being developed, there is a long road ahead to find better ways to individualise treatments based on tumour type and the inherent biologic behaviour of different types of ovarian malignancies. Further genetic and molecular research is likely to lead to major screening, prognostic and therapeutic advances in the future.

Under the microscope

Dr Louise Farrell
FRANZCOG

Cervical screening in the era of human papilloma virus vaccination: is the Pap smear test still the best technique available?

In 2006, the Gardasil® human papilloma virus (HPV) vaccine became available in Australia. In 2007, the government program for free vaccination for young women was commenced. Initially, there was a catch-up program for young women up to 26 years of age and there is the ongoing program for girls aged 12–13 years. Overall, there has been good take up of the vaccine. It protects against infection with HPV 16 and 18, which in Australia represents more than 70 per cent of cervical cancers and approximately 50 per cent of high-grade squamous intraepithelial lesion (HSIL) abnormalities. There is also some cross protection against some other high-risk (HR) HPV types.

We expect that we will see a drop in the numbers of high-grade abnormal cytology within a fairly short time frame.[1] In low-prevalence populations cervical cytology does not perform as well as in populations with high levels of cervical disease.[2] The principle strength of cervical cytology is, while it may have low sensitivity, it generally has good specificity. HPV testing, on the other hand, has excellent sensitivity with poorer specificity. For many women, HPV carriage is transient and it is only persistent carriage that results in intraepithelial lesions developing in the cervix. The specificity of HPV testing, however, does improve in women over the age of 30 years.

> 'It has become apparent that various HPV detection methods vary in their clinical performance, with specificity varying substantially.'

There have been many trials comparing HPV testing with cervical cytology either as a standalone screening method or as a triage tool where cytology is inconclusive, including:

- New Technologies in Cervical Cancer (NTCC)[3];
- ARTISTIC trial[4];
- POBASCAM[5];
- Sweedscreen[6]; and
- Finnish trial[7].

These trials have confirmed that HPV testing is more sensitive than cytology in detecting HSIL lesions and the negative predictive value of an HR HPV test is about six per cent higher than that of a negative cytology test. The improved negative predictive values should allow for longer screening intervals. In the studies that followed women over two screening rounds, an average reduction of about 50 per cent in the HPV arm was shown in the second screening round. The NTCC trial was sufficiently powered to show a significantly better prevention of cervical cancer in the HPV arm.

So the Pap smear, which has been the screening tool for cervical cancer since cytology-based programs were introduced in the mid-20th century and has resulted in a significant reduction in cervical cancer in screened women, has come under threat as unequivocally the best tool for primary screening. In 2011, the Netherlands Health Council advised the Ministry of Health in the Netherlands to implement HR HPV testing as the primary test in cervical cancer screening for women aged 30–60 years, with cytology triage for those testing positive. It has suggested that screening be performed at 30, 35, 40, 50 and 60 years of age. With this screening program, the Netherlands will become the first country with an HR HPV-based screening program and triage with cytology that involves only five lifetime screening rounds.[8]

HPV tests suitable for clinical use became available in the 1990s. Some countries (such as New Zealand, the UK and USA) incorporate their use in triage for colposcopy in women with inconclusive or low-grade changes on cytology. In Australia, in 2006, the National Health and Medical Research Council (NHMRC) recommended HPV testing only for test of cure after treatment for high-grade abnormalities.

In New Zealand, the National Cervical Screening Programme guidelines recommend HR HPV testing in three clinical situations:

1. women 30 years and older with ASC-US or low-grade changes, to help assist risk of progression (as they use liquid-based cytology in New Zealand, this is performed reflexly by the laboratory);
2. women (all ages) treated for a high-grade lesion, to help assess whether the lesion has been completely resolved; or
3. where colposcopy has shown discordant results from cytology, to help interpret these results.

The last few years have seen an increase in the number of alternative tests for detection of HR HPV DNA. It has become apparent that various HPV detection methods vary in their clinical performance, with specificity varying substantially.

There have been a number of methods by which the specificity of the HPV test can be improved. One is genotyping. For the ALTS trial it was recognised the HPV carriage with types 16 and 18 carried far greater significance than HPV carriage with one of the other high-risk types.[9] Some of the newer tests do allow for identification of HPV 16 and 18.

Viral load is known to be significant. It is important that HPV tests are not so sensitive that they pick up clinically unimportant infections

with low viral loads that are generally not associated with HSIL.[10] However, higher viral loads are known to be associated with a higher risk of HSIL.

Another marker of significant disease has been over expression of $p16^{INK4a}$. In the NTCC if only women with over expression of p16 were referred for colposcopy, there was no increase in referral for colposcopy, but HPV testing still gave an improved sensitivity of 1.53 over cytology.[3]

Testing RNA of E6 and E7 has also shown promise, as levels increase with lesion severity. There is available a nucleic acid sequence-based amplification (NASBA) based assay detecting E6/E7 transcripts from the five most common HR HPV types (PreTect, HPV-Proofer, NorChip AS are some of these). Gen-Probe is currently developing the APTIMA® HPV Assay targeting E6/E7 mRNA from 14 HR HPV types.[11]

There are three principle technologies used for HR HPV DNA detection assays:

1. hybridisation followed by signal amplification
   hybrid capture 2: RNA probe cocktail (HC2; Qiagen)
   invader technology: third-wave invader HPV test (Cervista);
2. broad spectrum PCR
   DNA amplification with consensus primers or multiplex format (some labs have in-house PCRs; Abbott - Real time HPV test, Amplicor HPV & Linear Array HPV Genotyping); and
3. in situ hybridisation (ISH)
   used for years for research into HPV (Ventana Inform the only commercially available and recommended for histological material only).[13]

The following HPV tests are available in Australia:

- Digene or Hybrid Capture® 2 (HC2) – used in the ALTS trial, there is a lack of internal control for input DNA and it does have some cross reactivity with low-risk types. It will not identify specific HPV types.
- In house PCR – this is the most sensitive technique, it allows for testing on samples with fewer cells. Contamination can be an issue. It is capable of type distinction. There is no external validation.
- Cervista (Hologic) FDA approved (invader technology) can distinguish HPV 16 and 18 from other high-risk types. There is internal control for input DNA.
- Abbott Real time HPV test (PCR) provides the most accurate type-specific measure of viral load.
- Roche Cobas 4800 HPV test – used in the Athena trial, it has an internal control and can identify HPV 16 and 18 infections.

The cervical screening program in Australia has been hugely successful; leading to the country having one of the lowest rates and mortality for cervical cancer in the world. However, our understanding of the disease, and the technologies available, has increased dramatically since the introduction of the screening program. We have fallen behind the rest of the world in embracing new technologies. Fortunately, a review of the entire cervical screening program has begun and it is likely that there will be great changes.

I believe that, ultimately, HPV testing will become part of the routine screening program in Australia, as it is in New Zealand, but there are many developments and advances in this testing. The positive predictive value of HPV testing will also decline in the vaccinated population due to removal of all the HPV 16 and 18 lesions, which have much higher association with significant lesions than the other non-vaccine high-risk types. Thus it will become important to use and expand the other methods of improving specificity of HPV testing if it is to be used as a screening tool.

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Risk-reducing surgery

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Prophylactic risk-reducing surgery is being performed more frequently as women and their medical practitioners become more aware of the genetic and hereditary factors involved in some gynaecological malignancies.

Even before the identification of the BRCA1 gene, in 1994, and BRCA2, in 1995, linkage studies had clearly shown a heritable risk factor in some cases of ovarian and breast cancer. This has been extended with the identification of mis-match repair (MMR) gene abnormalities in Lynch Syndrome and the increased risk of ovarian and endometrial cancer in this condition.

The mechanics of risk-reducing surgery (RRS) are only a minor part of the overall treatment of women being counselled about this intervention. In general, a woman who perceives her risk of gynaecological malignancy is sufficiently high to warrant surgical intervention should:

- have a thorough family history taken, which includes male relatives; and
- consider referral to a Familial Cancer Clinic (FCC) to try and define the actual risk, not only for the woman herself, but also for other family members.

This may include specific genetic testing, but there are many situations where this may not be possible or the results are uninformative. However, the involvement of a FCC does broaden the perspective by looking at other associated malignancies and options for screening and early intervention for the patient and her family. A comprehensive overview of recommendations for the management of women at high risk of ovarian cancer is available at the Cancer Australia website: http://guidelines.nbocc.org.au/guidelines/high_risk_ovarian/ .

> 'The mechanics of surgery are only a small part of the process of RRS in high-risk or potentially high-risk women.'

Initial discussions with a woman about RSS will often focus on the surgery itself. What should be removed and how will this be performed? An essential part of the surgery is careful inspection of the 'at risk' peritoneal cavity and complete removal of the at-risk structures. Numerous case reports of malignancy in residual ovarian tissue in women who had undergone oophorectomy highlight the importance of complete removal of all ovarian and extra-uterine fallopian tube. This effectively means a vaginal-only approach to the surgery is inadequate. There is no evidence to support either laparoscopy or laparotomy as being superior in terms of malignancy risk reduction and the decision as to the mode of surgery should be made on the basis of the usual risk factors and operator experience. The mechanics of surgery are only a small part of the process of RRS in high-risk or potentially high-risk women. Apart from discussing the nature, aims and risks of the surgical procedure, many other issues will need to be clarified prior to performing any surgical procedure.

Is a hysterectomy required?
Despite initial concerns about an increased risk of serous endometrial cancer in women with BRCA mutation, this has not been shown to be true in subsequent studies. There is no current evidence to support routine prophylactic hysterectomy as an effective part of RRS for potential high-risk or known BRCA mutation carriers.

As Lynch Syndrome is associated with more than 50 per cent lifetime risk of endometrial cancer and ten per cent lifetime risk of ovarian cancer, hysterectomy is an essential component of RRS in this condition.[1]

What is the risk of malignancy after RRS?
Removal of the tubes and ovaries is associated with a marked reduction in the risk of ovarian cancer. Domchek et al have reported a marked reduction in gynaecological cancer and death in women with a BRCA mutation undergoing RRS.[2] Rarely, primary peritoneal cancer can occur after RRS. The risk of primary peritoneal cancer after gynaecological RRS appears to be approximately one per cent and there is no evidence that screening for this condition after RRS is effective or beneficial.[1]

There is limited data published on the efficacy of RRS in Lynch Syndrome, but what is available supports a marked reduction in the frequency of gynaecological cancer after RRS.[1]

A secondary effect of RRS with removal of the ovaries in pre-menopausal women with BRCA mutation is a significant reduction (approximately 50 per cent) in the risk of breast cancer.[1,3]

Several studies on prophylactic bilateral salpingo-oophorectomy (BSO) in women with BRCA mutations have reported occult cancer in four to 12 per cent of cases. It is therefore important to explain that a small number of women undergoing RRS may require further treatment.

Management of menopausal symptoms.
Women with surgically induced menopause more commonly report night sweats, sleep disturbance, hot flushes and decreased libido and have significantly more severe vasomotor symptoms than women who go through natural menopause.[4] However, Finch et al reported that physical and mental health-related quality of life for most women did not deteriorate after RRS in BRCA mutation carriers.[5]

Hormone replacement therapy (HRT) appears to control some, but not all, of these symptoms. There is no apparent increase in risk of breast cancer in BRCA1/2 mutation carriers, unaffected by breast cancer, who take short-term HRT after RRS performed before the age of 50 years compared to those who do not take

HRT. Domcheck reported that HRT following RRS for BRCA mutation carriers was not associated with an increased risk of breast cancer, however, the length of follow up is limited.[6]

There is no reason to believe that non-hormonal measures to control menopausal symptoms after RRS would have different efficacy or risks compared to those seen in the general population. Longer term implications of premature menopause and possible interventions to prevent or deal with these problems should also be clearly explained and, if necessary, implemented.

Despite the effects of RRS on hormonal function in premenopausal women, follow up at 12 months suggests that less than five per cent regret the decision to proceed with surgery and the reduction in anxiety about developing ovarian cancer was a major factor in this overall level of satisfaction.[7]

Timing of surgery

The risk of ovarian cancer in BRCA1 carriers starts to increase from the age of 40 years and several years later for BRCA2 carriers. RRS should be considered from the age of 40 years and include complete removal of the extra-uterine component of both fallopian tubes as well as ovaries.

The beneficial effects of RRS on the overall reduction in breast cancer risk are seen only in premenopausal women and are most apparent when RRS occurs at about 40 years.

Lynch Syndrome is associated with an increasing risk of endometrial cancer from the mid 30s and ovarian cancer from the early 40s. There is no evidence to support screening for endometrial cancer in Lynch Syndrome so RRS to remove the uterus, tubes and ovaries should be considered from the mid 30s.

Our understanding of the pathogenesis of ovarian cancer has changed markedly in recent years and we are now aware that many supposed ovarian cancers probably arise in the fimbrial part of the fallopian tube.[8] Microscopic malignancy identified at the time of prophylactic BSO in BRCA mutation carriers appears to show that a significant number (50–60 per cent) of high-grade serous tumours arise in the fimbria without involvement of the ovary.[9] This finding has led to some speculation that prophylactic salpingectomy may be appropriate RRS but there is no data to support this procedure as being equivalent to prophylactic BSO at this time.

These recent findings have significant implications for clinical practice for both the surgeon and pathologist. The possibility that a microscopic tumour may be present in the delicate fimbrial tissue means that tubes and ovaries need to be handled with care during the operative procedure and removed intact to allow for thorough pathological examination. Morcellation of tubes and ovaries during delivery through laparoscopic ports should be avoided.

The pathologist should be made aware of the reason for the prophylactic surgery. Occult cancers involving the tubes and/ovaries will frequently go unrecognised unless ultrasectioning of the specimens is undertaken.[10] This will only occur if the gynaecologist informs the pathologist of the reason for the surgery. The finding of an occult tubal or ovarian cancer has significant impact on the woman's need for further treatment and ultimate prognosis.

RRS for gynaecological malignancy is a far more complex event than just removing the 'at risk' organs.[11] The treating gynaecologist should never regard this as just a technical exercise and time must be spent with the patient and often her family explaining the reason for surgery, the benefits and risk of intervention and ensuring the long-term sequelae are dealt with adequately.

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The genetics of cancer

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Attempts to understand the genetics of cancer have revealed, in considerable depth, mechanisms of tumorigenesis and drug resistance. Rapid technological advances will further improve our ability to study genes and their impact on cancer and its treatment. However, the interpretation of this story requires ever-increasing care, with important implications for clinical trial design.

The genetics underlying cancers are relevant for both inherited and non-inherited (sporadic) cancer. Inherited predisposition can be proven (as in the case of a person proven to have inherited a pathological mutation in a cancer predisposition gene), inferred (from a pedigree consistent with a dominantly inherited mutation in a high-penetrance predisposition gene, even if such a gene has not yet been documented in that family) or surmised, in a group of families in which the incidence of two related cancer types, for example, seems to be higher than predicted for that general population.

On the other hand, a 'sporadic' case of cancer is diagnosed in a family with no other relevant family history. However, we know that in some families one case may be the harbinger of a subsequent family constellation of related cancers, for which an inherited family-specific mutation in a relevant cancer predisposition gene may eventually be identified. For example:

1. a young case of osteosarcoma, suggestive of a 'Li Fraumeni' family in which a mutation in the guardian of the genome, p53 may be present, if subsequent cases of breast cancer are diagnosed[1,2];
2. a woman developing triple-negative breast cancer, aged less than 35 years at diagnosis[3], followed by other breast and/or ovarian cancer cases; or
3. a woman with high-grade serous ovarian cancer, aged less than 50 years at diagnosis[4], followed by other breast and/or ovarian cancer cases.

High-penetrance founder mutations, such as in BRCA1/2, occurring in either the Ashkenazi Jewish[5] or Icelandic[6] populations, involve a higher than expected rate of carriage of the relevant mutations compared with the general population. More confusingly, even with mathematical modelling, are population effects of what are presumed to be moderate-strength or low-risk cancer predisposition alleles, the latter having been identified in genome-wide association studies.[7] At present, the impact of mutations in moderate-risk predisposition genes (CHEK2, ATM, BRIP1, PALB2 and NBS1)[8] or low-risk alleles are difficult to interpret. It is even more difficult to accurately estimate, at a population level, the precise impact of such genes on the rate of cancer in a given population. It is thought these alleles may act in concert, for example, with three or more genes potentially predisposing to a particular type/subtype/s of cancer (polygenic risk).[8] However, to accurately determine the effects of potentially inheriting a set of such alleles, for one woman, or one family, remains beyond our reach. It is worth noting, therefore, that proving that a particular case of cancer is indeed 'sporadic' could be quite difficult.

Much has been learned from studying inherited cancer predisposition genes. The way in which our knowledge of cancer genetics has developed over the last three decades has illustrated many salient points important for our general understanding of disease today. We have stumbled across important genes and later learned their function, by following the flags of rare, obviously inherited cancers. In doing so, we have learned much that is now of critical relevance for larger populations of patients who have cancer that is deemed to be sporadic in origin. This is exemplified by the discovery of genes underlying some breast and ovarian cancers, as described below.

Of great importance are the functions associated with the list of inherited, in many cases rare, cancer predisposition genes.[9] Together these functions highlight most of the important 'machinery-gone-wrong' malfunctions involved in the genesis, propagation and, often, drug resistance underlying the lethality of sporadic cancer. Historically, the function of many of these genes was elucidated following a lengthy period of basic research, made possible by the identification of the gene underlying a striking inherited familial phenotype, for example that of the Retinoblastoma gene (Rb)[10], or of familial breast and ovarian cancer (BRCA1)[11] or familial female and male breast cancer (BRCA2).[12]

Many genes important enough to cause a high-penetrant cancer syndrome are tumour suppressor genes with crucial roles in regulation of the cell cycle, DNA repair and programmed cell death or apoptosis.[9] Much rarer are examples of inherited oncogenes, such as the RET oncogene that causes the MEN2 syndrome, including tumours such as medullary thyroid cancer.[13] What we do not understand well, is why some genes, involved in such critical processes, affect only certain tissue types. Most of the known familial cancers have 'diagnostic' specificity, for example: BRCA1 is associated with breast, ovarian and prostate cancers[11] (perhaps all hormonally linked); BRCA2 is associated with breast, ovarian (to a lesser extent than for BRCA1), prostate, melanoma and pancreatic cancer[14]; indeed, the guardian of the genome itself, p53, is associated predominantly only with soft-tissue sarcoma, breast cancer and haematologic malignancies[15]; PTEN is involved in Cowden Syndrome, involving thyroid cancer and breast cancer[16]; and the Lynch Syndrome genes (MLH1, MSH2, MSH6) are involved in bowel, uterine and ovarian cancer and cancers of the uroepithelial tract.[17] Such tissue specificity is relatively strict and yet the molecular basis for it is largely unknown.

In order to illustrate many of the principles outlined above, the story begins with the analysis of the very well-documented large kindreds involving breast and ovarian cancer that resulted, in 1994, in the identification of BRCA1 (so-named because it was the first gene to be associated with inherited breast cancer).[11] It was thought the identification of BRCA2, 3, 4 and so on would rapidly follow and yet even BRCA2 remained elusive until pedigrees involving another discrete phenotypic feature were studied, that of the inclusion of male as well as female breast cancer.[12] In fact, BRCA3 and 4 remain as yet undiscovered, in the sense that, although we have identified additional breast cancer susceptibility genes associated with breast and/or ovarian cancer, such as ATM, PALB2 and RAD51C and D, each of these accounts for only a very small number of families and is thought to confer mostly moderate risk (higher risk in some families), leaving the bulk of families, especially, with 'breast cancer only' as yet unexplained in a genetic sense.

Following the discovery of these genes, much basic research ensued that rapidly defined essential roles for BRCA1[18] and BRCA2[19] in DNA repair, particularly in the high-fidelity pathway of homologous recombination (HR). The defect in DNA repair was present only in the cancer cell (which had obligate loss of the wildtype allele), but not in the rest of the patient's body (in which the cells were heterozygote for the gene concerned and therefore retained normal protein and DNA function). It was logical to hypothesise that a defect in one important DNA repair pathway might be exploited by creating a 'synthetic lethal' setting, with the addition of a pharmacologically driven defect in a complementary DNA repair pathway.[20,21] This approach led to the development of potent inhibitors of PARP, important for Base Excision Repair (reviewed in[22]). Indeed, results to date of PARP inhibitors in high-grade serous ovarian cancer are impressive, both in patients documented to carry a mutation in BRCA1 or BRCA2[23] and in patients with 'sporadic' high-grade serous ovarian cancer (reviewed in[22]). It is likely that up to approximately 50 per cent of high-grade serous ovarian cancers have a 'BRCAness-like' defect, due to a variety of molecular mistakes in wiring of the DNA repair machinery.[24] A functional test or easy molecular test to identify this phenotype is not yet available, but would be of great utility.

The likelihood that we could improve the targeting of PARP inhibitors in ovarian cancer is suggested by two important recent observations:

1. In ovarian cancers, established mutations in either BRCA1 or BRCA2 can, under pressure to evade treatment, with cisplatin or PARP inhibitor, undergo 'mutation reversion'.[25-27] This means any cancer cell in which by chance the DNA is subsequently altered to result in the BRCA1 or BRCA2 mutation going back 'in frame' at the DNA level, will be able to survive treatment and clonally expand, causing drug resistance and tumour recurrence.
2. Another source for resistance to PARP inhibitor treatment lies in the recent demonstration that a related DNA repair pathway, called non-homologous end joining (NHEJ), known as the 'poor sister' of DNA repair because it is not of high fidelity, is unexpectedly essential for the killing by PARP inhibitors in cells lacking DNA repair by HR.[28] Initially counterintuitive, it appears in the absence of HR, PARP normally prevents this poor-sister error-prone pathway from getting out of control. But, in the presence of a PARP inhibitor and the absence of functional HR, this NHEJ pathway does indeed spiral out of control, causing marked genomic instability that results in death of that cell. As such, any HR-deficient cell lacking intact machinery for NHEJ would be predicted to be resistant to PARP inhibitor therapy. It would seem logical that in this setting, PARP inhibitor therapy would be best avoided for that patient.

Understanding the molecular pathways that result in successful killing of cancer cells, by targeting a specific weakness in that cancer cell, is likely to drive the great therapeutic success stories of the next few decades. However, in order to take advantage of the current 'genomics explosion' we must ensure that clinical trial design evolves to enable tissue analysis both pre- and post-therapeutic exposure to putative targeted drugs. Only in this way will we collect tissue, both clinically and molecularly annotated, and – together with molecular pathologists and genomicists – be in a position to fast-track novel therapies with a sufficient understanding to ensure a high response rate and a low drug-resistance or drug-failure rate. In this way, the genetics of cancer has the potential to address the great unknowns that currently preclude effective cancer treatment, ultimately, resulting in improvement in treatment outcomes for our patients.

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Triage of pelvic masses

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Pelvic masses are routinely encountered in gynaecological practice and pose diagnostic and management challenges for both general practitioners and gynaecologists.

While the majority of pelvic masses are benign and may not require active intervention, a small proportion harbour malignancy that requires timely and appropriate surgical management. Pelvic masses can be of both gynaecological and non-gynaecological origin; therefore, it is paramount that clinicians be aware of the differential diagnosis and have an understanding of the significance and accuracy of diagnostic techniques (see Table 1).

Why triage?

The purpose of triage is to differentiate benign from malignant masses, develop a suitable management strategy and facilitate referral to a gynaecological oncologist. Gynaecologic oncologists are specifically trained to complete the operative management of malignant and suspected malignant conditions of the female genital tract. In the presence of a malignant or clinically suspicious mass, a pre-operative consultation with a gynaecological oncologist is important so that the patient can receive a realistic explanation of their cancer risk and understand the potential extent of surgical procedures, including associated risks and benefits of gastrointestinal or genitourinary surgery. It also obviates the likelihood of re-operation when an unstaged or incompletely cytoreduced malignancy is diagnosed.[1-6] Furthermore, studies confirm that women treated by a gynaecological oncologist in a multidisciplinary setting have decreased morbidity and mortality and increased overall survival.[4-6]

After excluding malignancy, the goal is then to differentiate masses that would require active surgical intervention from those that can be managed medically or observed clinically for spontaneous resolution, for example, follicular cysts, corpus luteal cysts and hemorrhagic cysts of the ovary. Functional ovarian cysts arise from unruptured follicle or corpus luteum and invariably undergo spontaneous resolution. An internal haemorrhage within these cysts may delay resolution as it progresses through the stages of acute haemorrhage, clot formation, clot retraction and complete resolution. Physiological cysts are commonly seen in young girls and women in the reproductive age group; however, they can also be encountered in perimenopausal women who are amenorrhoeic, but rarely in postmenopausal women. Meanwhile, pelvic inflammatory diseases, tuberculosis and endometriomas can be managed with medical treatment, occasionally requiring surgery in exceptional circumstances.

For triage, epidemiological and genetic risk factors, evaluation of clinical symptoms and clinical examination with careful selection and interpretation of diagnostic tests should be considered and applied accordingly in a given clinical context.[1-3]

Risk factors for ovarian cancer

The lifetime risk of ovarian cancer in the general population of women is 1.4 per cent and the age-adjusted incidence rate is 12.9 cases per 100 000 women.[7] Nulliparity, early menarche, late menopause, infertility and a BMI $\geq$30kg/m^2 are some epidemiological factors associated with an increased risk of ovarian cancer. Meanwhile, the use of oral contraceptive pills,

Table 1. Differential diagnoses of pelvic masses.

Functional or physiological	Ovarian follicles Haemorrhagic cyst Corpus luteum	
Inflammatory	Pelvic inflammatory disease Endometrioma	
Other benign conditions	Paratubal cysts Para-ovarian cysts Hydrosalpinx Polycystic ovaries Ectopic pregnancy Ovarian torsion	
Benign neoplasms	Germ cell tumours	Mature cystic teratoma
	Sex cord stromal tumour	Fibroma Thecoma
	Epithelial	Serous cystadenoma Mucinous cystadenoma Brenner tumour
Malignant neoplasms	Epithelial ovarian cancer	Borderline or low malignant potential tumour Invasive epithelial adenocarcinoma
	Germ cell tumour	Dysgerminoma Immature teratoma Yolk sac tumour (Endodermal sinus) Choriocarcinoma
	Sex cord stromal tumour	Granulosa cell tumour
	Fallopian tube carcinoma	
Non-gynaecological	Diveritculitis Appendicular mass Colon/rectal cancer Krukenberg tumours (metastasis from gastric, breast primary)	

breastfeeding, multiparity and tubal ligation are some protective factors associated with reduced risk of ovarian cancer.

Age is the most important independent risk factor for epithelial ovarian cancer (EOC). The median age of diagnosis is 60 years old for sporadic cases and ten years earlier in women with a hereditary ovarian cancer syndrome (BRCA or HNPCC/Lynch syndrome).[7,8]

EOC is uncommon in women <40 years of age. Low malignant potential tumours or borderline tumours occur more frequently in younger premenopausal women compared to post menopausal women. Similarly, sex cord stromal tumours and germ cell tumours are more common in younger women aged 10–30 years.

Family history

Of women with ovarian cancer, ten to 15 per cent have an inherited germline mutation in a tumour suppressor gene. BRCA1, BRCA2 and hereditary nonpolyposis colorectal cancer (HNPCC) are the most common germline mutations. The risk of EOC is increased by 40–45 per cent with BRCA1, ten to 25 per cent with BRCA2 and nine to 12 per cent with HNPCC gene mutations. In the absence of formal genetic testing, family history can provide an insight into the risk of cancer. A woman with a single relative affected by EOC has a four to five per cent risk of developing the disease, while one with two affected relatives has a seven per cent risk. In contrast, women with hereditary ovarian cancer syndromes, defined as having at least two first-degree relatives with EOC, have a lifetime probability as high as 25–50 per cent for developing EOC.

Hence, it is very important for the clinicians to thoroughly evaluate a patient's family history and be alert if a patient has either multiple relatives or a first-degree relative with early age onset (<50 years) of breast and/or ovarian cancer (with BRCA1/2 mutations) or colon, endometrial, gastrointestinal, pancreatic or renal malignancies (with Lynch/HNPCC syndrome).[7,8]

Symptoms and clinical examination

The non-specific nature of the symptoms of ovarian cancer has led to it being termed the 'silent killer'. Studies suggest that approximately 93 per cent of women experience symptoms prior to diagnosis; therefore it is vital to establish symptoms and signs and initiate diagnostic tests that allow women to be directed towards an appropriate clinical pathway. The following symptoms are commonly experienced by women with ovarian cancer[9]:

- Abdominal or pelvic pain
- Abdominal bloating
- Abdominal distension
- Abdominal mass/swelling
- Urinary frequency or urgency
- Postmenopausal/abnormal bleeding
- Loss of appetite

These symptoms may indicate ovarian cancers, especially if they are new and occur frequently: more than 12 times per month.[10] Although symptom assessment is not an efficient screening tool for the general population, persistent symptoms in high-risk patients with or without a palpable pelvic mass should raise the index of suspicion for malignancy.[1-3]

Pelvic examination

In premenopausal women, only five to 18 per cent of palpable pelvic masses prove to be malignant, in contrast to 30–60 per cent in postmenopausal women. The higher predictive value for discrimination of malignant from benign disease in postmenopausal women is due to the higher prevalence of cancer and lower prevalence of disorders that mimic malignancy.[11,12]

The presence of a solid, irregular, fixed pelvic mass or nodularity in the posterior vaginal fornix on pelvic examination is highly suggestive of an ovarian malignancy. If the physical examination identifies the presence of ascites, the patient should immediately be referred to a gynaecological oncologist.[2,3]

In my experience, a thorough examination – including a general physical examination, breast examination, per-abdominal, per-speculum, per-vaginal and a per-rectal examination – often helps in reaching a correct diagnosis.

Imaging

Ultrasound (US) scan through both transabdominal (TA) and transvaginal (TV) routes has a well-established role in the initial evaluation of an ovarian mass or pelvic symptoms. The technique has many advantages as it is widely available, inexpensive, involves no exposure to radiation and can be used effectively to differentiate a benign from a complex mass and facilitate triage of patients with a suspicious mass. Besides providing multiplanar imaging, TVUS has a higher resolution, which allows better visualisation of the ovaries independent of body habitus and is associated with a relatively short examination time. However, the sensitivity of US is to an extent observer dependent. Size, morphologic features such as presence of septae, irregular cyst wall, thickness, internal vegetations, solid areas and mural nodules are taken into consideration while interpreting USS results and ovarian volumes of 20cm^3 in premenopausal women and 10cm^3 in postmenopausal women are taken as upper cut-off limits.[13,14]

Both TAUS and TVUS, however, have low specificity for detecting malignancy, owing to overlap in the imaging appearances of benign, borderline and malignant diseases. Thickened cyst walls, internal separations and mural nodules are sometimes present in benign cyst adenomas, haemorrhagic cysts and cystadenofibromas of the ovary. Similarly benign fibromas, Brenner tumours and fibrothecomas of the ovaries often appear as solid tumours. However, if there are associated ascites, hydronephrosis or peritoneal implants diagnosis of malignancy is more likely.[14] Supplementation of Doppler arterial measurements to morphologic features of the ovary improves specificity, thereby decreasing the number of false-positive cases ending up in surgery.[15] The use of both non-targeted and targeted micro bubbles is being evaluated to analyse their ability to discriminate between benign and malignant ovarian lesions. The contrast agents increase the reflectivity of blood, which helps assess blood flow and tissue perfusion at the microvascular levels enabling better detection than the conventional US Doppler.[16,17]

A computed tomography (CT) scan, although not a primary imaging tool in early diagnosis of ovarian cancer, is a common imaging modality used after the US, because of its widespread availability. It provides information about peritoneal and lymphatic dissemination of ovarian cancer in the thorax and upper abdomen. A magnetic resonance imaging (MRI) scan helps to define indeterminate lesions on US masses. It has a specificity of 98 per cent versus 82 and 87 per cent with US and CT scan, respectively. Contrast-enhanced MRI with soft tissue contrast results in better tissue characterisation and accuracy when diagnosing endometriomas and dermoid cysts.[18]

Tumour markers

The serum glycoprotein CA-125 concentration (normal <35 units/mL) values are found to be elevated in 30–50 per cent cases with

Table 2. Risk of malignancy index (RMI).

RMI combines three pre-surgical features	Ultrasound score (U) Menopausal status (M) Serum CA-125 level (IU/ml)
U is scored one point for each of the following characteristics	Multi-locular cysts, solid areas, bilateral lesions, ascites and intra-abdominal metastasis 0 = no abnormality 1= one abnormality 3 = two or more abnormalities
M is scored by menopausal status	Premenopausal = 1 Postmenopausal = 3
RMI score = U x M x CA 125 value. Score ≥200 = high risk of malignancy.	

Table 3. Risk of malignancy algorithm (ROMA).

Uses CA-125 value, HE4 value and menopausal status. Calculates the risk percentage using the following equations:	
Premenopausal	Predictive index (PI) = -12.0+2.38*LN(HE4)+0.0626*LN(CA-125)
Postmenopausal	PI= -8.09+1.04*LN(HE4)+0.732*LN(CA-125) Predicted probability exp (PI)/[1+ exp(PI)]
Cut off values (specific to Abbott Laboratory)	
Premenopausal	≥7.4% High risk of finding EOC <7.4% Low risk of finding EOC
Postmenopausal	≥25.3% High risk of finding EOC <25.3% Low risk of finding EOC

early-stage ovarian cancer and in over 80 per cent of women with advanced ovarian cancer. It has the advantages of being non-invasive, reproducible and relatively inexpensive and is the first test to be performed in presence of a pelvic mass. However, its specificity is limited, with the levels elevated in one per cent of healthy women, fluctuating during menstrual cycle and being elevated in the presence of benign and other malignant conditions, such as endometriosis, pelvic inflammatory disease, fibroid uterus, ulcerative colitis, liver cirrhosis, pericardial and pleural diseases and cancers of the endometrium, breast, lungs and pancreas. The test is more useful for predicting malignancy in postmenopausal women, in whom it has sensitivity of 69–87 per cent, specificity of 81–100 per cent and positive predictive value (PPV) of 73–100 per cent.[19] CA-125 combined with sonographic features of the adnexal mass has a higher specificity for ovarian malignancy than CA-125 alone.[12,19,20]

Human epididymis protein 4 (HE4) is a protein expressed in clear, serous and endometriod ovarian cancer tissues. In contrast to CA-125, it is minimally expressed in normal or benign ovarian tissue; hence it is not elevated in women with endometriosis. Studies suggest that the addition of HE4 testing to ovarian cancer risk assessment with CA-125, pelvic imaging and menopausal status increases the sensitivity for detection of malignant pelvic masses. HE4 is superior to CA-125 in triaging patients with an incidental finding of a pelvic mass who are asymptomatic and medically compromised, thus sparing elderly and unfit patients from surgery. While patients with high CA-125 and negative HE4 can be referred to a gynaecologist, all patients with a normal or positive CA-125 and positive HE4 should be referred to a gynaecological oncologist.[21-23]

The tumour markers AFP (alpha-fetoprotein), LDH (lactate dehydrogenase) and beta human chorionic gonadotrophin are exclusive to endodermal sinus tumour, dysgerminoma and nongestational choriocarcinomas, respectively, and should be performed routinely in young women with a solid or solid and cystic adenexal mass to exclude these germ cell tumours.

Other tumour markers, such as carcino-embryonic antigen (CEA), may be elevated in the presence of gastrointestinal and especially colorectal malignancies and this helps in the differential diagnosis of pelvic masses of non-gynaecological origin. Further evaluation by proper history, risk assessment, colonoscopy and or upper GI endoscopy may be required for accurate diagnosis.

Risk stratification

Individual tests alone are not sufficient for triage. The combination of elevated CA-125 value and ultrasound morphology provides better specificity of ovarian malignancy rather than the individual tests alone.[19,20] Various combined methods for evaluating the risk of malignancy have been proposed. The risk of malignancy index (RMI) was originally developed in 1990, based on menopausal status, ultrasound and CA-125 (see Table 2).[20] Patients with a RMI score greater than 200 had, on average, 42 times the background risk of cancer compared to those with a lower value.[20]

A number of modifications to the RMI have been proposed and scoring systems have incorporated additional variables such as pelvic examination, Doppler studies and serum Ca 72.4 values.[12] All of these systems rely to a greater extent on expertise in ultrasonography, and even with a specificity of 92 per cent it does not help avoid unnecessary surgery in women with benign masses.

Combination of CA-125 and HE4 has the greatest sensitivity of 76.4 per cent and specificity of 95 per cent and outperforms every other tumour marker in regards to prediction of malignancy, making it the most effective dual combination.[21,23] A combination of CA-125 and HE4 can be used as an aid in risk stratification for women presenting with pelvic mass by using the risk of ovarian malignancy algorithm (ROMA). The ROMA value estimates the probability of ovarian cancer in women with a pelvic mass, based on the patient's HE4 and CA-125 levels and their menopausal status. There are two different ROMA formulas and cut offs based on the patient's menopausal status (see Table 3).[22] Women with ROMA levels above the cut off

have an increased risk of ovarian cancer and should be evaluated by a gynecological oncologist. In a study by Moore et al[24], ROMA was compared to RMI and found to have higher sensitivity than RMI for detecting epithelial ovarian cancer.[24] Studies have shown HE4 and ROMA to improve the detection of ovarian cancer, however, further studies and validation is required in different population subsets.

Conclusion

A methodical approach is best for the management of pelvic masses. While the majority of theses masses are benign, it is of utmost importance that malignant cases are diagnosed efficiently and managed with proper investigation and interventions. Intermediate-risk adenexal masses pose various diagnostic challenges. For appropriate triage and management of these cases, careful consideration of clinical risks, evaluation of clinical symptoms, clinical examination (general physical, breasts, per abdominal, per vaginal, per rectal) and correct interpretation of diagnostic procedures is essential. When presented with a diagnostic dilemma one should not be hesitant in seeking an opinion from gynaecological oncology colleagues.

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Robotic surgery

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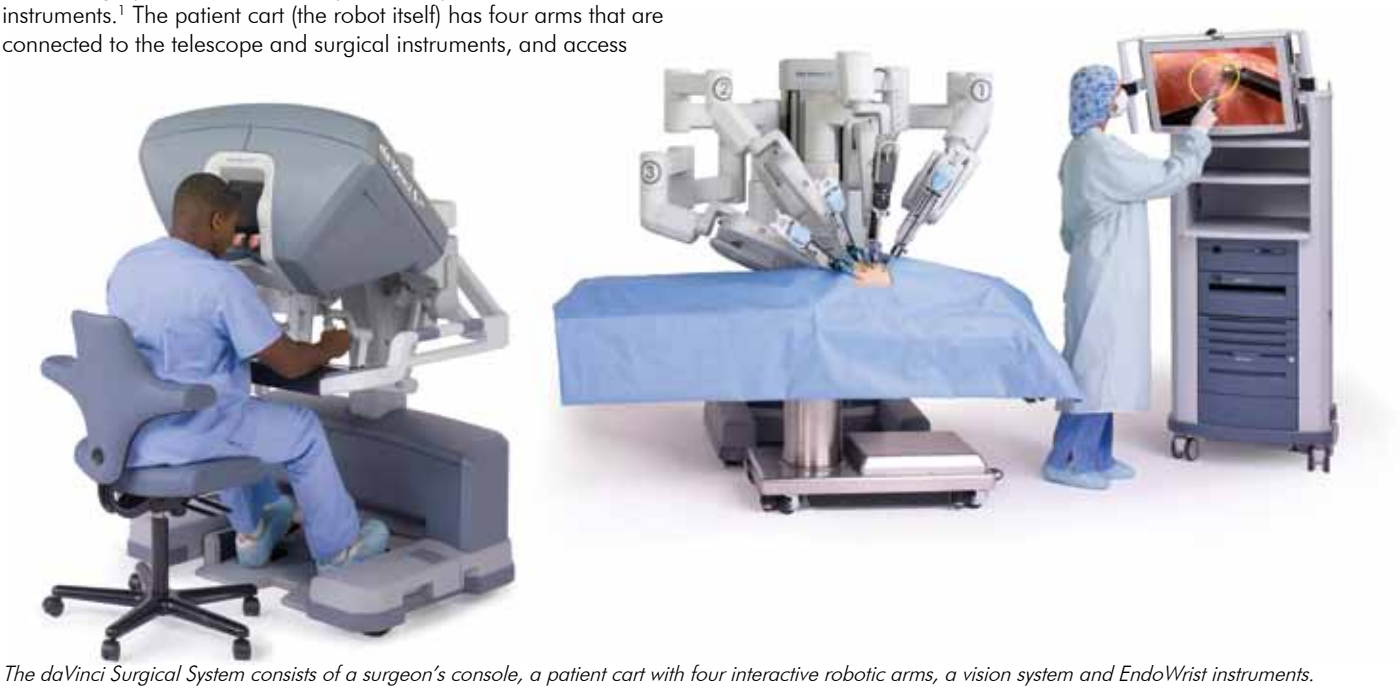
More than 300 000 robotic surgical procedures were performed worldwide in 2011. What role is there for robotic surgery in gynaecological oncology in our region?

Urologists have been the early adopters of robotic surgery, with more than 90 per cent of prostatectomies in the USA now being performed robotically. Despite this head start, gynaecology has caught up and, in the USA at least, more robotic gynaecology procedures are now performed than robotic urology procedures. Australia has been slower to adopt the technology and currently there are only three gynaecologists (two of them gynaecological oncology subspecialists) accredited by Intuitive Surgical® as robotic surgeons, although several are currently proceeding along the accreditation pathway.

The initial research and development for robotic surgery was undertaken by a collaboration from Stanford University, NASA and the US military, who envisioned a system by which emergency battlefield surgery could be undertaken by robots located close to the action during wartime, while the surgeons who controlled the robots were able to remain safely behind the frontline. Ultimately, the military recognised this as a flawed concept and sold it to a private consortium (Intuitive Surgical) that has continued to develop and refine the system to what we today know as the daVinci® Surgical System. Although there have been a number of, essentially, false starts by other companies with prototypes, the daVinci Surgical System is currently the only commercially available robotic surgical system. It seems unlikely that any comparable robotic systems will appear in the short term.

The daVinci Surgical System consists of an ergonomically designed surgeon's console, a patient cart with four interactive robotic arms, a high-performance vision system and patented EndoWrist® instruments.[1] The patient cart (the robot itself) has four arms that are connected to the telescope and surgical instruments, and access the body cavity via laparoscopic ports. The console at which the surgeon sits, remote from the patient, includes the 'masters' (or hand controls for the robotic instruments); foot pedals that control some of the functions; and a viewing box in which the surgeon has a three-dimensional view of the operative field. Lastly, the system includes a tower that houses the insufflator, light, energy sources and other electronic components. The surgical assistant, nursing staff, anaesthetist and others can view the surgery on standard laparoscopic monitors, but unlike the surgeon they do not see the surgery in three dimensions.

The robot is nothing more than a tool to facilitate laparoscopic surgery, albeit a very sophisticated tool. As such, it conveys many of the established benefits of laparoscopic surgery over laparotomy, including smaller incisions, better cosmesis, less pain, quicker recovery, shorter hospital stay and fewer complications.[2] In addition, the robot provides the surgeon with a number of features far superior to its standard laparoscopic counterpart. These include better vision, better instrumentation and better ergonomics. The robotic telescope has two telescopes in its shaft and two cameras, thus projecting a true three-dimensional image for the surgeon's view. The surgeon's experience of looking into the viewing box is thus of a high-resolution, magnified, three-dimensional view of the surgical field that encompasses the surgeon's entire visual field. Compare the robotic surgeon, to whom the operative field comprises his entire visual field and gives the surgeon the sensation of being immersed within the pelvis, to the laparoscopic surgeon who views a small, two-dimensional screen a couple of metres across the operating table that comprises a small part of the visual field. In standard laparoscopic surgery, the greater part of the surgeon's visual field is filled with all of the potential distractions elsewhere in the operating theatre that must be filtered out.



The daVinci Surgical System consists of a surgeon's console, a patient cart with four interactive robotic arms, a vision system and EndoWrist instruments.

Because laparoscopic surgery uses the abdominal wall as a fulcrum, it requires counterintuitive movement by the surgeon. This means that laparoscopic surgeons must teach their hands to do the opposite movement to that which the brain is indicating they should. This requirement for counterintuitive motion is eliminated by the software in the robotic system (as is any surgeon tremor), so that the robot instruments mimic exactly the surgeon's hand movements. Further, the robotic instruments are 'wristed' and thus can perform movements that mimic the human hand, but at a much finer scale. The EndoWrist instruments have seven degrees of freedom; one more than the human hand. Compare this with the simple open-and-close movement allowed by conventional 'straight sticks' laparoscopy. Finally, the robotic surgeon sits comfortably at a console and operates without the need to lift, stretch or strain. This ergonomic improvement results in a much lower potential for surgeon fatigue or injury compared to laparoscopy.

The advantages afforded by the robot will apply to most cases, however, simple procedures may still be undertaken very satisfactorily using conventional laparoscopic equipment and do not justify the extra set up times and expense of robotic surgery. The benefit of the robot will become increasingly apparent as the degree of difficulty of the surgery increases, especially in cases involving morbid obesity, significant pelvic adhesions, large fibroids, severe endometriosis or staging of malignancy requiring pelvic or para-aortic lymph node dissection. Anyone who has performed laparoscopic surgery on morbidly obese patients and struggled against the weight of the abdominal wall to achieve each movement of the handheld instruments would envy the relaxed demeanour of the robotic surgeon, who requires no more physical effort to operate on a 150kg patient as on a 50kg patient. Further, the robotic instruments are able to hinge at the 'wrist' and do not use the abdominal wall as a fulcrum, so that the abdominal wall is less traumatised, resulting in less bruising and pain.

For any cancer surgery, the primary objective is to safely achieve cure. Other objectives such as recovery time, cost and cosmesis must be secondary. While the published data has been almost universally encouraging, so far there have been no prospective randomised controlled trials validating robotic surgery with reference to these objectives in gynaecological oncology.

Endometrial cancer

The significant benefit of laparoscopic surgery versus open surgery has been convincingly demonstrated by the LACE trial.[3] It is likely that the robotic approach will offer similar improvements in outcome for women with endometrial cancer. The more important question is in regard to the comparison of robotic surgery to laparoscopic surgery in endometrial cancer. The recent Cochrane meta-analysis[4] concluded that robotic surgery results in less blood loss compared to either laparoscopy or laparotomy. The robotic platform has been shown to provide similar or increased lymph node yields compared to laparoscopic surgery[5], and the adequacy of surgery is improved in the case of morbidly obese patients compared to laparoscopic surgery.[6] Obesity is a major causative factor for endometrial cancer and the incidence of both is increasing dramatically in Australia. Weinberg's group[7] concluded that robotic surgery becomes increasingly advantageous over laparoscopic surgery for women with endometrial cancer as the potential complexity of the surgery is increased by co-morbidities such as obesity, larger uteri and previous abdominal surgery. The role for robotic surgery in endometrial cancer in Australia is thus likely to increase.

Cervical cancer

The increased surgical finesse, range of motion and three-dimensional vision offered by the robot provides significant advantage to the surgeon especially in the parametrial and ureteric dissection and in preserving the autonomic nerve supply to the bladder when undertaking radical hysterectomy for cervical cancer. Many published reports[8-11] have demonstrated the safety and feasibility of robotic radical hysterectomy and pelvic lymph node dissection in the management of early-stage cervical cancer. These reports have consistently demonstrated that robotic surgery is associated with longer operating times than open surgery, but shorter than laparoscopic surgery and with less blood loss than either. Robotic fertility-sparing surgery (radical trachelectomy) for selected cases of early cervical cancer has been described[12,13] and is likely to be easier to master than the equivalent vaginal radical trachelectomy. The overall role for robotic surgery for early-stage cervical cancer in Australia is likely to increase initially as more gynaecological oncologists are trained in robotic surgery. However, in the longer term, the incidence of early cervical cancer will diminish due to the effectiveness of screening programs and HPV vaccination.

Ovarian cancer

The management of ovarian cancer requires optimal surgical cytoreduction (debulking) in advanced stage disease and, less commonly, a definitive staging procedure in apparent stage I disease. While robotic surgery can achieve these surgical goals within the pelvis, its limitation is in its relative inability to operate simultaneously and extensively within the abdomen and pelvis. The literature contains only a few case reports and small series. Magrina[14] has published a retrospective series of 25 patients undergoing primary surgery performed robotically for ovarian cancer and concludes that limitations of robotic technology will probably prevent its widespread application in patients with ovarian cancer.

Training and accreditation

There is currently no universally recognised training or credentialling requirement for gynaecologists wishing to perform robotic surgery in Australia. As is stands, each hospital currently maintains its own requirements. Nevertheless there has been some consistency. Most hospitals in Australia have, thus far, required a gynaecologist intending to take up robotic surgery to first demonstrate proficiency in advanced laparoscopic procedures, to undertake case observations and/or assisting other surgeons with cases, to practice on a robotic simulator and complete an industry-run standard training module. This training module is a two-day workshop consisting of didactic lectures and hands-on live surgery in an animal laboratory and is run by Intuitive Surgical at various sites in the USA, Europe and Hong Kong. Then the first three robotic surgery cases must be performed with the supervision of an experienced proctor. In order to be recognised by Intuitive Surgical as a robotic surgeon, one must perform a minimum of 20 robotic cases in the first 12 months and 20 cases in every 12 months thereafter.

The learning curve for robotic surgery will be different for each individual surgeon; however, it has been estimated that between 20 and 50 cases are required to obtain proficiency.[15] The learning curve continues and individual surgeons report continuous improvements to their technique up to and beyond 100 cases.[16] The learning curve will be much steeper for surgeons who are not already proficient in laparoscopic surgery, as they will be learning new surgical techniques at the same time as they are learning to use the robotic system, in contrast to experienced laparoscopists who can apply their existing laparoscopic skills that will be extended and enhanced by the adoption of robotics.

Costs and limitations

There is no doubt that, in the learning phase, robotic surgery cases take longer to set up than the equivalent open or laparoscopic procedure. This can be largely overcome by engaging a consistent

team of committed theatre staff, including anaesthetist, surgical assistant, scrub and scout nurses and theatre technicians.

Cost is the major limitation to the introduction and widespread acceptance of robotic surgery in gynaecological oncology practice. The capital outlay for a daVinci system is around $3m, with additional annual service costs. The EndoWrist robotic instruments have a lifetime of ten uses and must thereafter be disposed of, adding around $3000 to the cost of each case. There are currently no HIC item numbers specific to robotic surgery. Many private health insurance funds will cover the cost of the disposable equipment, some will not. The funding arrangements are complex and the business model will be different for each institution. Nevertheless, the cost has not been a disincentive to the introduction of robotic surgery in my own private practice where I have completed over 100 cases. Dr Martin Oehler, at Royal Adelaide Hospital, has introduced a successful robotic gynaecologic oncology program into a public hospital system, working within these financial constraints, and has completed more than 150 cases.[17]

The future

One of the main barriers to the implementation of robotic surgery in gynaecological oncology practice in Australia has been limitation of access, as few hospitals had purchased robotic systems and those that did were often already fully utilised by urologists. This is changing rapidly and there are currently five robots in Melbourne alone, with 12 in Australia overall, three in New Zealand and more on the order books. The second barrier has been the cost. Every nation's health budget is under strain and it is important that all new technologies be justified with respect to the cost/benefit equation. A number of US[18-20] studies and at least one[21] European analysis of robotic surgery costs have concluded that robotic surgery is more expensive than either laparoscopic or open surgery, however, the difference is minimised when a high volume of cases is undertaken robotically in order maximise amortisation of the capital outlay.[20] These analyses have not taken into account the societal cost of surgery, such as the cost of time off work to the employer, to the family and to the individual. While the cost modelling is unlikely to be directly transferable to the Australian healthcare system, the conclusions are likely to be similar. Nevertheless, at some time in the future, a competitor may enter the marketplace as an alternative robotic system is developed. Competition will dissolve the current monopoly and inevitably lead to reductions in cost.

It is almost inevitable that successive generations of robots will become more compact, even easier to use and incorporate other technologies, such as ultrasound probes or other imaging modalities to identify anatomy deep to the surgical field. A single port robot system has been produced in prototype form only and may offer even greater benefits.[22]

Robotic surgery is feasible and safe for the management of endometrial cancer and early cervical cancer. Data from further well-constructed trials will emerge to better define its role in gynaecological cancer surgery. There is likely to be a steady and consistent uptake of robotic surgery by gynaecological oncologists in Australia as more hospitals acquire the technology.

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Epithelial ovarian cancer

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Ovarian cancer is the ninth most common cancer diagnosed in Australian women, with one in 80 being diagnosed by age 85, and is the seventh most common cause of cancer death. It is the most lethal gynaecological cancer, with around 1300 women diagnosed each year and around 850 deaths.[1]

In over 90 per cent of women with localised disease, surgery alone is curative, but unfortunately the majority of women have advanced disease at diagnosis. Although there has been an apparent improvement in five-year survival in the last 20 years, from 33 to 40 per cent, this has probably been the result of improved long-term survival with disease rather than an increase in cure rate. In the absence of any useful methods to diagnose the disease at an earlier stage, prevention should be a primary aim.

Adjuvant chemotherapy with platinum and paclitaxel remains the standard of care following surgery, but newer agents that target specific biological markers are being developed and, with advances in gene profiling, individualisation of treatment is the hope of the future.

Prevention

1. The oral contraceptive pill (OCP) reduces the risk of ovarian cancer in the general population by up to 80 per cent with long-term use. The OCP also appears to reduce the risk of ovarian cancer in gene mutation carriers, such as BRCA1/2 (in case-controlled studies only), with 40 per cent reduction with long-term use and no apparent increase in breast cancer risk.[2]
2. Hysterectomy reduces the relative risk by 50 per cent.
3. Tubal ligation reduces the relative risk by 50 per cent.
4. Bilateral salpingo-oophorectomy (BSO) reduces the risk by 95 per cent. The residual risk lies in developing primary peritoneal cancer.

Screening

Screening is not effective in the diagnosis of precancerous lesions or early-stage ovarian cancer based on available information, although results of a large randomised trial of ultrasound versus CA-125 versus expectant management in over 200 000 postmenopausal women in the UK is expected in the next 12 months (UKTOCS). Although CA-125 is usually elevated (over 90 per cent) in advanced epithelial ovarian malignancies, it is elevated in only 50 per cent of early-stage cancers of the ovary, which limits its use in screening as well as diagnosis.

Transvaginal ultrasound is the other investigation commonly used as a screening tool, but at present lacks both sensitivity and specificity.

As a result of current knowledge of available screening tests, the 2011 National Breast and Ovarian Cancer Centre guidelines, endorsed by RANZCOG, do not recommend screening in the general population or in women at increased risk due to family history or a known gene mutation.[3]

There is ongoing promising research assessing multiple markers that may be indicative of early ovarian cancer, but none of these, to date, have undergone full evaluation in a population setting.

Diagnosis

CA-125 measurement is helpful in investigating a postmenopausal woman with a pelvic mass as, in this situation, an elevated CA-125 indicates malignancy in around 90 per cent of cases, whereas pre-menopausally, endometriosis, adenomyosis, menstruation, fibroids, ovulation and pregnancy can all raise the CA-125 level, limiting its interpretation.

Carcinoembryonic antigen (CEA), CA 19-9 and CA 15-3 may be elevated in mucinous tumours, but these account for less than five per cent of epithelial malignancies and if elevated are more likely to indicate a gastro-intestinal, pancreatic or breast primary. Serum inhibin is also often elevated in mucinous tumours, but is most helpful in the management of granulosa cell tumours. Currently, the timeframe for obtaining the results of inhibin assays makes this relatively unhelpful at the time of primary diagnosis.

In most situations, pelvic masses still present a diagnostic dilemma. Around 20 per cent of ovarian cancers occur before menopause and differentiating between functional, benign and malignant masses remains problematic, particularly in the setting of endometriosis in which clear cell and endometrioid tumours of the ovary may arise. Ultrasound, in the hands of trained gynaecologists, can help clarify suspicious features, particularly the complexity of a mass and solid areas with low-resistance blood flow (indicating neovascularisation), nodularity in the pouch of Douglas and free fluid indicative of ascites. Newer magnetic resonance imaging (MRI) technology using weighted diffusion images, in experienced hands, can differentiate endometriosis from malignancy, increasing the specificity of imaging and reducing the intervention for benign disease[4], but differentiating borderline from malignant tumours is not reliably possible and frozen section remains the best method of planning intra-operative management. However, frozen section may still under-call the situation, particularly in the setting of very large complex masses and this must be discussed pre-operatively with the woman. The most important aspect of managing these masses is not to convert a stage IA cancer into an advanced cancer. If masses are to be removed they should be removed intact or in a retrieval bag, if at laparoscopy. Morcellation of solid masses intraperitoneally should be avoided.

Treatment

Surgery

If an ovarian mass clinically confined to the ovary is found to be malignant at frozen section or final histopathology, then full surgical staging (including para-aortic lymph node dissection, omental sampling and peritoneal sampling with peritoneal washings) is required for both treatment planning and prognosis. If there is tumour rupture or surface involvement, adjuvant chemotherapy is usually recommended. Fertility-sparing surgery may be considered in women wanting to conceive, but this should only occur after extensive counselling and only for stage IA cancer and stage IC disease with favourable histological features.

Advanced ovarian cancer requires cytoreduction, with the amount of residual disease being one of the strongest prognostic factors. Leaving no macroscopic residual disease is now considered optimal

cytoreduction. If there is no macroscopic residual disease at the completion of surgery the median progression-free survival (PFS) is around 100 months, compared to the historical mean of 18 months.[5]

To achieve optimal cytoreduction to no macroscopic residual, more aggressive surgical procedures are commonly required, such as rectosigmoid resection, splenectomy and liver mobilisation to aid resection of hepatic and diaphragmatic disease, including pleural resection. Patient selection is important in terms of identifying candidates for these morbid procedures, as miliary small bowel or mesenteric disease, porta hepatis disease, high para-aortic nodal disease or extensive distant metastases may preclude optimal cytoreduction and render this surgery futile. Extensive ascites (over 1000ml) appears to be a predictor of inability to cytoreduce to no macro residual. In these situations neo-adjuvant chemotherapy for stage IIIC and stage IV disease is often preferred with the aim of maximal cytoreduction after three cycles of chemotherapy. A recent randomised controlled trial in Europe showed no adverse effect on disease-free survival or mortality and a reduction in surgical morbidity utilising neoadjuvant chemotherapy in this group of patients.[6]

Chemotherapy

Standard chemotherapy for advanced epithelial ovarian cancer remains six cycles of intravenous (IV) combination carboplatin and paclitaxel given every three weeks. This treatment has a response rate of 80 per cent and a PFS of 18/12. New modes of administration of chemotherapy such as intraperitoneal (IP) administration have been investigated and preliminary trials have shown an improvement in PFS but with increased toxicity. Trials are ongoing to assess whether less morbid IP regimens are more effective than our current mode of intravenous administration.

Changing the schedule of administration of chemotherapy may also alter its effectiveness. A large Japanese study showed that a regimen of paclitaxel given weekly was more effective than three-weekly administration, increasing PFS from 17 to 28 months, but unfortunately also was more myelosuppressive, probably due to a higher overall dose of paclitaxel than with the standard chemotherapy regimen.[7] This regimen is currently being assessed in Western populations.

New biological agents

Newer agents, such as angiogenesis inhibitors (for example, bevacizumab), target the tumour micro-environment, not the tumour itself, and in randomised controlled trials have shown activity in the adjuvant and recurrent setting, extending PFS by four to six months with prolonged use.[8] Bevacizumab has also shown activity as a single agent in the treatment of bulky recurrent disease and extensive ascites, but has to date demonstrated no improvement in overall survival. This agent is often associated with side effects, such as hypertension, diarrhoea, abdominal pain, fatigue and asthenia, with serious side effects including bowel perforation, haemorrhage and arterial thrombo-embolism. It is also expensive, costing around $10 000 per month. There is no biomarker currently available to determine which patients would benefit from its use.

Poly (ATP-ribose) polymerase inhibitors (PARPIs) (for example, olaparib, iniparib) are also proving useful in the treatment of BRCA mutation related high-grade serous ovarian cancer (around 20 per cent of these high-grade serous tumours) and also prolong PFS by around four months in advanced disease.[9]

The real hope for individualisation of treatment lies in new technology that allows the measurement of expression of thousands of genes, with the ability to demonstrate their clinical phenotypes. Differences in intrinsic, as opposed to acquired, chemoresistance of ovarian tumour cell lines has already been demonstrated. Several studies have tried to identify gene expression signatures correlating with survival and relapse and the new challenge is to develop gene expression profiles that could be used to develop early detection or screening tests and determine individual treatment plans.

Conclusion

Ovarian cancer remains one of the deadliest female cancers, with over two-thirds of women having advanced disease when diagnosed. Disease prevention is the ideal, with the OCP providing significant risk reduction as do pregnancy, tubal ligation and hysterectomy.

Subtypes of ovarian cancer

It has become increasingly obvious that there is a great variation in ovarian cancer and its behaviour. Ovarian cancer can no longer be considered to be one disease. Molecular biology has improved our understanding of the traditional subtypes.

1. Serous ovarian cancers (80 per cent) can be separated into two types:
   a. Low-grade Type 1 with mutations in K-Ras, BRAF, PTEN, CTNNB-1, b-catenin that probably arise from ovarian cortical inclusion cysts; and
   b. High-grade Type 2 with mutations in p-53. There is increasing evidence that the fallopian tube may be the origin of many of these high-grade serous tumours.[10] The ovarian epithelial surface accounts for only one per cent of the total ovarian mass despite over 90 per cent of primary ovarian tumours being epithelial in origin. P-53 signatures can be found in benign appearing tubal epithelium and tubal intraepithelial cancer has been found in five to ten per cent of women with serous ovarian cancers and in BSO specimens of women having prophylactic surgery who are at high risk of ovarian cancer. BRCA mutations have been found in 18 per cent of women diagnosed with high-grade serous cancer, regardless of their family history. Prophylactic tubal removal in women who have completed childbearing and who are undergoing pelvic surgery for benign reasons should be seriously considered.
2. Endometrioid ovarian cancers (ten per cent) are associated with endometriosis. Risk is reduced with increased parity, OCP use, breastfeeding and tubal ligation. Steroid receptors are commonly positive and response to progestogens has been described.
3. Clear cell ovarian cancers (five per cent) are associated with endometriosis and obesity. Reduced risk occurs with OCP use and increased parity. Mutations in ARID1 and PIK3CA are common. Of these, 40–60 per cent are diagnosed with early stage disease, but recurrence is common with a median PFS of 12/12. If disease is advanced at diagnosis, 50 per cent progress on first line standard chemotherapy with an overall complete response rate of only 11 per cent.
4. Mucinous ovarian cancers (less than five per cent) are rare as primary ovarian tumours and gastro-intestinal metastasis must always be excluded. They are associated with smoking and obesity. There is now some evidence for progression from benign to borderline to invasive disease. They uncommonly metastasise to lymph nodes.[11]

In women at high risk of developing ovarian cancer, screening is currently ineffective and prophylactic surgery with BSO is the only effective risk-reducing mechanism available, but this must be balanced by the morbidity of surgery and surgical menopause. Prophylactic removal of the fallopian tubes should be discussed with all women who have completed their families and are undergoing pelvic surgery for benign disease.

First-line treatment of epithelial ovarian cancer has not changed in principle, with the aim of optimising cytoreduction to no macroscopic residual. Increased utilisation of more extensive surgery, including liver, spleen, diaphragmatic and pelvic rectosigmoid resection, affords dramatically improved outcomes for the women in whom this is possible. Adjuvant chemotherapy with platinum and paclitaxel remains the standard of care, but new administration routes and scheduling are under investigation. Newer biological agents targeting angiogenesis and other molecular targets delay tumour growth, and many new agents are under investigation. However, the challenge for ovarian cancer lies in the development of effective screening or early detection tests and also individualisation of treatment, particularly as more information suggests that the subtypes of epithelial ovarian cancer are heterogenous in their gene expression and thus in their response to treatment.

Acknowledgement
I wish to thank Prof Michael Quinn who proofread and edited this article.

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Cervical neoplasia

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This article presents an overview of current detection and treatment options, written by a certified gynaecological oncologist practising in Queensland.

Australia has the lowest mortality (1.7 per 100 000 women) and second-lowest incidence (6.9 per 100 000 women) of cervical cancer in the developed world; largely because of its National Cervical Screening Program, which costs $138m annually. This involves two million women per year undergoing screening, of whom 100 000 will have an abnormal Papanicolaou (Pap) smear report. Of this group with Pap smear abnormalities, around 30 per cent will have a histological abnormality, half of which are high grade. In the last decade, both incidence and mortality for cervical cancer have declined by over 50 per cent. Compared to the incidence of squamous cell carcinoma, the incidence of adenocarcinoma of the cervix has remained unchanged, mostly due to its relative inaccessibility to detection techniques.

The two age groups that account for the majority of cervical cancers are women 30–39 years old, and women 60–69 years old. There are some differences geographically within Australia in incidence and mortality, but these differences are narrowing. However, Indigenous women are still six-times more likely to die from cervical cancer than non-Indigenous women. The introduction, in 2006, of a vaccine against the human papilloma virus (HPV) may represent our best chance of changing this statistic.

HPV

Over 99.7 per cent of cervical cancers have detectable HPV DNA, and this sexually acquired infection, if persistent, appears to be a necessary step in developing cervical cancer. This progression is slow and the overwhelming majority of women clear the infection spontaneously in eight to 14 months. Almost 25 per cent of young, sexually active women at any given time will have active HPV infection. Lifetime risk of exposure to genital strains of HPV is up to 85 per cent.

There are over 150 types of HPV, some of which cause warts on the skin of the vulva, vagina, cervix, inside the urethra, on the penis and anal region. Of these HPV strains, 15 cause cervical cancer. The HPV types that cause common skin warts and visible genital warts do not cause cervical cancer.

Vaccination

High-risk strains, including HPV 16 and 18, are involved in 60–80 per cent of cancers, and these are the strains targeted in recently released vaccines. It is important to remember that vaccination against HPV does not replace regular Pap smears, which are still necessary, though ultimately there should be a reduction in the number of abnormal smears reported. HPV vaccines are now available to females aged nine to 26 years old and males aged nine to 15 years old. These vaccines prevent 70 per cent of HPV strains that cause cervical cancer and 90 per cent of those that cause anogenital warts. Women up to the age of 45 can also be vaccinated as they have up to a 14 per cent incident infection with HPV.

Detection

The detection of HPV is facilitated by recent advances in molecular biology, although none of these detection methods is in general use currently for diagnosis in an individual patient. HPV detection is used commonly as a 'test of cure' in patients treated for high-grade lesions, in other words cervical intraepithelial neoplasia (CIN) 2 to 3. This is currently recommended to be tested at 12 months post-treatment and again annually, along with cytology, until both are negative on two consecutive occasions, at which time the patient can return to a normal two-year screening interval.

Screening

Cervical cytology screening programs can detect pre-invasive, as well as invasive, cellular changes of the cervix. Cervical cancer typically has a long pre-invasive state (often a decade or more) and the treatment for pre-invasive disease is effective; therefore, screening programs can potentially prevent the occurrence of invasive cervical cancer.

Pap smear test

The Pap smear is the current standard screening test for lower genital tract neoplasia. Sensitivity ranges from 55 to 80 per cent for high-grade lesions and specificity is generally over 90 per cent. Up to 50 per cent of Pap smears taken in a setting of invasive carcinoma will be negative. Therefore, a clinically abnormal macroscopic cervical appearance, abnormal bimanual examination and feel of the cervix and/or symptoms of persistent abnormal bleeding or discharge should mean referral to a gynaecologist regardless of smear result.

Liquid-based cytology

Newer liquid-based cytologies, such as the ThinPrep Pap Test, will increase the yield of adequate Pap smear readings and may reduce the false negative rate in patients with chronic cervicitis, blood or inflammation, which may obscure a reading, repetitive possible low-grade Pap smear reports and HIV infection. These liquid-based technologies also enable HPV testing to be done on the same sample. New technologies and combinations of HPV testing and cytology do not have significant additional benefits on life expectancy compared to conventional cytology when used as an annual screening tool, but are more costly. However, they may be cost effective when incorporated into less frequent screening programs (for example, every three years). This may become an option for vaccinated patients in the future. Liquid-based cytology appears to detect glandular lesions better than conventional Pap smears, which have not been effective for lowering the incidence of, or death rate owing to, endocervical adenocarcinoma in screened versus unscreened populations, and may be useful in this group.

Screening guidelines

Current screening guidelines in Australia are that all women who

have ever been sexually active should commence having Pap smears between the ages of 18 and 20 years and then continue doing so until age 70. Regrettably, around 35 per cent of eligible women fail to comply with these recommendations and over 90 per cent of invasive cancers come from this group.

Pre-invasive disease

As for all screening tests, results of the Pap smear cannot be used to make a definitive diagnosis or initiate treatment. The function of the Pap smear is solely to screen for cellular abnormalities that are associated with an increased risk for the development of cervical cancer. Thus, it selects those women who should have further evaluation, such as colposcopy and/or biopsy. Treatment decisions are then made based on diagnostic results from histological examination, usually from colposcopically directed biopsies.

Low-grade cytological abnormalities

Low-grade cytological abnormalities are now accepted as representing acute HPV infection. Up to 80 per cent of low-grade lesions regress by 12 months, and less then four per cent progress to high-grade lesions in the same time period. The National Health and Medical Research Council (NHMRC) guidelines – Screening to prevent cervical cancer: guidelines for the management of asymptomatic women with screen-detected abnormalities (2006) – reflect this finding. The NHMRC recommends initial conservative follow up of low-grade squamous intraepithelial lesions on Pap smear with a repeat smear in 12 months, unless the patient is over 30 years old with no preceding negative smear history. If the patient is over 30 years old with no preceding negative Pap smear history, or the repeat Pap smear is again low grade, referral for colposcopy is required. If a low-grade lesion (CIN1 or less) is confirmed on colposcopy, conservative follow up is now the norm and should result in a around 30 per cent fewer excisional procedures (wire loop excision) taking place in the younger age group, which has obvious benefits for future fertility needs.

High-grade pre-invasive changes

High-grade pre-invasive changes (CIN2 to 3) are treated via diathermy (wire loop excision), laser or cryotherapy. Single treatment is usually extremely effective. A cone biopsy involves a larger excision of cervical tissue and is generally reserved for adenocarcinoma in situ (the glandular 'equivalent' of CIN3), disease going up the cervical canal that cannot be fully visualised at colposcopy, or if invasive disease is suspected.

Follow up

Treatment of pre-invasive disease is highly effective, and follow up is important to ensure no recurrence of disease. Follow up usually takes the form of a repeat colposcopy and Pap smear at six months, then repeat Pap smear and HPV testing at 12 months. Providing this is normal, it is repeated annually until both HPV and cytology are normal. When this occurs for two consecutive years, cytology can then be reduced to every two years, as for the general population. Patients treated for adenocarcinoma in situ, despite clear margins on cone biopsy, are at ongoing risk for developing further pre-invasive or invasive disease long term, and are therefore advised to have a completion hysterectomy (with ovarian conservation) once childbearing is completed.

Cervical cancer

Risk factors

Risk factors for cervical cancer include: smoking, early coitus, multiple partners, multiple pregnancies, poor general health, poor nutrition and a genetic predisposition to cervical cancer.

Lifestyle factors predisposing women to cervical cancer include prolonged stress, eating disorders, poor diet, excessive exercise and inadequate rest. Illnesses that increase a woman's risk include diabetes and immune disorders. Immunosuppressent agents also increase a woman's risk.

Presenting symptoms

The most common presenting symptom is abnormal vaginal bleeding or bloodstained discharge, which may smell offensive in the presence of secondary infection. Symptoms may be precipitated by contact, for instance coitus. All persistent postcoital bleeding should be investigated. Pain (particularly sciatic type pain), pressure symptoms and sometimes vaginal passage of urine or faeces are usually signs consistent with advanced disease.

Pre-treatment work up

Staging

Cervical cancer is staged clinically, apart from intravenous pyelogram (IVP) and X-ray examination of the lung and skeletal systems. This is because, worldwide, most patients are treated in areas that do not have access to high-level imaging techniques and most are treated with radiation only. Therefore, computerised tomography (CT) and magnetic resonance imaging (MRI) of the abdomen and pelvis cannot alter the clinical stage assigned at the time of initial evaluation, but are very useful in determining the extent of the disease and, therefore, treatment planning. The initial evaluation to determine stage and treatment plan usually consists of an examination under anaesthetic, cystoscopy, proctoscopy, cervical biopsy or cone biopsy, and curettage with both a gynaecological oncologist and radiation oncologist present.

Imaging

MRI scans are becoming the preferred imaging technique to define the extent of a tumour, because of their high resolution of pelvic anatomy. They are also useful in pregnancy, as MRI poses no risk to the fetus. Positron emission tomography (PET) scans, which use a radionuclide-labelled sugar to detect sites of malignancy (which are avid users of glucose), are increasingly used in helping to define the extent of disease and therefore the most appropriate therapy, particularly in more advanced disease. Ultimately, if other distant sites of potential tumour are discovered on imaging, fine needle aspiration cytology is then required to confirm this, in order to make any therapeutic decisions.

Treatment

Surgery and chemoradiation are the mainstays of treatment for cervical carcinoma. Stage for stage, the success rates for the two treatment modalities are identical and the type of treatment is usually selected by stage, extent of disease, patient preferences and co-morbidities (for example, if a pelvic kidney is present, surgery is preferable, if possible). Surgical treatment (if suitable) is generally preferable for premenopausal women, as it enables preservation of ovarian function and also probably has less sexual dysfunction associated with it.

The extent of surgery varies depending on the stage and fertility wishes as described below.

Early stage disease

- Stage IA1: lesion is <3mm invasion and <7mm wide. Perform cone biopsy only if no extensive lymph vascular space invasion (LVSI) is present, endocervical curette is negative and future fertility is desired. If fertility is not required, perform a simple hysterectomy. No lymph node dissection is required.

- Stage IA2: lesion is between 3mm and 5mm invasion and <7mm wide. Perform radical hysterectomy (see below) and pelvic lymphadenectomy if fertility is not required. If fertility is desired, perform a radical trachelectomy and pelvic lymphadenectomy (see below).
- Stage IB1: tumour is >7mm wide or 5mm deep, or macroscopically evident with a diameter of up to 4cm. Perform a radical hysterectomy (or radical trachelectomy up to 2cm in those desiring fertility) with pelvic lymphadenectomy or chemoradiation.
- Stage IB2: tumour is >4cm diameter. The optimal management of women with primary tumours measuring 4cm or more in diameter is controversial. Proposed treatment strategies include: primary chemoradiation with the option of subsequent completion hysterectomy (currently the most used option); neoadjuvant chemotherapy, followed by radical hysterectomy and pelvic radiation, pending pathology findings; primary radical hysterectomy and lymphadenectomy followed by tailored chemoradiation.
- Stage IIA: tumour extends onto upper vagina. If cervical tumour is small, in other words <4cm, consider surgical option as above or chemoradiation.

Locally advanced disease

- Stage IIB: tumour extends into parametrial tissues, but not to sidewall (tissue lateral to cervix).
- Stage IIIA: tumour has spread to lower one-third of vagina, but nowhere else.
- Stage IIIB: tumour has spread to the pelvic side wall, or has blocked a ureter.
- Stage IVA: tumour has spread to the rectum or bladder. These patients may require surgical diversion of the bladder or bowel before definitive chemoradiation.
- Stage IVB: tumour has spread to distant organs, for instance lungs.

Women with locally advanced cervical squamous cell cancer are best treated with primary chemoradiation, as surgery alone will not provide adequate clearance and will still require adjuvant radiation. It is desirable to minimise side effects to avoid dual radical treatments if possible (in other words, surgery plus chemoradiation). Patients are still potentially curable up to stage IVA (up to 15 per cent five-year survival).

Definitions

- Radical hysterectomy: compared to a simple hysterectomy to achieve adequate clearance from the tumour, a vaginal and paracervical cuff of tissue is excised in continuity with the cervix. Much of the morbidity of this procedure comes from the additional dissection required to attain lateral clearance (bladder and bowel dysfunction) but this is usually temporary. In addition to a laparotomy, this procedure can also be completed entirely laparoscopically (with or without a robot) and an international randomised trial we are participating in is currently evaluating this against the conventional laparotomy route.
- Radical trachelectomy: in patients with no lymph vascular invasion (LVSI) and tumours <2cm who want ongoing fertility, this procedure involves radical excision of the cervix with a vaginal and paracervical cuff, with reanastamosis of the vagina to the isthmus of the uterus with or without cerclage. This procedure enables the patient to undergo future childbearing, can be performed vaginally, laparoscopically or abdominally, and is combined with a pelvic lymphadenectomy.
- Chemoradiation: definitive radiation with concomitant chemotherapy (weekly cisplatin 40mg/m^2). Chemoradiation compared to radiation alone for the treatment of cervical cancer has been shown to provide a 30–50 per cent reduction in the risk of death, and is now the preferred option for the treatment of cervical cancer.

Follow up

Following therapy, patients should be monitored every three months for two years, every six months until five years, and then annually. The majority of recurrences occur in the first two years after treatment.

Recurrent disease

The incidence of failure is closely related to stage. The prognosis with recurrent disease largely depends on the site of recurrence and how well localised it is. Central recurrences without evidence of distal disease may be amenable to an anterior or posterior exenterative surgical procedure, or may necessitate a total exenterative surgical procedure, depending on distribution of recurrence. The anterior procedure involves removal of the bladder with ileal conduit formation, vagina with or without reconstruction, and possibly the uterus and cervix if still present and affected by tumour recurrence. The posterior procedure involves removal of bowel and tumour, and construction of a colostomy. If it is feasible to proceed with these 'rescue' procedures, there is approximately a 40–50 per cent five-year survival rate, but adequate preoperative counselling is essential for the enormous psychosexual challenge facing the patient. Definitive chemoradiation may also be used for recurrent disease when the patient has initially undergone surgical treatment alone.

Cervical neoplasia in pregnancy

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Cervical cancer in pregnancy is often an emotionally charged, challenging situation in which the risks of all the various options available to the woman need to be considered and carefully explained.

Cervical intraepithelial neoplasia and pregnancy
Five per cent of pregnant women will develop abnormal cervical cytology. The assessment and management of these women can present unique challenges. There is no evidence to suggest that the natural history of cervical neoplasia is altered by pregnancy and, therefore conservative management of non-invasive cervical lesions is considered safe.[1] Biopsy and treatment can usually be safely delayed until after delivery.

Principles of management
The primary task of the colposcopist is to exclude invasive cervical disease. This is not always easy since the physiological changes of pregnancy make colposcopic assessment difficult. In addition, fewer women are now undergoing colposcopy in pregnancy. This is most likely due to a decrease in opportunist cervical screening in the first trimester, and the recognition that colposcopic assessment can be deferred until after delivery for most women with low-grade squamous abnormalities. Fewer colposcopists have extensive experience and expertise in colposcopic assessment in pregnancy and gynaecologists are advised to seek out the opinion of an expert colleague if they have concerns.

Referral for a colposcopy in pregnancy will usually follow similar guidelines as for the non-pregnant woman (see Table 1).[1,2] The asymptomatic pregnant woman with cervical cytology suggestive of a productive HPV infection does not require immediate investigation and subsequent management can be safely postponed until after delivery.[3] However, anxiety in the pregnant woman may lead to referral for reassurance. Several large series confirm that regression rates are high for low-grade abnormalities in pregnancy and that asymptomatic women with such Pap smears are very unlikely to harbour occult invasive disease.[3]

Women with cervical abnormalities suggestive of high-grade squamous lesions do require colposcopic assessment to exclude invasive cervical cancer. The clinician needs to be reminded that a small percentage of women with cervical cytology suggesting a high-grade squamous abnormality will harbour invasive cervical cancer. Cervical intraepithelial neoplasia (CIN) 2 and 3 can be managed conservatively during pregnancy, but most series suggest a high likelihood of persistence postpartum and treatment is usually required after the pregnancy is completed.

Table 1. Management of an abnormal Pap test during pregnancy.

Pap smear results	Suggested management
PLGSIL or LGSIL	Women should be managed in a similar manner as for the non-pregnant women with a repeat Pap test in 12 months
High-grade squamous lesions and possible high-grade squamous lesions	Refer to colposcopy/exclude invasive disease
All glandular lesions	Refer to colposcopy
Concerning cervical appearance/persistent postcoital bleeding.	Refer to colposcopy

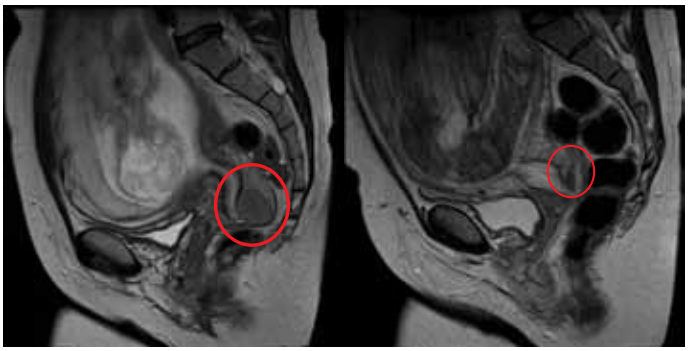
It is also important to remember that a woman with unexplained persistent bleeding in pregnancy, especially postcoital, should have a speculum examination, cytology and colposcopy, if warranted.

Advice for the colposcopist
A significant degree of experience and technical expertise is required to perform colposcopy in pregnancy. The cervix is hypertrophied and hyperaemic and there is markedly increased vaginal laxity. Women should be reassured concerning the safety of colposcopy in pregnancy and, as with any surgical procedure, consideration should be given to the likely challenges of the examination before proceeding. A large (broad and long) Cusco speculum is usually necessary and retraction of the vaginal walls, using a glove finger or condom with the end removed, is usually more comfortable for the women than a vaginal wall retractor.

There are several pitfalls for the less experienced colposcopist. Deciduosis in pregnancy can have an appearance suggestive of malignancy and the features of squamous metaplasia may be exaggerated, as are vascular changes. The goal is to exclude malignancy and this may or may not require a targeted biopsy. Biopsy is considered relatively safe in pregnancy, but is not necessarily considered part of standard management. Cervical biopsy can usually be avoided in pregnancy and the experienced clinician will be more comfortable with making a 'clinical' diagnosis of exclusion of invasive disease. A second opinion from a more experienced colleague can be most reassuring for the clinician and the patient, and should be sought whenever the colposcopist is uncertain about the appearance of the cervix.

The diagnosis of a frank malignancy must be confirmed by target biopsy. The more challenging situation for the colposcopist is when early invasive disease is suspected. In this situation a larger biopsy is required, which may take the form of a wedge biopsy, needle diathermy or knife cone, or diathermy loop excision. Many surgeons advocate use of additional haemostatic sutures or cerclage to reduce the significant risk of haemorrhage and subsequent pregnancy loss. These procedures are usually carried out under general anaesthesia, in hospital. Many authorities suggest that such surgery is performed between 12 and 20 weeks, but this advice is based on practices that predate the widespread use of ultrasound for pregnancy dating and viability. The precise risks for the mother and pregnancy are difficult to define, with only small case series available with varying results, but obviously pregnancy loss and significant haemorrhage can occur.[4]

Cervical ACIS in pregnancy
Rarely a woman is discovered with adenocarcinoma in situ (ACIS) either on cytology or biopsy in pregnancy. Cytological interpretation and colposcopy have limited roles in the management of the non-pregnant women with ACIS and the physiological changes of pregnancy only heighten the deficiencies of these tools. Australian data suggest that at least 16 per cent of women with ACIS on Pap will harbour an invasive cancer, the majority cervical. Only a proportion of these lesions will be obvious at colposcopy.[5] Guidance as how to best care for women in this situation is scarce, and care has to be individualised. Expert cytologic review of the referral Pap smear and biopsies may be most helpful prior to proceeding to excisional



MRI image of cervical squamous cell carcinoma (ringed) diagnosed 18–20 weeks (left) and taken at 34 weeks after three courses of neoadjuvant chemotherapy (right). Images courtesy Robin Harle, Royal Hobart Hospital.

procedures in pregnancy. A large excisional biopsy may be required in the second trimester in order to determine the extent of the lesion and inform subsequent care, or this may be delayed until the post-partum period, depending on the gestation the diagnosis is made.[6,7]

Key points

- Colposcopy in pregnancy may be difficult.
- The main aim of colposcopy in pregnancy is to exclude invasive cancer.
- Seek a second opinion when there is uncertainty about the diagnosis.
- Cervical biopsy is not usually necessary in pregnancy.
- Treatment of CIN2/3 should be deferred until after pregnancy.

Invasive cancer of the cervix in pregnancy

When invasive cervical cancer is suspected on Pap smear or colposcopy or confirmed by biopsy in the pregnant woman, the further assessment and management should be carried out by a certified gynaecologic oncologist. The incidence of invasive cervical cancer in pregnancy is around 1/10 000 and is declining. The gestational age at diagnosis, tumour type, stage and extent of disease and the woman's wishes will influence advice and care. A recent international consensus meeting agreed that: 'the limited experience with an invasive cervical cancer diagnosis in pregnancy renders every treatment proposal other than established standard therapy for the non-pregnant patient experimental.'[8] Certainly, when continuation of the pregnancy is desired, women should be informed of the 'experimental nature' of the cancer treatment and associated risks for her and the pregnancy.

Women with FIGO stage IA1 (confined to the cervix with <3mm invasion) disease can be treated by a shallow cone biopsy in the second trimester.[9] For more advanced disease, diagnosed in the first or second trimesters, staging is advised. Pelvic examination remains the basis of FIGO staging for cervical cancer, however, other techniques may be considered to inform on the extent of disease and assist decision-making. Pelvic magnetic resonance imaging (MRI) is widely used in pregnancy and thought to be safe. Although this will inform of the size and local extent of the tumour, MRI is a poor predictor of lymph node status. Since lymphatic spread is a major determinant of prognosis it has recently been proposed that when pregnancy-sparing treatment is preferred, pelvic lymphadenectomy (either extra peritoneal or laparoscopic) should be considered in the second trimester to define lymph node status.[9,10] It is also suggested that sentinel node biopsy can be safely performed in pregnancy and this may play a role in the future.[10] For high-risk node positive disease it is then advisable to terminate the pregnancy via hysterotomy and treat the women aggressively with standard chemoradiation.

For women with operable node negative cancers (FIGO ≤IB1: confined to the cervix and less than 4cm is diameter) there are several options. Trachelectomy has been performed in pregnancy, although associated with significant haemorrhage and pregnancy loss. Most frequently, a radical caesarean hysterectomy is considered once fetal maturity is reached.[10,11] The use of neoadjuvant (NACT) platinum chemotherapy is reported in the literature to shrink disease and theoretically minimise metastatic spread while awaiting fetal maturity.[12] Timing of the delivery should be decided in conjunction with neonatal and obstetric advice.

NACT may also be considered for more bulky higher stage disease (≥IB2) while awaiting fetal maturity, subsequent caesarean delivery and definitive treatment with chemoradiation. Vaginal delivery is seldom considered an option unless the cervix is free of tumour. Fatal recurrences in episiotomy scars have been reported.

Most gynaecologic oncologists rarely encounter pregnant women with cervical cancer. It is often a difficult situation in which the risks of all the various treatment options available need to be fully considered and carefully explained. Broad multidisciplinary discussion involving histopathologists, oncologists, neonatal and obstetric colleagues is important to assist the lead clinician and the individual woman.

Key points

- When invasive cervical cancer is suspected in the pregnant woman, the further assessment and management should be co-ordinated by a certified gynaecologic oncologist.
- Discussion across multiple disciplines is frequently necessary to fully inform the women of her choices.

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Investigating the borderline

Dr Susan Bigby
MBChB, FRCPA

Ovarian mucinous borderline tumours of intestinal type – a pathologist's perspective.

'Mucinous tumors of ovary are among the most difficult ovarian neoplasms for surgical pathologists to interpret.' Hart WR.[1]

Mucinous tumours of the ovary comprise an estimated 10–15 per cent of all primary ovarian epithelial tumours. These tumours are characterised by mucinous differentiation of the lining epithelium, and encompass a spectrum from benign cystadenomas and cystadenofibromas to carcinomas. There is geographic variation in incidence, with mucinous tumours comparatively more common in Asian than in Western populations.[2] Significant changes in classification and diagnostic criteria have occurred over the last 20 years. There remain controversies over aspects of classification and outcome.

The category of borderline tumour was introduced in 1971, to identify a subset of tumours with histological features intermediate between benign and malignant tumours. These tumours display epithelial proliferation that exceeds that seen in their benign counterparts, but lack the destructive growth of invasive carcinomas. This subgroup is associated with a significantly better outcome than invasive carcinomas. Synonymous terms include mucinous tumour of low malignant potential, cystadenoma of borderline malignancy and atypical proliferative tumour. The term 'borderline tumour' has been adopted by the WHO.[3] The majority (about 85–90 per cent) of mucinous borderline tumours (MBT) are lined by epithelium showing intestinal differentiation, usually in the form of goblet cells; however, there is often a spectrum of cell types present. The remainder are lined by epithelial cells resembling endocervical (Mullerian) epithelium. These two subgroups appear distinct, with differing epidemiological and clinical features.

MBT of intestinal-type occur predominantly in reproductive-age women with a mean of 45 years; however, the age range is wide (between nine and 88 years).[1,2] They are almost always unilateral, with only five per cent occurring bilaterally. MBT are typically the largest of all ovarian tumours, and can measure up to 30cm in dimension (see Figure 1). Gross appearances cannot reliably distinguish benign, borderline and malignant tumours. Typically, the cut surface shows multiple cysts filled with mucin, often with a gelatinous appearance (see Figure 2).

Tumorigenesis

The cell of origin of most primary ovarian mucinous tumours is not clear. These tumours are distinct from other ovarian epithelial tumours, with differing morphology, immunohistochemical and molecular profiles. About five per cent are associated with cystic teratomas (dermoid cysts), and may be benign, borderline or malignant[4] (see Figure 3). This association suggests that some mucinous tumours may represent monodermal teratomas of germ cell origin. Occasional mucinous tumours are also seen in association with other types of ovarian tumours such as Brenner tumours, carcinoids and Sertoli-Leydig cell tumours (see Figure 4). A recent study hypothesised that both mucinous and Brenner tumours share a cell of origin in the transitional cell nests located at the tubal-peritoneal junction.[5] Tumours with a pure mucinous appearance may, in some cases, have outgrown and obliterated any co-existing Brenner tumour.

Mucinous tumours are presumed to develop sequentially from benign cystadenomas to borderline tumours and finally carcinomas, similar to an adenoma-carcinoma sequence seen in the bowel. Intermediary stages are borderline tumours with intraepithelial carcinoma (MBT with IC) and borderline tumours with microinvasion or microinvasive carcinoma (MBT with MI). Evidence for this hypothesis comes from morphological appearance and molecular studies. Borderline and malignant tumours are histologically heterogeneous, with a spectrum ranging from benign to proliferative and malignant, suggesting progression. K-ras mutations have been identified in mucinous tumours and are distinct from mutations seen in other types of

Figure 1. Mucinous borderline tumours may be very large. This tumour measured 38cm in maximum dimension.

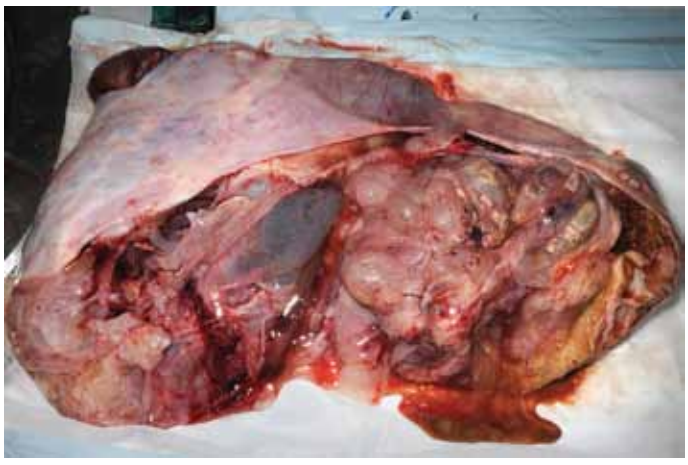

Figure 2. Typically, the cut surface shows multiple cysts filled with mucin.

ovarian tumours.[6] K-Ras mutations have been identified more frequently in malignant, as opposed to borderline or benign, tumours. Identical mutations have been reported in benign, borderline and malignant areas of the same tumour.[7,8] This mutation is a presumed early event in tumorigenesis.

Microscopic assessment

MBTs are typically composed of multiple cysts lined by epithelium that ranges from benign to proliferative with stratification, areas of tufting and papillary growth (see Figures 5 and 6). Cells show mild to moderate atypia and mitotic activity. The lower and upper ends of the spectrum are not well defined. At the lower end, benign and borderline tumours are distinguished by the degree of epithelial proliferation or atypia. 'Minor' foci of proliferation are acceptable in a benign tumour, with proliferation exceeding ten per cent used by many, but not all, as an arbitrary quantitative cut off.[9] Tumours with proliferation below the ten per cent threshold are designated mucinous cystadenomas with focal proliferation or focal atypia. The significance of lesser degrees of proliferation is uncertain with few studies addressing this question.[10]

MBT at the top end of the spectrum may show either intraepithelial carcinoma or small foci of invasion (microinvasion or microinvasive carcinoma).

MBT with IC

Intraepithelial carcinoma is the presumed precursor to invasive tumour and is characterised by epithelium showing areas of severe atypia (carcinoma in situ) without evidence of invasion. If present, the tumour should be more extensively sampled to exclude invasion. Where intraepithelial carcinoma is extensive it may be difficult to distinguish from invasion with an expansile pattern.

MBT with MI

Microinvasion is reported in up to nine per cent of mucinous borderline tumours of intestinal-type.[1] Invasive foci may consist of single cells, small clusters, glands or foci of confluent or cribriform growth within the stroma (see Figure 6). The generally acceptable maximum permissible size of each focus is 10mm^2 in area, or 3mm in maximum dimension. Some investigators have used different maximum dimensions (2mm and 5mm).[11,12] If invasion exceeds this, the tumour is classified as a carcinoma. The maximum size of individual foci has not been validated, nor has the number of permissible individual foci been specified.[10] Foci of microinvasion should be distinguished from stromal mucin extravascation following cyst rupture. Fragmented, non-invasive epithelium may be associated with these mucin granulomata.

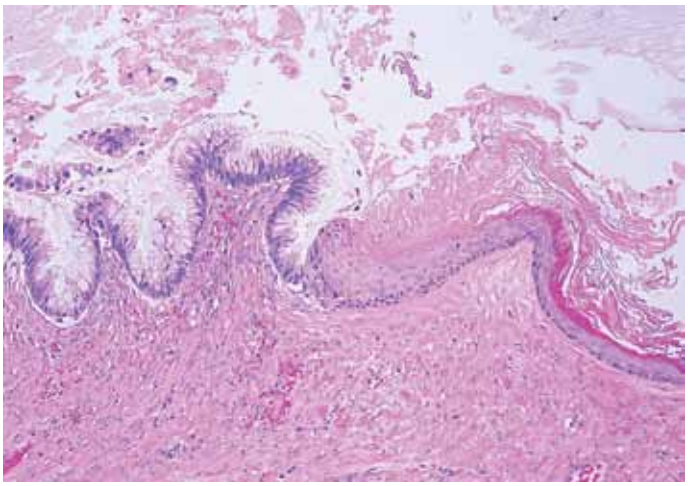

Figure 3. Mucinous tumours may arise in association with teratomas. This cyst is lined in part by mucinous epithelium (left), and by keratinizing stratified squamous epithelium (right).

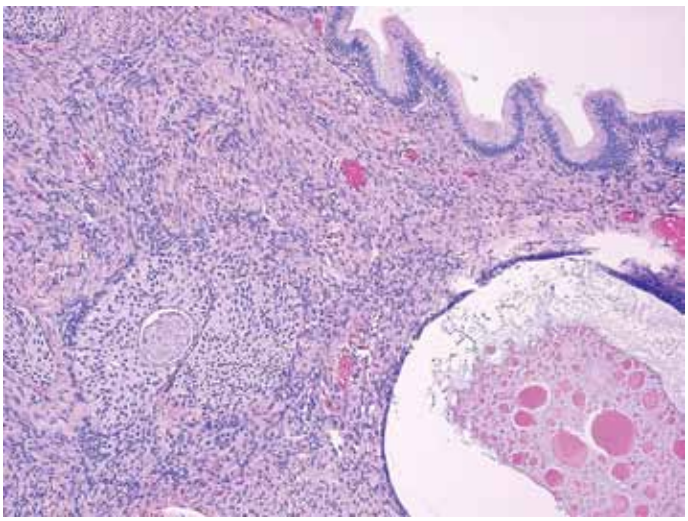

Figure 4. Mucinous tumours may co-exist with Brenner tumours. Nests of transitional-type cells typical of a Brenner tumour are seen in the ovarian stroma beneath a cyst lined by simple mucinous epithelium.

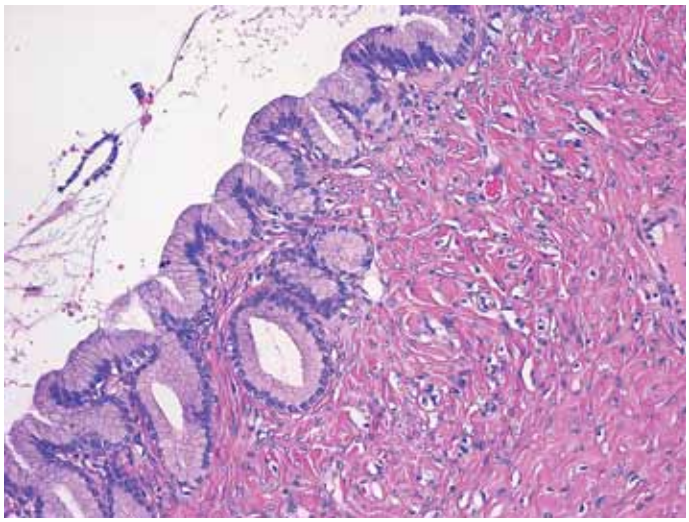

Figure 5. This cyst is lined by benign epithelium consisting of a single layer of cells showing mucinous differentiation.

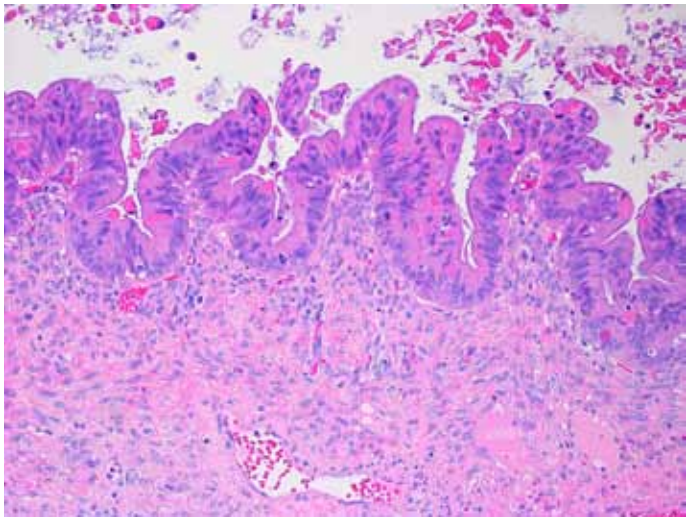

Figure 6. Mucinous borderline tumour with an area of epithelial proliferation showing epithelial stratification, nuclear atypia and mitotic activity.

Some investigators distinguish between microinvasion and microinvasive carcinoma, while others use the terms synonymously. 'Microinvasion' has been used to describe cases where tumour cells have low-grade nuclear features, whereas 'microinvasive carcinoma' refers to invasive foci showing high-grade cytology.[1] This distinction is controversial and the significance remains unresolved. No prognostic difference was observed between these two groups in a recent study.[13]

Borderline tumours with mural nodules

Rare mucinous tumours have mural nodules that may be either reactive or malignant. Reactive nodules are often multiple and may occur in benign, borderline or malignant tumours. Malignant nodules, by contrast, almost always occur in borderline or malignant tumours. These may be either solitary or multiple, and have either a carcinomatous, sarcomatous or mixed appearance. The presence of malignancy is associated with a poor outcome.

Outcome

Borderline tumours of all types generally have an extremely good prognosis. Analysis of more recent studies with detailed histopathological review showed an overall risk of recurrence of two per cent (1.2 per cent, 1.9 per cent and 5.1 per cent in MBT without adverse histological features, MBT with IC, and MBT with MI, respectively).[13] Recurrence is strongly associated with stage, and no women with stage IA tumours recurred, even where adverse histological features were present. Women who recurred all had stage IC tumours, with recurrence rates of 4.2 per cent, 16.7 per cent, and 25 per cent, respectively, in the three tumour subgroups. While overall numbers are small, tumour-related deaths were observed. An age-related risk was also identified, with all recurrences occurring in women aged <45 years.[13] This age-related risk has not been widely studied.

Correct classification of mucinous tumours requires thorough sampling and exclusion of metastases. Tumours are typically large and histologically heterogeneous, necessitating extensive sampling. Current recommendations are that at least one section per centimetre of tumour be processed, with additional sampling reaching two sections per centimetre in tumours measuring over 10cm, or with complex cystic or solid areas, or those that show intraepithelial carcinoma, microinvasion or tumour perforation.[14] This level of sampling was not reached in many earlier studies of outcome where aggressive behaviour in MBT was reported.

The vast majority of mucinous carcinomas, and some tumours with a borderline appearance, are now recognised as metastatic from extra-genital sites, particularly gastrointestinal tract. Tumours arising in the pancreas and biliary tract may be especially bland and histologically indistinguishable from mucinous borderline tumours. Presentation with an ovarian mass may precede diagnosis of the primary tumour. With the rare exception of teratoma-associated mucinous tumours, pseudomyxoma peritonei (mucinous ascites and/or mucinous peritoneal nodules) is invariably due to an extra-ovarian neoplasm, usually appendiceal, with secondary involvement of the ovary.[4] When metastatic tumours are excluded, primary mucinous carcinomas are very uncommon. Immunohistochemistry may assist in interpretation of likely site of tumour origin, however there is considerable overlap in immunoprofile and clinical correlation is always required. Features favouring metastasis include bilaterality, size <10cm, surface involvement by tumour or the presence of surface mucin, an infiltrative pattern of invasion, nodular growth pattern, signet ring cells or single cell invasion, vascular invasion, ovarian hilar involvement, pseudomyxoma ovarii and pseudomyxoma peritonei. Dirty necrosis is often associated with metastatic colonic tumours. Knowledge of the patient's clinical history and radiological findings are essential in assessment.

Summary

Our understanding of the pathogenesis and behaviour of mucinous tumours of the ovary has evolved significantly over the last few decades. The excellent prognosis of most MBT has resulted in suggestions that MBT be reclassified as benign. Others believe this term should be retained because it better reflects their intermediate position in tumorigenesis.[15] Further, a number of persistent controversies remain unresolved, particularly those involving the clinical significance of histologically adverse features. Current outcome data are based on small patient numbers. Stratifying borderline tumours into those with and without adverse histological features allows for further studies of outcome in these subgroups. This will enhance our understanding of these problematic tumours and help guide clinical follow-up and long-term recommendations.

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Meetings Calendar Autumn 2012

LEGEND

A	RANZCOG Approved Meetings – evidence of attendance required
A/P	Practice Review & Clinical Risk Management (PR&CRM) activity associated with meeting
P	Practice Review & Clinical Risk Management (PR&CRM) activity
O	Category to be determined
B	Other meetings category

Australia
2012 onwards

March 2012

16-17 Mar 2012 – O
AGES Pelvic Floor Conference 2012
Melbourne VIC
Contact Conference Connection 282 Edinburgh Road Castlecrag Sydney NSW
(t) +61 2 9967 2928
(f) +61 2 9967 2627
(e) conferences@ages.com.au
(w) www.ages.com.au

18-21 Mar 2012 – O
FAOPS & PSANZ Congress 2012
Sydney NSW
Contact Nina Grange
(t) +61 3 9320 8604
(e) faopspsanz@eventplanners.com.au
(w) www.faopspsanz2012.eventplanners.com.au

22 Mar 2012 – A
Drugs in Pregnancy and the Newborn
Sydney NSW
Contact Koti Hawarth National Drug and Alcohol Research Centre
(t) +61 421 035 579
(e) k.haworth@unsw.edu.au
(w) http://www.cvent.com/d/bcqmfs

22-23 Mar 2012 – O
BSS Basic Surgical Skills Gynaecology
Crawley WA
Contact CTEC University of Western Australia
(t) +61 8 6488 8044
(w) www.ctec.uwa.edu.au

26-30 Mar 2012 – O
Advanced Gynaecological Laparoscopic Surgery Course (SWEC)
Sydney NSW
Contact Workshop Administrator SWEC Suite 1 2 Pearl St Hurstville NSW 2220
(e) sweconline@gmail.com or doc@drgregorymcario.com.au

28 Mar-1 Apr 2012 – O
ASUM Ultrasound Multidisciplinary Workshop 2012
Adelaide SA
Contact www.asum.com.au

30 Mar-1 Apr 2012 – O
ASUM Annual O&G Ultrasound Symposium 2012
Adelaide SA
Contact (w) www.asum.com.au

April 2012

16-19 Apr 2012
MRANZCOG Pre-Examination Course
Brisbane QLD
Contact Lee-Anne Harris Executive Officer Queensland Regional Committee
(t) +61 7 3252 3073
(e) lharris@ranzcog.edu.au

20 Apr 2012 – O
MRANZCOG MCQ Writing Workshop
Melbourne VIC
Contact Lyn Johnson Director Education and Training RANZCOG 254-260 Albert St East Melbourne 3002
(t) +61 3 9412 2944
(f) +61 3 9419 7817
(e) ljohnson@ranzcog.edu.au

28-29 Apr 2012 – O
ASCCP Colposcopy Course
Sydney NSW
Contact Mary Sparksman YRD Event Management
(t) +61 7 3368 2422
(e) mary@yrd.com.au
(w) www.asccp.com.au

28-29 Apr 2012 – A
2012 Provincial Fellows Annual Scientific Meeting
Mackay QLD
Contact Melissa Glogolia 254-260 Albert St East Melbourne VIC 3002
(t) +61 3 9412 2912
(f) +61 3 9415 9306
(e) mglogolia@ranzcog.edu.au
11 points

May 2012

4-6 May 2012 – O
2nd International Conference on the Science of Nutrition in Medicine and Healthcare
Melbourne VIC
Contact ACNEM
(t) +61 3 9597 0363
(e) info@nutritionmedicine.org.au
(w) http://www.nutritionmedicine.org.au

7-8 May 2012 – O
Refresher Obstetric Ultrasound Course
Ivanhoe VIC
Contact Oriana Tolo PO Box 317 Ivanhoe VIC 3079
(t) +61 418 506 878
(f) +61 3 9497 4441
(e) http://www.ultrasoundtraining.com.au/courses/category/refresher-obstetric-ultrasound

18 May 2012 – O
Anatomy of Complications Workshop
Crawley WA
Contact CTEC University of Western Australia
(t) +61 8 6488 8044
(w) www.ctec.uwa.edu.au

18-20 May 2012 – O
Sydney GPCE Primary Care
Sydney NSW
Contact (t) 1800 358 879
(w) www.gpce.com.au

24-26 May 2012 – O
4th Biennial Breathing New Life into Maternity Care Conference
Melbourne VIC
Contact (e) events@remark.com.au

24-27 May 2012 – O
19th WONCA Asia Pacific Regional Conference
Jeju Korea
Contact WONCA Jeju 2012 Secretariat 1F Haroreum Bldg 748-5 Yeoksam-dong Gangnam-gu Seoul 135-925 Korea
(t) +82 2 566 6031
(f) +82 2 566 6087
(e) admin@woncaAP2012.org
(w) www.woncaAP2012.org

28 May–1 Jun 2012 – A
MRANZCOG Course
Melbourne VIC
Contact: Ms Fran Watson Executive Officer Victorian and Tasmanian Committees RANZCOG
(e) fmwatson@ranzcog.edu.au

30 May-1 Jun 2012 – O
XXII AGES Annual Scientific Meeting 2012 in conjunction with APAGE
Sydney NSW
Contact Conference Connection 282 Edinburgh Road Castlecrag Sydney NSW
(t) +61 2 9967 2928
(f) +61 2 9967 2627
(e) conferences@ages.com.au
(w) www.ages.com.au

June 2012

21-22 Jun 2012 – O
4th Annual Obstetric Malpractice Conference
Melbourne VIC
Contact (e) info@iir.com.au
(w) www.iir.com.au/obstetric

21-22 Jun 2012 – O
14th Flinders Private EndoGynaecology 'Mastering Laparoscopic Suturing' Workshop
Adelaide NSW
Contact Dr Robert O'Shea
(t) +61 8 8326 0222
(f) +61 8 8326 0622
(e) rtoshea-isge@adam.com.au

22 Jun 2012 – O
Anatomy of Complications Workshop
Crawley WA
Contact CTEC University of Western Australia
(t) +61 8 6488 8044
(w) www.ctec.uwa.edu.au

July 2012

16-20 Jul 2012 – O
Advanced Gynaecological Laparoscopic Surgery Course (SWEC)
Sydney NSW
Contact Workshop Administrator SWEC Suite 1 2 Pearl St Hurstville NSW 2220
(e) swecaustralia@hotmail.com or doc@drgregorymcario.com.au

18-20 Jul 2012
DRANZCOG Course
Melbourne VIC
Contact: Ms Fran Watson Executive Officer Victorian and Tasmanian Committees RANZCOG
(e) fmwatson@ranzcog.edu.au

September 2012

4-8 Sep 2012 – O
International Urogynaecological Association 2012 Congress
Brisbane QLD
Contact (w) www.iuga2012.com

5-6 Sep 2012 – O
2012 GPET Convention
Melbourne VIC
Contact (w) www.agpt.com.au

9-12 Sep 2012 – O
RANZCOG 2012 ASM
Canberra ACT
Contact Ms Kylie Grose RANZCOG 254-260 Albert Street East Melbourne VIC 3002
(t) +61 3 9412 2922
(f) +61 3 9419 0672
(e) kgrose@ranzcog.edu.au
(w) www.ranzcog2012asm.com.au

11-13 Sep 2012 – O
SimHealth 2012: Innovation, Education and Research in Healthcare Conference
Sydney NSW
Contact (w) www.simhealth.com.au

14-16 Sep 2012 – O
Brisbane GPCE Primary Care
Brisbane QLD
Contact (t) 1800 358 879
(w) www.gpce.com.au

October 2012

5 Oct 2012 – O
Anatomy of Complications Workshop
Crawley WA
Contact CTEC University of Western Australia
(t) +61 8 6488 8044
(w) www.ctec.uwa.edu.au

12-14 Oct 2012 – O
16th Australian Menopause Society Congress
Melbourne VIC
Contact AMS 2012 Congress Managers GPO Box 128 Sydney NSW 2001
(t) +61 2 9265 0700
(f) +61 2 9267 5443
(w) http://www.ams2012.com.au
(e) menopause@arinex.com.au

8-12 Oct 2012 – O
Advanced Gynaecological Laparoscopic Surgery Course (SWEC)
Sydney NSW
Contact Workshop Administrator SWEC Suite 1 2 Pearl St Hurstville NSW 2220
(e) swecaustralia@hotmail.com or doc@drgregorymcario.com.au

25-28 Oct 2012 – O
Rural Medicine Australia 2012
Fremantle WA
Contact www.acrrm.org.au

26-28 Oct 2012 – O
ASUM 2012 Annual Scientific Meeting
Sydney NSW
Contact (w) www.asum.com.au

November 2012

19-20 Nov 2012 – O
Refresher Obstetric Ultrasound Course
Ivanhoe VIC
Contact Oriana Tolo PO Box 317 Ivanhoe VIC 3079
(t) +61 418 506 878
(f) +613 9497 4441
(w) www.ultrasoundtraining.com.au/courses/category/refresher-obstetric-ultrasound

16-17 Nov 2012 – O
AGES Focus Meeting 2012 in conjunction with NASOG
Gold Coast QLD
Contact Conference Connection 282 Edinburgh Road Castlecrag Sydney NSW
(t) +61 2 9967 2928
(f) +61 2 9967 2627
(e) conferences@ages.com.au
(w) www.ages.com.au

16-18 Nov 2012 – O
Melbourne GPCE Primary Care
Melbourne VIC
Contact
(t) 1800 358 879
(w) www.gpce.com.au

2013

23-26 Feb 2013 – O
10th International Congress on Andrology
Melbourne VIC
Contact WALDRONSMITH Management
(t) +61 3 9645 6311
(w) www.ica2013.com

25-29 Mar 2013 – O
Advanced Gynaecological Laparoscopic Surgery Course (SWEC)
Sydney NSW
Contact Workshop Administrator SWEC Suite 1 2 Pearl St Hurstville NSW 2220
(e) swecaustralia@hotmail.com or doc@drgregorymcario.com.au

15-19 Jul 2013 – O
Advanced Gynaecological Laparoscopic Surgery Course (SWEC)
Sydney NSW
Contact Workshop Administrator SWEC Suite 1 2 Pearl St Hurstville NSW 2220
(e) swecaustralia@hotmail.com or doc@drgregorymcario.com.au

8-12 Sep 2013 – O
RANZCOG 2013 ASM
Sydney NSW
Contact Ms Kylie Grose RANZCOG 254-260 Albert Street East Melbourne VIC 3002 (t) +61 3 9412 2922
(f) +61 3 9419 0672
(e) kgrose@ranzcog.edu.au

7-11 Oct 2013 – O
Advanced Gynaecological Laparoscopic Surgery Course (SWEC)
Sydney NSW
Contact Workshop Administrator SWEC Suite 1 2 Pearl St Hurstville NSW 2220
(e) swecaustralia@hotmail.com or doc@drgregorymcario.com.au

New Zealand 2012 onwards

March 2012

20 Mar 2012 – A
RANZCOG SAQ and MCQ Writing Workshop
Rotorua
Contact Bronwyn Robinson RANZCOG College House 254-260 Albert Street East Melbourne VIC 3002
(t) +61 3 9412 2949
(e) brobinson@ranzcog.edu.au
7 points

21-24 Mar 2012 – A
New Zealand Committee Annual Scientific Meeting
Rotorua
Contact Ms Kate Bell Level 3 Navigate House 69 Boulcott Street Wellington New Zealand
(t) +64 4 472 4608
(f) +64 4 472 4609
(e) k.bell@ranzcog.org.nz
19 points

30 Mar-4 Apr 2012 – O
International Fetal Medicine & Surgery Society 31st Annual Meeting 2012
Queenstown
Contact (w) http://www.confer.co.nz/ifmss2012/index.htm

April 2012

16th Apr 2012 – O
Ultrasound Physics and Technology Study Day
Hamilton
Contact Antegrade Ultrasound Solutions 22 Oakley Avenue Claudelands Hamilton 3214 NZ
(e) info@antegrade.net

June 2012

29 Jun-1 Jul 2012 – O
ASUM New Zealand 2012 Annual Scientific Meeting
Auckland
Contact (w) www.asum.com.au

August 2012

6-10 Aug 2012 – O
Advanced Wilderness Life Support Course
Queenstown
Contact Michelle Watts 642 Bainfield Road RD2 Myross Bush Invercargill 9872 Southland NZ
(t) +64 21 239 8069
(e) WildMed@xtra.co.nz
(w) www.wildmed.co.nz

November 2012

9-11 Nov 2012 – O
ANZ Vulvovaginal Society Biennial Scientific Meeting
Auckland
Contact Anne Fleming
(t) +61 3 9899 1686
(e) fleminga@bigpond.net.au

December 2012

5-9 Dec 2012 – O
Advanced Wilderness Life

Support Course
Queenstown
Contact Michelle Watts 642 Bainfield Road RD2 Myross Bush Invercargill 9872 Southland NZ
(t) +64 21 239 8069
(e) WildMed@xtra.co.nz
(w) www.wildmed.co.nz

Overseas 2012 onwards

March 2012

21-24 Mar 2012 – O
Society for Gynaecologic Investigation 59th Annual Scientific Meeting 2012 (SGI 2012)
San Diego USA
Contact (w) http://www.sgionline.org/index.php?option=com_content&view=article&id=27

24-27 Mar 2012 – O
ACC12 Annual Scientific Session and Expo
Chicago USA
Contact (w) www.accscientificsession.org/international

30-31 Mar 2012 – O
The 1st Biomarker Meeting in Reproductive Medicine: Emergence of a New Field
Valencia Spain
Contact (e) biomarker@comtecmed.com
(w) www.comtecmed.com/biomarker

April 2012

13-15 Apr 2012 – O
64th Annual Congress of Japan Society of Obstetrics & Gynaecology
Kobe Japan
Contact MA Convention Consulting Inc Dal2 Izumi-shoji Bldg 4-2-6 Kojimachi Chiyoda-ku Tokyo 102-0083 Japan
(t) +81 3 5275 1191
(f) +81 3 5275 1192
(e) info@macc.jp
(w) http://jsog.umin.ac.jp

25-28 Apr 2012 – O
7th International Congress on Minimally Invasive Gynecology 2012 (AAGL 2012)
Puerto Madero Argentina
Contact (w) http://www.aaglargentina2012.com

26-28 Apr 2012 – O
3rd International Video Workshop on Radical Surgery in Gynaecological Oncology
Prague Czech Republic
Contact Workshop Secretariat
(t) +420 284 001 444
(e) ivw2012@guarant.cz
(w) www.ivw2012.cz

May 2012

13-15 May 2012 – O
The International Conference on Integrative Medicine
Jerusalem Israel
Contact (w) www.mediconvention.com

17-20 May 2012 – O
The 2nd International Congress on Cardiac Problems in Pregnancy (CPP 2012)
Berlin Germany
Contact Sarah Krein CPP 2012 Marketing and Sales Coordinator Paragon Conventions
(t) +41 22 5330948
(f) +41 22 5802953
(e) skrein@paragon-conventions.com
(w) www.cppcongress.com

25-27 May 2012 – O
University Obstetrics & Gynaecology Congress 2012
Singapore
Contact (w) www.obgyn2012.com

31 May-2 Jun 2012 – O
Joint International Congress of the American Society for Reproductive Immunology and the European society for Reproductive Immunology 2012 (ASRI-ESRI 2012)
Hamburg Germany
Contact (w) www.asri-esri-2012.de

June 2012

5-8 Jun 2012 – O
RCOG 10th International Scientific Congress
Sarawak Malaysia
Contact Ms Zoe Scott A Working Title Events Sdn Bhd E-3-14 Block E Plaza Damas Jalan Sri Hartamas 1 50480 Kuala Lumpur Malaysia
(t) +60 3 6201 1858
(e) zoe@aworkingtitleevents.com
(w) www.rcog2012.com

13-16 Jun 2012 – O
XXIII European Congress of Perinatal Medicine
Paris France
Contact (w) www.ecpm2012.org

24-28 Jun 2012 – O
11th World Congress in Fetal Medicine 2012 (FMF 2012)
Kos Greece
Contact (w) www.fetalmedicine.com/fmf/courses-congress-conference/

July 2012

1-4 Jul 2012 – O
28th Annual Meeting of ESHRE
Istanbul Turkey
Contact www.eshre.eu

19-22 Jul 2012 – O
16th World Congress on Controversies in Obstetrics, Gynecology & Infertility 2012 (COGI 2012)
Singapore
Contact (w) http://www.congressmed.com/cogisingapore/

September 2012

9-13 Sep 2012 – O
World Congress on Ultrasound in Obstetrics and Gynaecology
Copenhagen Denmark
Contact (w) www.isuog.org/WorldCongress/2012

12-15 Sep 2012 – O
World Congress on Ovulation Induction and Ovarian Stimulation Protocols (WOOSP 2012)
Goa India
Contact IVF Foundation 101 1st Floor B-Wing 36 Turner Road opp Crossword Bandra (West) Mumbai 400050 India
(w) http://www.woosp.in/

October 2012

7-12 Oct 2012 – O
2012 XX FIGO World Congress of Gynecology and Obstetrics
Rome Italy
Contact Ms Marta Collins FIGO Suite 3 Waterloo Court 10 Theed Street London SE1 8ST UK
(t) +44 20 7928 1166
(f) +44 20 7928 7099
(e) marta@figo.org
(w) www.figo.org

13-16 Oct 2012 – O
14th Biennial Meeting of the International Gynecologic Cancer Society (IGCS)
Vancouver Canada
Contact Meeting Secretariat C/O Kenes International 1-3 Rue de Chantepoulet PO Box 1726 CH-1211 Geneva 1 Switzerland
(t) +41 22 908 0488
(e) igcs@kenes.com
(w) www.kenes.com/igcs2012

2013

19-23 Sep 2013 – O
10th Congress of the European Society of Gynaecology
Brussels Belgium
Contact (e) seg2013@btcongress.com

5-8 Oct 2013 – O
18th International Meeting of the European Society of Gynaecological Oncology (ESGO)
Athens Greece
Contact (w) www2.kenes.com/esgo18/Pages/Home.aspx

RANZCOG ASMs 2012-2016

9-12 Sep 2012 – O
2012 RANZCOG ASM
Canberra ACT
Contact Ms Kylie Grose RANZCOG 254-260 Albert Street East Melbourne VIC 3002
(t) +61 3 9412 2922
(f) +61 3 9419 0672
(e) kgrose@ranzcog.edu.au
(w) www.ranzcog2012asm.com.au

2013

8-12 Sep 2013 – O
2013 RANZCOG ASM
Sydney NSW
Contact Ms Kylie Grose RANZCOG 254-260 Albert Street East Melbourne VIC 3002
(t) +61 3 9412 2922
(f) +61 3 9419 0672
(e) kgrose@ranzcog.edu.au

2014

2014 RANZCOG ASM
WA

2015

2015 RANZCOG ASM
QLD

2016

2016 RANZCOG ASM
Tasmania

Provincial Fellows and Regional Committee ASMs

26-29 Apr 2012 – O
Provincial Fellows Annual Scientific Meeting
Mackay QLD
Contact Ms Kate Lawrey
(t) +61 3 9412 2971
(f) +61 3 9415 9306
(e) klawrey@ranzcog.edu.au

2013

10-13 Apr 2013 – O
New Zealand Committee Annual Scientific Meeting
Hawkes Bay New Zealand
Contact Ms Kate Bell Level 3 Navigate House 69 Boulcott Street Wellington New Zealand
(t) +64 4 472 4608
(f) +64 4 472 4609
(e) k.bell@ranzcog.org.nz

RCOG Meetings and Postgraduate Courses

For further information on RCOG Postgraduate Courses contact
Conference Office RCOG 27 Sussex Place Regent's Park London NW1 4RG
(t) +44 20 7772 6245
(f) +44 20 7772 6388
(w) www.rcog.org.uk/events

MRANZCOG Pre-Examination Courses

16-19 Apr 2012
MRANZCOG Pre-Examination Course
Brisbane QLD
Contact Lee-Anne Harris Executive Officer Queensland Regional Committee
(t) +61 7 3252 3073
(e) lharris@ranzcog.edu.au

22-26 Oct 2012
MRANZCOG Pre-Examination Course
Sydney NSW
Contact Chris Dowling Administrative Officer NSW Regional Committee RANZCOG
(e) cdowding@ranzcog.nsw.edu.au

22-23 Nov 2012
Sydney NSW
Contact Chris Dowling Administrative Officer NSW Regional Committee RANZCOG
(e) cdowding@ranzcog.nsw.edu.au

Women's Health Courses and Activities

21 Feb 2012
IUD Workshop
Family Planning WA
Contact Sandra Halloran
(t) +61 3 9257 0100
(f) +61 3 9257 0111
(e) shalloran@fpv.org.au
Category 1: 40 points

5-26 Mar 2012
Shared Care Pregnancy Management and Beyond
CSGPN Training Facility NSW
Contact Karen Wheeler
(t) +61 2 8752 4906
(f) +61 2 9799 0933
(e) kwheeler@csgpn.com.au
Category 1: 40 points

17 Mar 2012
Reproductive & Women's Health Seminar – Cairns QLD
Contact Vanessa Lahy
(t) +61 7 3833 1020
(e) vanessal@qfg.com.au
Category 1: 40 points

7 Apr 2012
Ambulatory Procedural Gynaecology Course VIC
Healthbridge Hawthorn Hospital
Contact Marissa Van Staden
(t) +61 438 754 989
(e) carissa@ades.com.au
Category 1: 40 points

21-22 Apr 2012
Education Course in Sexual Health for General Practice
HIV & HCV Education QLD
Contact Samantha White
(t) +61 7 3346 4813
(e) s.white@uq.edu.au
Category 1: 40 points

27 Apr 2012
Emergency Care of the Sick Neonate
Kununurra WA 6743
Contact Barbara Carter King
Edward Memorial Hospital
(t) +61 8 9340 1260
(f) +61 8 9381 7802 7802
(e) barbara.carter@health.wa.gov.au
Category 1: 40 points

18-20 May 2012
GPCE Sydney 2012
Contact Belinda Hoy
(t) +61 2 9422 2303
(e) belinda.hoy@reedmedicaleducation.com.au
Category 1: 40 points

19-20 May 2012
Women's Health Conference
Cairns QLD
Contact Zena Horton
(t) +61 7 3105 7800
(e) zhorton@healthworkforce.com.au
Category 1: 40 points

2 Jun 2012
Ambulatory Procedural Gynaecology Course VIC
Healthbridge Hawthorn Hospital
Contact Marissa Van Staden
(t) +61 438 754 989
(e) carissa@ades.com.au
Category 1: 40 points

27 Jun 2012
The Cutting Edge: Gynaecological Procedures
CTEC University WA
Contact John Linehan
(t) +61 8 6488 8049
(e) john.linehan@ctec.uwa.edu.au
Category 1: 40 points

16 Oct 2012
Emergency Care of the Sick Neonate
Kununurra WA
Contact Barbara Carter King
Edward Memorial Hospital
(t) +61 8 9340 1260
(f) +61 8 9381 7802 7802
(e) Barbara.carter@health.wa.gov.au
Category 1: 40 points

Various Dates
Advanced Life Support in Obstetrics (ALSO) Course
Various Locations
Contact Anne Taylor
(t) +61 2 9534 5655
(f) +61 2 8209 4949
(e) anne@mayhemcorp.com.au
Category 1: 40 points

Various Dates
Antenatal Clinical Attachment Southern Health Outpatients Clinic Victoria 3168
Contact Toni Lamarche
(t) +61 3 5970 3727
(e) tonil@monashdivision.com.au
Category 1: 40 points

Various Dates
Cervical Screening Skills Workshop – Queensland
Contact Diane Earl
(t) +61 7 3250 0242
(f) +61 7 3854 0294
(e) dearl@fpq.com.au
Category 1: 40 points

Various Dates
Chlamydia and health consequences in young adults (ACCEPT ALM/Program)
Contact Dr Dyani Lewis
(t) +61 3 9035 4268
(e) dlewis@unimelb.edu.au
Category 1: 40 points

Various Dates
Clinical Audit on Pap Smear (improving the data on "No Pap Smear recorded in the last 4 years) – GPs Practice
Contact Holli Davis
(t) +61 3 5754 1226
(e) hollid@nevicdgp.org.au
Category 1: 40 points

Various Dates
Clinical Facilitation Training FPQ Clinic Fortitude Valley QLD
Contact Diane Earl
(t) +61 7 3250 0242
(f) +61 7 3854 0294
(e) dearl@fpq.com.au
Category 1: 40 points

Various Dates
Counselling Skills Workshop Various Locations
Contact Donna Cowieson
(t) +61 3 9885 0855
(e) lrceducation@breastfeeding.asn.au
Category 1: 40 points

Various Dates
Early Detection of Breast Cancer by Mammographic Screening BreastScreen
South Australia
Contact Dr Frances Cumming
(t) +61 8 8274 7156
(f) +61 8 8357 8146

(e) frances.cumming@health.sa.gov.au
Category 1:40 points

Various Dates
Fetal Surveillance Education Program (FSEP)
Contact Sharon Chang
RANZCOG
(t) +613 9412 2958
(e) schang@ranzcog.edu.au
(w) http://www.fsep.edu.au
Category 1: 40 points

Various Dates
Fetal Surveillance Education Program (FSEP) Refresher Program
Contact Sharon Chang
RANZCOG
(t) +61 3 9412 2958
(e) schang@ranzcog.edu.au
(w) http://www.fsep.edu.au/
Category 2: 8 points

Various Dates
Introduction to Ultrasound in Obstetrics
AIU Ultrasound Training
Broadbeach QLD
Contact Mr Tony Davies
(t) +61 7 5526 6655
(e) tony@aiu.edu.au
Category 1: 40 points

Various Dates
IUD (Intra Uterine Device) Insertion Training
Various Locations
Contact Hilary Bower FPNSW
(t) +61 2 87752 4387
(f) +61 2 8752 4393
(e) education@fpnsw.org.au
Category 1: 40 points

Various Dates
IUD Insertion Training
Various Locations
Contact Diane Earl
(t) +61 7 3250 0242
(f) +61 7 3854 0294
(e) dearl@fpq.com.au
Category 1: 40 points

Master of Women's Health Care ECU Western Australia
Contact Eric Khong
(t) +61 8 6304 3512
(f) +61 8 6304 2254
(e) e.khong@ecu.edu.au
Category 1: 40 point

Various Dates
Neonatal Resuscitation Program
Western Australia
Contact Barbara Carter King
Edward Memorial Hospital
(t) +61 8 9340 1260
(f) +61 8 9381 7802 7802
(e) Barbara.carter@health.wa.gov.au
Category 1: 40 points

Various Dates
Obstetrics & Gynaecology Ultrasound FastTrack Workshop
AIU Ultrasound Training
Broadbeach QLD
Contact Mr Tony Davies
(t)+61 7 5526 6655
(e) tony@aiu.edu.au
Category 1: 40 points

Various Dates
Perinatal in Practice: Managing Perinatal Mood Disorders in General Practice
Various Locations
Contact Dr Katherine Denton
(t) +61 2 9382 4518
(e) k.denton@blackdog.org.au
Category 1: 40 points

Post Graduate Diploma of Women's Health Care
ECU Western Australia
Contact Eric Khong
(t) +61 8 6304 3512
(f) +61 8 6304 2254
(e) e.khong@ecu.edu.au
Category 1: 40 point

Various Dates
SH&FPA Certificate in Sexual Health & Reproductive Health - Short Course
Various Locations
Contact Iris Lawler FPNSW
(t) +61 2 8752 4335
(f) +61 2 8752 4393
(e) irisl@fpnsw.org.au
Category 1: 40 points

Various Dates
SH&FPA Certificate in Reproductive and Sexual Health
Various Locations
Contact Iris Lawler FPNSW
(t) +61 2 8752 4335
(f) +61 2 8752 4393
(e) irisl@fpnsw.org.au
Category 1: 40 points

Various Dates
Ultrasound Workshop
RANZCOG
Contact Debra O'Brien
(t) +61 3 9412 2982
(f) +61 3 9419 7817
(e) dobrien@ranzcog.edu.au
Category 1: 40 points

Online Media and Distance Education

1 Apr–1 Sep 2012

Sexual Health and Family Planning Australia Certificate
Contact Iris Lawler Family Planning NSW
(t) +61 2 8752 4335
(f) +61 2 9716 5046
(e) medicaleducation@fpnsw.org.au
Category 1: 40 points

Sep 2012-Apr 2013

Sexual Health and Family Planning Australia Certificate
Contact Iris Lawler Family Planning NSW
(t) +61 2 8752 4335
(f) +61 2 9716 5046
(e) medicaleducation@fpnsw.org.au
Category 1: 40 points

Beyond babyblues: Detecting and managing perinatal mental health disorders in primary care
Contact ThinkGP
(t) +61 2 8014 6050
(f) +61 2 9878 8065
(w) http://thinkgp.com.au/
Category 1: 40 points

Chlamydia Prevention and Testing in General Practice
Contact Rebecca McNaught
(t) +61 2 4933 3824
(e) Rebecca@hrdgp.org.au
Category 1: 40 points

Diagnosis and Management of PCOS
Contact Carolyn Wall
(t) +61 3 9562 6771
(e) carolyn.wall@jeanhailes.org.au
Category 1: 40 points

Managing Breast Symptoms
Contact GPlearning Help Desk
(t) +61 1800 284 789
(e) contactus@gplearning.com.au
(w) www.gplearning.com.au
Category 1: 40 points

Managing Breast Symptoms
Contact Clined Help Desk Help Desk (t) +61 1800 284 789
(e) contactus@clined.com.au
(w) www.clined.com.au
Category 1: 40 points

Maternal Health Clinical Audit
Contact Jennifer Hains
(t) +61 7 3011 3904
(e) jenny.hains@menzies.edu.au
Category 1: 40 points

Pap Smear Audit - Sullivan Nicolaides Pathology
Contact Margot Hill
(t) +61 7 3377 8442
(e) margot_hill@snp.com.au
Category 1: 40 points

Prescribing hormone replacement therapy: weighing up the evidence
Contact Carolyn Wall
(t) +61 3 9562 6771
(e) carolyn.wall@jeanhailes.org.au
Category 1: 40 points

Proactive Management of HPV Infection
Contact MDBriefcase Australia
Derek Bryan
(t) +61 437696544
(e) rprewitt@mdbriefcase.com
(w) www.mdBriefcase.com
Category 1: 40 points

For further information on Women's Health activities please use this link to visit the RACGP website http://www.racgp.org.au and follow the links

For further information on ACRRM Women's Health activities please use this link o visit the ACRRM website http://www.acrrm.org.au/ and follow the links

The events list will no longer be published in *O&G Magazine*.

The up-to-date events list is available online at: www.ranzcog.edu.au .

If you wish to add your event to the list, please contact:
Val Spark
CPD Senior Coordinator
(t) +61 3 9412 2921
(f) +61 3 9419 7817
(e) vspark@ranzcog.edu.au

The pitfalls of treatment

Dr Geoff Otton
FRANZCOG, CGO

Gynaecologists will be asked to manage women with a pre-invasive disease of the vulva at some point in time. It is essential that we are familiar not only with these conditions, but also with the potential pitfalls of assessment and treatment.

The two main pre-invasive conditions of the vulva are vulvar intraepithelial neoplasia (VIN) and, to a lesser degree, extra-mammary Paget's disease. These conditions are uncommon. However, there is evidence supporting an increased frequency of VIN. Over the last 30 years, there has been a reported 400 per cent increase in the incidence of the disease, especially in young women.[1] All gynaecologists will be asked to manage women with these conditions at some point in their career. There are four basic steps to avoid problems associated with diagnosis and treatment.

The first two of these steps are to establish the diagnosis and determine the extent of the disease before commencing treatment. This may sound obvious, but these steps are not uncommonly overlooked, which results in suboptimal care.

Most women with preinvasive disease of the vulva will have seen their general practitioner with long-standing symptoms such as pruritus, burning sensation, pain and dysuria. They may have noticed a lump or change in pigmentation of the vulvar skin. Occasionally, an asymptomatic lesion will be noticed by the GP at the time of an examination for some other reason. Delay in diagnosis is unfortunately common, as symptoms are often thought to be due to thrush. Frequently, women will have been treated with a variety of topical steroids and antifungal preparations with limited success.

Usually the diagnosis has not been made prior to the consultation with the gynaecologist. Therefore careful colposcopic examination, with application of five per cent acetic acid, of the entire lower genital tract, including the perianal skin, is essential. In younger patients, VIN is more likely to be multifocal, more extensive and human papilloma virus (HPV) related. In contrast, older women usually have more localised disease often arising in a background of lichen sclerosis (LS).[2] Biopsy is mandatory to establish a diagnosis. At times multiple biopsies may be required to determine the extent of the disease and to exclude occult invasion prior to treatment. In younger women, VIN and cancer may appear warty and be misdiagnosed as condylomata accuminata. In older women with chronic untreated LS, the entire vulva may appear abnormal and it can be difficult to determine the worst area. Cancer, if present, may be obvious, but occult invasion is difficult to determine clinically.

Paget's disease of the vulva has an eczematoid appearance. In the author's experience, however, it can be very subtle. This highlights the importance of histopathology prior to commencing treatment, especially in women with persistent symptoms who have not responded to the usual gamut of medical therapies.

The aims of treatment

The aims of treatment need to be considered, including:

- control of symptoms;
- preventing the progression to invasive cancer;
- preventing recurrence of the condition; and
- preserving as much normal vulvar anatomy and function as possible.

Keeping the aims of treatment in mind helps to set the foundations of treatment. For example, an elderly woman with 30 years of symptoms due to lichen sclerosis who then develops VIN may not object to more extensive surgery if there is a reasonable chance that her symptoms will improve and it reduces her risk of developing cancer, even if the clitoris is removed. Other options may need to be considered in younger women. The natural history of VIN will never be completely understood, but it is thought the risk of progression to cancer occurs in about four per cent of treated cases and up to 87.5 per cent of untreated cases.[4]

Treatment needs to be individualised

Finally, treatment options need to be considered. No one treatment modality is ideal for every patient and therapy should be individualised based upon the patient's diagnosis, age and comorbidities, the position and size of the lesion/s and the condition of the remaining vulvar skin.

Treatment options include surgical excision, carbon dioxide laser and Imiquimod cream. Surgical resection is the author's preferred option as it removes the lesion and allows histopathological assessment of the surgical margins, but also excludes occult invasive carcinoma. This is more relevant in older women. For VIN, a surgical margin of 5mm is considered reasonable, but it should be remembered that the lesion may extend beyond the visible margin.[5]

Primary closure is usually possible with small lesions where there is some mobility of the surrounding skin. However, where there would be excessive tension or the cosmetic/functional result would be inferior, a flap repair should be considered. A number of flap procedures have been described, but are beyond the scope of this article. In general, the ideal flap not only fills the resection defect, but also allows easy closure of the donor site.

Wound breakdown and delayed healing are recognised complications of treatment.[4] The best way to avoid this problem postoperatively is to ensure a tension-free wound at the time of surgery. Patients should also be given advice postoperatively to minimise physical activity for about three to four weeks. Depending upon the size of the defect after resection, the patient and the experience of the gynaecologist, consultation with a plastic surgeon may be appropriate.

Carbon dioxide laser ablation is used widely with similar recurrence rates. It is particularly useful in lesions close to, or involving, the clitoris and/or external urethral meatus. Some consider laser to be the treatment of choice, especially for young women.[3] Very large lesions can be extremely painful after laser ablation and patients need to be warned of this. In addition, it is important to rule out invasive cancer prior to commencing this therapy. Care should be taken using any ablative treatments in those women past the menopause because they are at higher risk of squamous cell carcinoma (SCC) at diagnosis.[2]

Aldara Cream (five per cent Imiquimod), a topical immune response modifier, has been used increasingly in women with VIN and there is evidence for its efficacy, especially in young women with human papilloma virus (HPV)-related disease. As is the case with other treatment modalities, it is more efficacious with small lesions. It also preserves vulvar anatomy. Response rates of up to 64 per cent have been reported. However, about 25 per cent will have limited response and require additional ablative or surgical resection. Recurrence rates of 25 per cent have been reported.[6] Care must be taken to exclude invasive cancer before using this option.

Informed consent

Consent is an essential part of the therapy. Surgery on the vulva can result in significant anatomical distortion and psychosexual dysfunction. The extent of any procedure needs to be explained clearly. It is essential to work out what the patient understands about their procedure, especially if there will be loss of the clitoris and/or labia minora. The clinician cannot assume the woman understands her external genital anatomy and she may not fully comprehend what is being treated or removed. Nor can it be assumed a woman has ceased sexual activity based upon her age. A sexual history is important in developing treatment options and ensuring women consent to the side effects of treatment.

The loss of the labia minora can also result in spraying of urine on to the inner thighs rather than in a directed stream. This can be an awkward side effect of surgery. Some women will go on to develop a dermatosis from chronic exposure to urine, very similar to 'nappy rash'.

It is reasonable to also warn patients of the possibility of recurrence. This is more likely if surgical margins are involved and further treatment may be required. However, provided the macroscopic lesion is completely removed, further surgical excision is usually not warranted in the short term. In the event that a malignancy is detected, the initial step would be to, at least, discuss the case with a gynaecologic oncologist and have the pathology reviewed to determine if any further treatment is required.

Patients require follow up

Recurrence rates of VIN in the order of 15–50 per cent have been reported.[2] Accordingly, women who have been treated will require follow up. However, there are no evidence-based guidelines as to what constitutes appropriate surveillance. It is the author's practice to colposcopically examine women every six months for two years and then yearly up to five years after treatment, depending upon the age of the patient and condition of the remainder of the vulva. For example, a young woman with a localised lesion that has been fully excised is at lower risk of recurrence than an older woman with extensive LS. There is evidence to suggest older women are at increased risk of recurrence.[2]

Immunocompromised patients

Women who are immunosuppressed are at higher risk of HPV-related disease of the lower genital tract. Long-term steroid use and immunosuppressents used in organ transplant recipients are the more common contributing factors; however, women with HIV infection or some forms of congenital immunodeficiency syndrome remain at risk of developing preinvasive disease and cancer. These women may actually have a 'field' defect with disease involving the cervix, vagina, vulva and perianal skin. Close, life-long follow up is required in these women.

In summary, preinvasive disease of the vulva can be difficult to manage. Care must be taken as, not surprisingly, patients are often anxious and frustrated. They need adequate counselling (sometimes formally with a psychologist) and preparation. Treatment should be individualised with an aim to not only treat the disease, but also preserve as much normal vulva as possible. Developing adequate skills to manage these problems is difficult due to their infrequent presentations.

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Vulvar and vaginal cancers

Dr Gregory Robertson
FRCOG, FRANZCOG

Carcinomas of the vulva and vagina are some of the most uncommon. This article discusses diagnosis, staging and treatment options.

Carcinoma of the vulva is uncommon in Australia, with 280 new cases being diagnosed each year or two women per 100 000. It accounts for less than one per cent of all cancers in women. It usually occurs in women between the age of 55 and 75 years old and is associated with irritant conditions such as lichen sclerosus et atrophicus. In younger women it is associated with human papilloma virus (HPV) infection and smoking.

Diagnosis

Vulvar cancers usually present as a raised lump or ulcerated area. In making the diagnosis it is preferable that either a Keyes punch biopsy or a small wedge biopsy, including adjacent normal skin, is performed. Excising the entire lesion may compromise the patient's care, either by making the site of the lesion difficult to detect due to superior healing of the area or limiting the use of sentinel groin node detection. This is especially true of the smaller lesions. As vulvar carcinoma is often associated with cervical carcinoma (ten per cent), cervical cytology should also be performed at diagnosis.

Management

Surgery remains the key for localised disease. Obtaining a 1cm surgical margin and dissecting down to the inferior fascia of the uro-genital diaphragm is uncommonly associated with recurrence, whereas if the margin is less than this up to 50 per cent will recur locally. The risk of groin node metastases is related to depth of invasion (see Table 1). Usually the ipsilateral nodal group is at risk, except for lesions that involve midline structures such as the anterior labia minora or clitoris, in which case both groins are at risk and need to be assessed.

If the groin nodes are negative then the survival rate is very high. The number of positive groin nodes remains the single most important prognostic factor. The presence of a single nodal metastasis of less than 5mm in diameter still carries a good prognosis compared to more than two groin nodes involved or extracapsular spread of the metastases from the node, where prognosis falls to a 50 per cent five-year survival. Pelvic nodal metastases, the next echelon of nodal spread, are associated with an 11 per cent five-year survival.

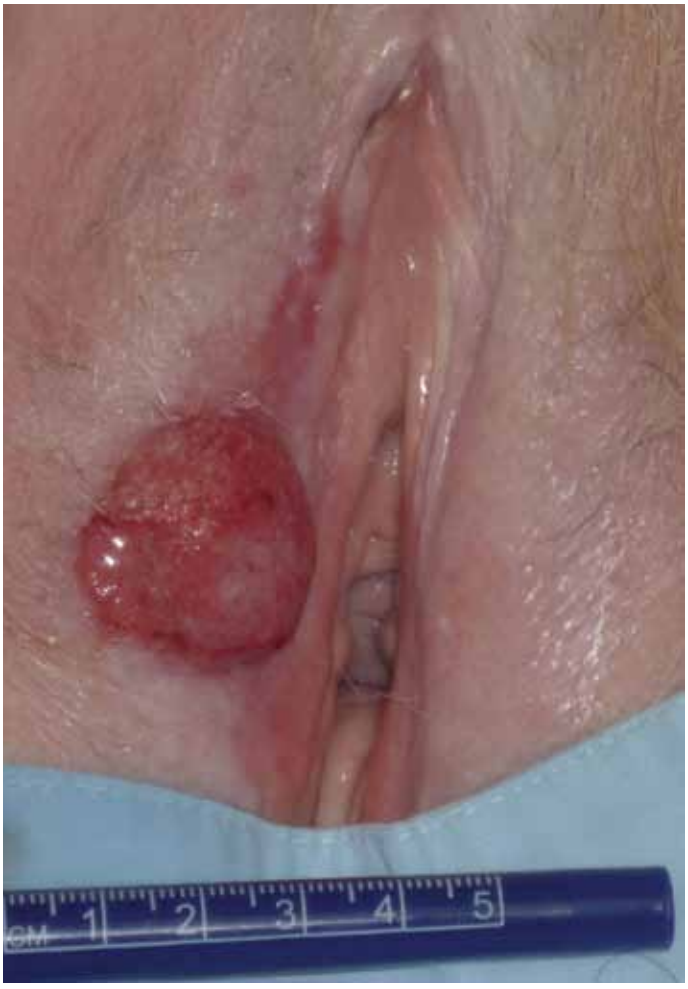
Adjuvant radiotherapy to the groin and pelvic nodes is utilised with more than two positive nodes. Where it is not possible to achieve local vulvar clearance, it may also be used in an adjuvant setting or in advanced disease it may the primary treatment modality followed by resection of residual disease. The morbidity associated with radiation to the vulva requires a skilled radiation oncologist to nurse the patient through her treatment; frequently with breaks in the treatment so she can tolerate the complete course.

Sentinel groin node biopsy in vulvar cancer

The standard of care for vulvar lesions of greater than 1mm invasion and in the absence of obvious nodal metastases is a radical vulvar excision achieving at least a 1cm margin, together with either ipsilateral or bilateral groin node dissection, depending on the location of the tumour. As with breast cancer, the concept of detecting the sentinel node in the groin is highly attractive, because of the high morbidity associated with complete node dissection. However, with lesions less than 4cm in size up to 80 per cent of nodes will be negative. The confounding factor is

Table 1. Risk of nodal metastases based on depth of invasion in vulvar cancers <2cm (T1) (taken from Berek & Hacker 3rd Ed Practical Gynecologic Oncology).

Depth of invasion	Percentage risk of groin node involvement
<1mm	0
1.1–3mm	8 per cent
3.1–5mm	26 per cent
>5mm	35 per cent



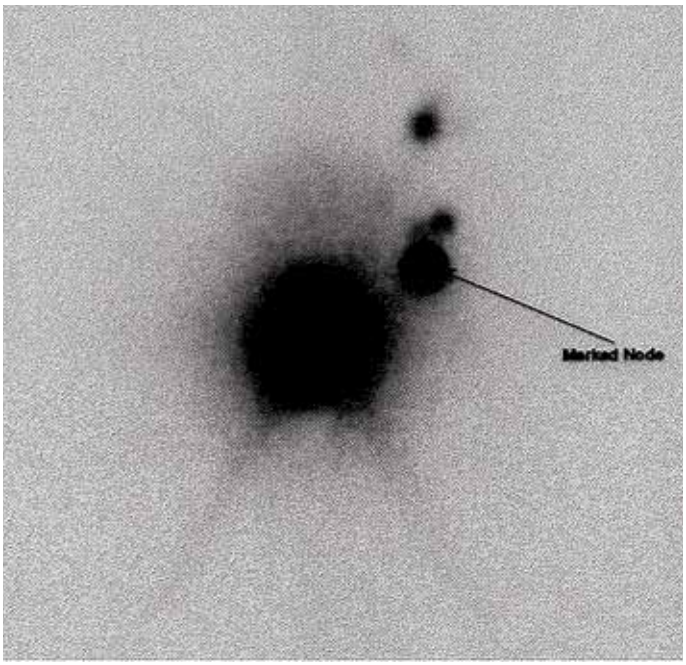
Carcinoma of the vulva.

Table 2. FIGO staging 2009: carcinoma of the vulva.

I	A		Tumour confined to the vulva or perineum, ≤2cm in size with stromal invasion ≤1mm, negative nodes
I	B		Tumour confined to the vulva or perineum, >2cm in size or with stromal invasion >1mm, negative nodes
II			Tumour of any size with adjacent spread (1/3 lower urethra, 1/3 lower vagina, anus), negative nodes
III	A		Tumour of any size with positive inguino-femoral lymph nodes
		1	One lymph node metastasis greater than or equal to 5mm
		2	One to two lymph node metastasis(es) of less than 5mm
	B	1	two or more lymph nodes metastases greater than or equal to 5mm
		2	three or more lymph nodes metastases less than 5mm
	C		positive node(s) with extracapsular spread
IV	A		Tumour invades other regional structures (2/3 upper urethra, 2/3 upper vagina), bladder mucosa, rectal mucosa or fixed to pelvic bone
			Fixed or ulcerated inguino-femoral lymph nodes
	B		Any distant metastasis including pelvic lymph nodes

that 90 per cent of women will die if they recur in an undissected groin. So what false negative rate do you accept and at what risk to your patients?

The technique involves the injection of technetium 99-labelled albumin colloid around the lesion then performing scintigraphy with a gamma scan to determine the first draining inguinal lymph node. Vital blue is often used, again injected around the lesion at time of surgery, to assist with identification of the sentinel node together with the use of a handheld gamma probe. It should be reserved for patients with tumours of less than 4cm diameter and in whom no suspicious inguinal lymph nodes are present.



Gamma scan one hour post injection of Technichium into the vulva.

Two large studies have shown a false negative rate of 5.9 per cent and 6.9 per cent, while other institutions trying to replicate these studies have reported a 17 per cent false negative rate. It is fair to say this technique is not universally applied in all Australian institutions, but some do use sentinel lymph node examination alone. Some studies have looked at patient reaction to the risk of death associated with recurrence in an undissected groin and suggest patients would not be prepared to expose themselves to that risk, instead opting for a traditional full groin node dissection.

Staging in vulvar cancer

The International Federation of Gynecology and Obstetrics (FIGO) staging was modified, in 2009, to improve the prognostic groupings in terms of survival and to add further sophistication to the staging to reflect the significance of lymph node morphology (see Table 2). Several studies have confirmed that, in comparison to the 1988 staging system, the introduction of differentiation between the number of nodes involved and the presence of extra-capsular spread does stratify survival more accurately.

Carcinoma of the vagina

This is an uncommon cancer, accounting for less than 0.5 per cent of all cancers affecting women. Squamous cell carcinoma is the most common, although clear cell carcinoma secondary to maternal diethylstilbestrol (DES) exposure is probably the most well known among gynaecologists. Survival is not as good as it is for cervical carcinoma with a 70 per cent five-year survival for stage I disease through to 18 per cent for stage IV disease.

The precursors of vaginal carcinoma are not well known – vaginal intraepithelial neoplasia (VAIN) is thought to account for at most five per cent, although approximately 30 per cent of women with a diagnosis of vaginal carcinoma have a history of pre-invasive or invasive cervical carcinoma treated within five years of diagnosis. In the author's limited experience, VAIN needs to be respected and treated aggressively, particularly in more mature women in whom, if it develops into vaginal carcinoma, it is often resistant to chemoradiation. Prior pelvic irradiation is also a risk factor.

Given that screening is inappropriate for primary detection of this disease, the current screening recommendation is for vaginal vault smears in women with a past history of cervical dysplasia on a two-yearly basis post hysterectomy.

Presentation is usually with either screen detection or painless vaginal bleeding. Most lesions are confined to the upper posterior vagina, but are often missed because of masking of the lesion by the blades of the speculum. In patients who have persistent high-grade smears, but negative colposcopy, an examination of the entire vagina with Lugo's iodine under general anaesthetic may be appropriate. In postmenopausal women, the use of vaginal oestrogen before the procedure may aid visualisation of the lesion.

Management

The care of patients is very individualised and best done in an oncological centre. Given the incidence of pelvic nodal metastases may be as high as 28 per cent and groin node metastases in the order of 30 per cent in patients with lower-third vagina disease, it is important to treat each case on its merits. Younger patients may benefit from surgery, if possible, otherwise radiotherapy using a combination of pelvic radiation and brachytherapy is widely used. Concurrent cisplatin is the standard in most units.

Post-treatment vaginal stenosis either due to surgery or concomitant radiotherapy remains the largest difficulty for most patients wishing

to preserve sexual function. However, bowel and bladder toxicity remain real problems given the high dose of radiotherapy delivered. Survival is poorer than that found with cervical cancer.

Diethylstilboestrol exposure

The use of diethylstilboestrol (DES), a synthetic nonsteroidal oestrogen first synthesised in 1938, is a fascinating story, beginning with its use in prostate cancer in 1941. It was always used in tablet form varying in dose from 5–125mg, not as an injectable as progestagens were. Its initial indication for usage was gonorrheal vaginitis, atrophic vaginitis, menopausal symptoms and postpartum lactation suppression to prevent breast engorgement. In 1947, it was approved for use in pregnancy to prevent miscarriage although it had been used off label for the same indication since the early 1940s. It was recommended to be used at 5mg per day then increased ultimately to 125mg per day by the 35th week of pregnancy. Studies in the 1950s showed that it did not prevent miscarriage, but nevertheless was still prescribed.

In 1970, Herbst and Scully reported on seven young women aged between 15 and 22 years old with clear cell carcinoma of the vagina. All were the child of a woman who had been prescribed DES in pregnancy. The risk of clear cell carcinoma of the vagina was estimated to be one per 1000, with 70 per cent being diagnosed as stage I vaginal adenocarcinomas. This represents a 40-fold increase in risk and is the only known transplacental carcinogen. Other changes occur such as vaginal adenosis in 45 per cent of women and structural changes such as the so called cockscomb, transverse vaginal septum, cervical hypodysplasia or other such changes, in 25 per cent of women. Exposure after 22 weeks was associated with insignificant change.

More recently a report by Hoover et al has suggested that first-generation exposure is associated with infertility, preterm labour, first and second trimester miscarriage, pre-eclampsia, stillbirth and early menopause as well as a higher risk of breast cancer. In males it can be associated with testicular cancer, infertility and urogenital abnormalities in development, such as cryptorchidism and hypospadias.

Women exposed to DES are recommended to have annual colposcopy and vaginal cytology.

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The psychology of cancer

Dr Brett Daniels
PhD, MBBS, FRANZCOG

Diagnosis with a gynaecological cancer is traumatic for many women. An understanding of the psychology of cancer can assist us to provide better care for these women and their families.

Like most of us, I have been fortunate to never receive the words 'I'm sorry, you have cancer' from my doctor. However, I have delivered these words to patients and felt inadequate in my ability to console, reassure or empower them. To some extent I'm not certain what the purpose of the 'I'm sorry, you have cancer' conversation is. Is it simply to inform or should there be more to it? Certainly, if somehow you fail to communicate the diagnosis clearly, then you have failed the patient in the interaction. But what then? What should you add? What should the patient say? Are there normal and abnormal responses to the 'I'm sorry, you have cancer' statement? Should you be reassuring patients, or letting them find their own path? Does any of it make a difference in the long run?

The psychology of cancer is controversial. Practitioners of one school have had successful careers with techniques others will decry as untested and illogical. This article will focus on two areas of interest to people working with women with gynaecological cancer. The first is the idea of a normal grief process experienced by people diagnosed with a terminal illness; the second is the effect of a positive attitude on the outcome of cancer. It should of be borne in mind that while much of this article focuses on patients facing a terminal illness, for many women the diagnosis of a gynaecological cancer is not necessarily a death sentence. It is just as vital that we communicate effectively the relatively positive prognosis of early-stage endometrial cancer as we sensitively explain the consequences of disease with a worse outcome.

> '...a compulsory 'one size fits all' provision of counselling after a major traumatic event harms more people than it helps.'

Grief

People may experience grief in many situations. The death of a loved one is perhaps the purest example of the process, however, loss of other important aspects of life, such as a relationship or job, can also elicit a grief response. The reaction of a person to receiving a diagnosis of terminal illness such as cancer can also be understood as a grief process.

The work of Swiss-American psychiatrist Elisabeth Kubler-Ross on patients' psychological response to terminal illness has been influential since its publication in 1969.[1] For many practitioners and patients, her work remains useful in understanding the effect of a diagnosis of cancer on our patient's psyche.

Kubler-Ross described the stages of grief thus:

- Denial: ' there must be a mistake, this can't be happening to me.'
- Anger: 'why me, who can I blame?'
- Bargaining: 'if I can just survive this then I'll be a better person.'
- Depression: 'what's the point in doing anything?'
- Acceptance: 'I know that I'm going to die, how can I prepare myself?'

Kubler-Ross believed not all people went through all five stages or went through them in the same order. She believed every person went through at least two stages and that people could go back and forth between stages. The idea of stages of grief, and the desirability of moving from the earlier to later stages, underlies much of the traditional approach to grief counselling. Anecdotally, however, many of us have had experiences with people who appeared to grieve in an adaptive way, not in the order described by Kubler-Ross. A 2007 study of 233 bereaved people confirmed this, with the most common initial stage being acceptance, rather than disbelief.[2]

More recently, the research of George Bonanno has revealed that the five stages of grief are not universally applicable or necessary. Bonanno performed large empirical studies on populations of people suffering loss and bereavement. Two major facets of his work are the idea of resilience and of the four trajectories of grief. Psychological resilience refers to the ability of some individuals to deal with apparently major losses or trauma without going through a recognisable grief process. These people do not appear to experience any of the five stages of grief and do not suffer long-term psychological sequelae. An important part of Bonanno's work related to this was his finding that a compulsory 'one size fits all' provision of counselling after a major traumatic event harms more people than it helps.

Bonanno identified four trajectories of grief[3]:

1. Resilience: in which an individual maintains stable, healthy levels of physical and psychological function, despite exposure to an event of loss or threat.
2. Recovery: in which there is a temporary period of clinical or subclinical psychopathology, such as depression or post-traumatic stress disorder, before return to a pre-event level of function.
3. Chronic dysfunction: prolonged suffering and inability to function.
4. Delayed grief or trauma: in which a person appears initially to have coped well, with symptoms appearing later.

In practice, both models provide important lessons. Bonanno's description of the variety of trajectories of grief highlights that there is not a single correct way of dealing with grief, including receiving a diagnosis of cancer. People respond in many different, yet ultimately adaptive, ways and clinicians should not try and mould them into a 'correct' method of grieving. On the other hand,

Kubler-Ross' stages provides one possible model by which clinicians and their patients may begin to understand the psychological effect of their illness.

Positive psychology and cancer

While grief may be seen as an effect of cancer on a person's psychological state there is the converse consideration of whether psychological state can change the progression of a person's physical disease. Proponents of positive psychology cite the positive influences of 'fighting spirit' and optimism on survival and other outcomes of cancer, and describe personal growth and 'benefit finding' experienced by some patients with cancer.

Positive psychology, like many areas of psychology, has vehement supporters and critics. Unfortunately, controlled studies are few and academic literature fails to reach a convincing conclusion. A series of articles published in 2010 highlights these divisions.[4-7] Although evidence for an improvement in survival attributable to fighting spirit or other positive psychological factors has not been demonstrated reliably, it appears short-sighted to deny that there may be other, non-survival based benefits, which some patients may experience from maintaining a positive psychological outlook.

> 'There is no optimal way to talk to your patient with cancer. There is no right way for them to grieve and no right attitude for them to have towards their cancer.'

Conclusion

In medicine, theory only leads us so far. We read the literature and make our plan, but there always comes a time to act. Ultimately, we have to cut or not cut, treat or not treat, speak or not speak. There is no optimal way to talk to your patient with cancer. There is no right way for them to grieve and no right attitude for them to have towards their cancer. Person-centred Rogerian therapy uses the terms 'genuineness' and 'empathy' to describe the therapist's honesty and desire to understand their patient's internal frame of reference; these are qualities beneficial to any doctor talking to their patients. In practice, we do more good carefully listening to our patients – and supporting them as they make their own personal choices about their grief and their disease – than we will do attempting to prescribe a course of action for them.

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helping to drive research excellence in women's health

'Ab umbris ad lumina vitae' a short history of colposcopy

Prof Caroline de Costa
FRANZCOG

While the College motto is generally regarded as applying to the process of normal birth, it is also an appropriate reference to the history of colposcopy. Much of the research that underpins our current understanding of cervical pathology took place in the concentration camps of Nazi Germany.

The history of colposcopy begins in Hamburg, Germany, in the early 1920s. German gynaecologists were beginning to understand that cancer of the cervix might have a precursor condition, which they termed 'carcinomatous surface coating'. In 1921, the professor of gynaecology at Hamburg University, Von Franqué, assigned his assistant, Hans Hinselmann, to the study of this cervical surface. In particular, he advised him to look at the leukoplakias that, it had already been observed, could be seen with the naked eye, adjacent to many small cervical cancers.

Hinselmann realised that to see these small lesions properly some magnification was needed. As he would later write: 'the examination of the cervix and vagina with the unaided eye does not meet the demands of scientific appraisal. The use of magnification [is required].' With the help of technicians from the Leitz Company, the predecessor of Leica, manufacturers of cameras and microscopes, he devised the first binocular colposcope. This was a cumbersome creation, but it enabled him to gain an excellent view of the cervical epithelium. However, instead of the tiny ulcer, surrounded by leukoplakia, that he had expected to find preceding cervical cancer, he discovered a range of distinctive surface appearances that reflected histological changes in the epithelial tissues beneath them. Thus began his lifelong study of the cervix and the development of the science and terminology used by colposcopists today.

Hinselmann published his first paper on colposcopy in 1925, and the first textbook of colposcopy in 1933; the latter included a description of mosaic patterns in lesions that Hinselmann recognised as pre-cancerous. In 1930, he became director of his own gynaecological clinic, the Frauenklinik Altona in Hamburg. Gynaecologist Dr Helmut Wirths, whose brother Eduard was also a doctor, worked with him.

In the years before the Second World War, gynaecologists in a number of countries became interested in colposcopy and in Hinselmann's work. They included Babes in Romania; Levy, Emmert, Broders and Sacks in the USA; Usandizaga in Spain and Shaw in the UK. In the USA, Papanicolau's work on vaginal cytology and its ability to detect cervical abnormalities was also gaining currency, although at first it seemed to clinicians that the two techniques were in competition rather than potentially complementary. Colposcopy was introduced to Argentina by Jakob in 1932. He established the first colposcopy clinic in South America, a part of the world where the techniques and science of colposcopy have flourished ever since.

By the late 1930s, a substantial number of US gynaecologists were taking an interest in the possibilities the colposcope offered. There were some reservations; in 1934 Sacks commented on 'the cumbersome binocular endoscope of Hinselmann'. Another American, Gelhorn, in 1936 praised Hinselmann as having 'added a new chapter to gynaecologic diagnosis', but he also felt that: 'the size, clumsiness and great expense of Hinselmann's colposcope mitigates against its universal adoption.' However Farrar, writing in 1938, pointed out that: 'It takes time and patience to acquire skill with a new technique, and one must learn what a normal cervix looks like when viewed with low and then high magnification.' Farrar was also one of the first writers in English to describe the transformation zone as the site of pre-malignant change: 'Early carcinoma of the cervix…begins in the majority of cases in the unbroken epithelium of the external os on the borderline between the columnar epithelium of the cervical canal and the squamous epithelium of the portio, and spreads laterally. It is simple, white in color, and its borders are sharply defined from the adjacent tissue.'

Meanwhile, in Switzerland, Schiller in 1936 introduced the use of iodine, still often applied today to demarcate abnormal areas. Two years later Hinselmann himself described the use of acetic acid for the delineation of cervical abnormalities visible colposcopically. What prompted Hinselmann's use of vinegar in this unorthodox way? My own theory is based on the fact that douching was at the time a common habit, particularly among European women, for reasons of 'feminine hygiene' and attempts at postcoital contraception. Dilute household vinegar was a product commonly used for this purpose. Very possibly Hinselmann observed in one or more patients who had followed this practice the characteristic changes in the epithelial appearances. The use of acetic acid rapidly spread and, in 1939, Kraatz, working in Germany, devised the green filter, through which abnormal areas painted with dilute acetate are even more clearly demarcated. In England, Shaw acquired a colposcope and began the practice of colposcopy in the UK.

During the Second World War, Hinselmann remained in his clinic in Hamburg, as did Helmut Wirths. Contact with colleagues in Allied countries ceased. Eduard Wirths had joined the Nazi party while still a medical student and, in 1934, he joined the SS. When the war began he was first sent to the Russian front, but after a heart attack was transferred as medical director first to Dachau concentration camp and then to Auschwitz. There is good evidence to show that under Eduard Wirths' direction, a German-Jewish gynaecologist and prisoner, Maximilian Samuels, was compelled to perform colposcopies, using a Hinselmann colposcope, on Jewish women prisoners, take photos of the results, then remove the cervixes and despatch them to Hinselmann's clinic in Hamburg. It would seem that Helmut Wirths was also involved in this process and that he visited his brother in Auschwitz and performed some colposcopies there.

After the war, Hinselmann was found guilty by the Allies of having conducted forced sterilisations on Gipsy women at the Altona clinic

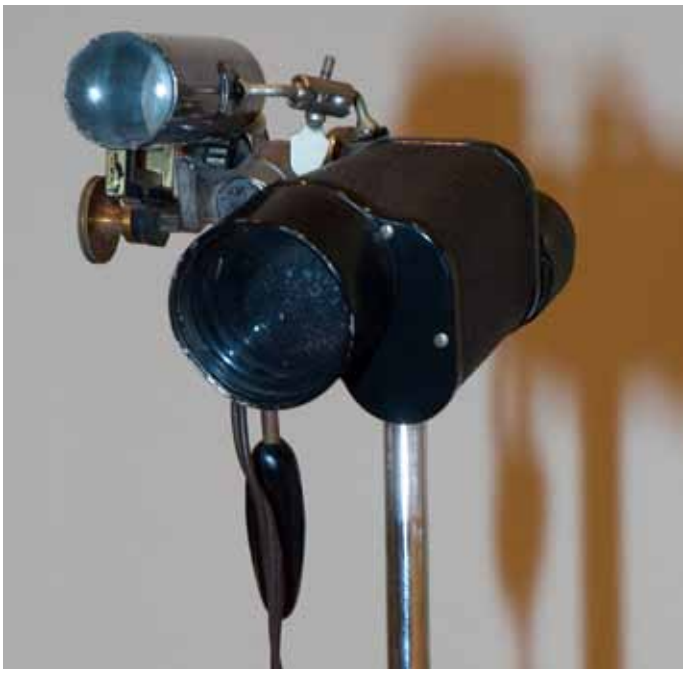

Figure 1. Colposcope 1970s from the RANZCOG Museum collection. Dr Mitchell used one half of a pair of field glasses and some ingenious welding techniques to create his unique instrument. Donation of Mrs Paul Mitchell, 1998.

and sentenced to three years' imprisonment. Viennese historian Ruth Jolanda Weinberger, who has conducted research into medical experimentation in Auschwitz using original documents from the camp hospital, has produced convincing evidence also linking Hinselmann to the study of the cervical tissues obtained from Auschwitz.

With the war over, there was renewed interest in colposcopy in Europe and North America, and renewed contact with colposcopists in South America. Hinselmann himself seems to have been rehabilitated by the late 1940s; he made several visits to South America and one to Spain to lecture and teach the techniques. Bolten, who has been called 'the father of modern colposcopy in the United States', came to the USA in 1953 from Germany, where he had been trained in colposcopy. First in Philadelphia and then in New Orleans, he trained others who formed a nucleus that led to the foundation of the American Society for Colposcopy and Colpomicroscopy in 1964. By 1977, it was estimated that some 3000 US gynaecologists had been trained in colposcopy, and colposcopy became integrated into teaching programs for residents in gynaecology. By the mid 1950s it was becoming acknowledged both in the Americas and in Europe that cytology and colposcopy could be complementary techniques in the diagnosis of cervical pre-malignancy.

In 1956, Stallworthy at the Radcliffe in Oxford acquired a colposcope. Not long after, the young Malcolm Coppleson arrived from Sydney as a registrar, rapidly mastered the use of the instrument and began a career that included world eminence in the field of cervical pathology and its management. Coppleson's first papers on the value of colposcopy in detecting precancerous lesions appeared in 1960; in 1967, he and Reid published a book on premalignant conditions of the cervix. In 1971, the first British colposcopy group was founded; in the same year Coppleson, Reid and Pixley published the first edition of their colposcopy text, which refined terminology and established the importance of the transformation zone. It was from this group that Australian colposcopy rapidly developed.

Figure 2. The FROGs travelling colposcope, which travels an average 1000km each working week.

Not everyone could afford an elegant imported German colposcope for their private practice. Undaunted, Dr Paul Mitchell of Brisbane made his own (see Figure 1) – now part of the RANZCOG College Collection. Perhaps other examples of such gynaecological ingenuity lurk unacknowledged in garages across Australia.

Colposcopy now plays an integral role in Australian and New Zealand gynaecological practice, and is part of the training of all gynaecologists. The travelling colposcope (see Figure 2) of the Far North Queensland Obstetric and Gynaecological Service (FROGS) is just one example of the use of smaller, easily-portable instruments in practice in rural and remote parts of the country.

We are much indebted to the original work of Hinselmann. However, we should also pay attention to the words of Weinberger, who wrote in 2007:

> 'Sixty-two years after the liberation of Auschwitz, the father of the colposcope remains a key figure in medical history, and for the untold number of lives he has saved he deserves credit. But for his complicity in the unbearable suffering inflicted on Jewish women in Auschwitz… Hinselmann deserves a qualified entry in the history books – and a moment of reflection from the millions of women who each year undergo a colposcopy.'

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Fetal death of a twin

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The management of single fetal death in a twin pregnancy can be difficult for any obstetrician.

Perinatal mortality in twin pregnancies is approximately five times higher than in singleton pregnancies. If both fetuses die the management is straightforward: delivery by the most appropriate means. Death of one of a twin pair is more challenging. The sequelae for the surviving co-twin may be significant, with risks of demise, premature delivery with its consequences and the risk of neurological impairment. Chorionicity, amnionicity, gestation and potential causation must all be considered when determining appropriate management.

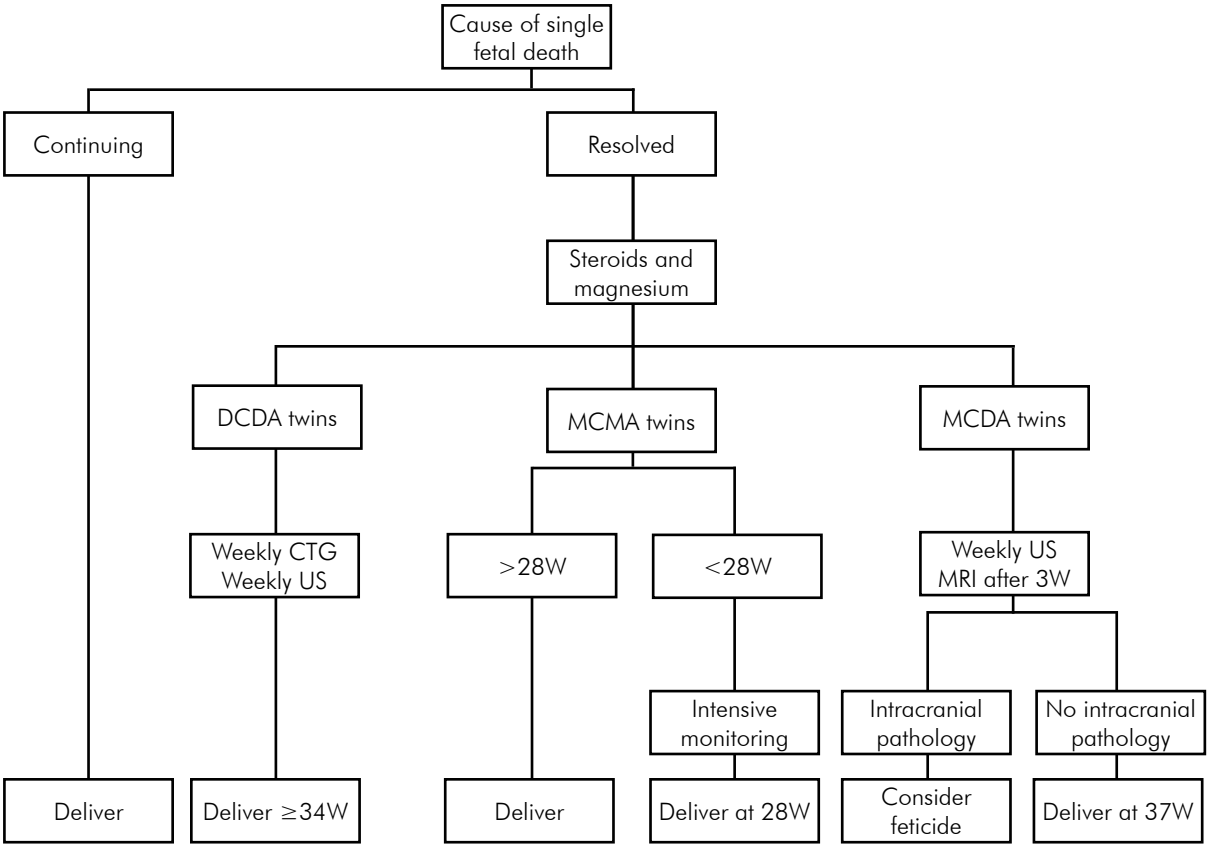
Prevalence

'Vanishing twin' is a term that has been used to describe the spontaneous loss of a twin during the first trimester. Around 23 per cent of twin pregnancies diagnosed by ultrasound at six-weeks gestation will be singleton pregnancies by 12 weeks. Bleeding or mild cramping may be noticed in the first trimester, but there are no longer term implications for the pregnancy. Grief for the lost twin may be significant and may need to be addressed.

The loss rate for a single twin during the second and third trimesters varies widely in reported series from 0.5 per cent to 11.6 per cent. Although monochorionic (MC) twins account for 30 per cent of all twin pregnancies they account for most of the fetal losses and the vast majority of adverse neurological outcomes. In several recent series, where accurate data is available, the loss rates for MC versus dichorionic (DC) twins has been reported as 3.9 per cent versus 1.3 per cent, 11.6 per cent versus 5.0 per cent and 6.5 per cent versus one per cent, respectively.

Aetiology

The aetiology of single fetal loss in a twin pregnancy varies by placentation and may be iatrogenic or spontaneous in nature.



A flowchart outlining treatment guidelines.

Fetal reduction

Single fetal loss in a twin pregnancy may be a consequence of either selective or multifetal pregnancy reduction. The former is performed for a fetal abnormality. The latter may be performed either because it is deemed medically unsafe to proceed with a twin pregnancy or because the parent(s) are unable to cope with a multiple birth.

Dichorionic diamniotic twins

Spontaneous single fetal loss in dichorionic diamniotic (DCDA) twins is usually a consequence of growth restriction, frequently unrecognised. The risk of fetal death increases with the degree of growth discordance, particularly when discordance exceeds 30 per cent.

Pre-eclampsia may result in the loss of one twin only – indeed, loss of the twin is often associated with a short-term improvement in the condition.

Other obstetric complications may result in the demise of only one of a twin pair: placental abruption, gestational diabetes, fetal abnormalities, intrauterine infections and cord accidents.

Monochorionic diamniotic twins

Twin-twin transfusion (TTTS) accounts for at least 50 per cent of all single MCDA twin deaths. Even with extensive and careful surveillance, the risk of sudden fetal death in the third trimester in these pregnancies is 1.2 per cent to six per cent, depending on the level of surveillance. Many have advocated planned early delivery to avoid this complication, but it is controversial.

Selective fetal growth restriction, particularly of the Gratacos type 2 and 3 variants, accounts for significant numbers of fetal deaths in MCDA twins.

Fetal anomalies, which are much more frequent in MC twins than either DC twins or singletons and include particularly cardiac and neurological abnormalities, account for a large proportion of MCDA single twin deaths. Most MC twins, although monozygotic, are discordant for fetal abnormalities.

Twin reversed arterial perfusion (TRAP) sequence is a rare complication of MCDA twins, but whether an acardiac twin can be counted as a fetal death is dubious.

Cord ligation to treat a fetal abnormality or TTTS is obviously lethal to the targeted twin. The procedure isolates the circulation of the co-twin and eliminates the risk of subsequent injury to the survivor. Clinical circumstances will determine if there may have been a pre-existing insult to the fetus.

Laser ablation of communicating vessels to treat TTTS not infrequently results in the demise of one of the twins. If the laser treatment has been successful, the placenta has been effectively dichorionised and there is again no risk of subsequent injury to the survivor, but there may be concerns about a pre-existing insult to the fetus.

Monochorionic mono-amniotic twins

Cord entanglement in monochorionic monoamniotic (MCMA) twins accounts for more than 50 per cent of all losses and may involve one or both twins.

Fetal abnormalities, particularly cardiac and neurological, complicate approximately 25 per cent of all MCMA twins. The abnormalities are frequently lethal, but the twins are usually discordant for the abnormality.

TTTS is less common in MCMA than in MCDA twins, but still contributes to fetal loss.

The same concerns about cord ligation and laser treatment apply to MCMA twins as to MCDA twins.

Complications of fetal death of a twin

Death of the co-twin

The risk of co-twin death following death of a twin after 20 weeks gestation is 12 per cent (95 per cent CI 7-18) for MC twins and four per cent (95 per cent CI 2-7) for DC twins. In a careful systematic review, where there was comparative data, the odds of MC co-twin death were six times higher than DC twins following a single in utero twin death: OR 6.04 (95 per cent CI 1.84-19.87).

Neurological sequelae

Chorionicity is the prime determinant of outcome when one twin dies. DC twins do not share a circulation and so are haemodynamically independent.

MC twins share a circulation with varying combinations of arterio-arterial (AA), arterio-venous (AV) and veno-venous (VV) anastomoses. Death of a MC twin may damage the co-twin by one of two mechanisms. The 'thromboplastin theory' proposes that the passage of thrombotic material from the dead to the surviving twin results in thromboses and subsequent neurological injury. The 'ischaemic theory' postulates that, immediately before it dies, the twin becomes profoundly hypotensive and partially exsanguinates its co-twin via placental anastomoses, resulting in a period of anaemia, hypotension and hypoperfusion for the twin that eventually survives. There is evidence for both theories, although the latter is probably the more likely explanation in the majority of cases. The neurological injuries may be seen from as early as six days to as late as six weeks after the fetal death. These changes include periventricular leucomalacia, multicystic encephalomalacia, porencephaly, hydrancephaly and microcephaly.

Preterm delivery

The risk of delivery before 34 weeks is higher for MC twins than for DC twins: 68 per cent (95 per cent CI 56-78) versus 57 per cent (95 per cent CI 34-77).

It is difficult to determine the average time between fetal death and the onset of labour as the timing of fetal death is rarely known with any precision. Labour often occurs spontaneously two to three weeks after the recognition of a fetal death, but may occur almost immediately — such as following a placental abruption – or may be delayed for many months.

The timing of iatrogenic preterm delivery is guided by the considerations described in the management discussion below.

Management

Again, the nature of the placentation determines precise management. In all circumstances consideration should be given to the use of corticosteroids to promote fetal lung maturity and magnesium sulphate for neuroprotection. A neonatal paediatric consultation should be arranged and close discussion between the parents, obstetrician and paediatrician over subsequent weeks is essential.

If the live twin is leading, well grown and is in a cephalic presentation, then vaginal delivery may be considered. If the live twin is malpresenting or is growth restricted, or if the dead twin is leading, caesarean section is preferred. Many parents prefer caesarean section regardless of these considerations and this obviously needs to be discussed, taking into account the whole circumstances of the couple.

The development of a coagulopathy if a dead fetus is retained for more than four weeks is remarkably uncommon if the co-twin remains alive. Nevertheless, consideration should be given to perform weekly fibrinogen levels with a platelet count and a partial thromboplastin time after four weeks of confirmed fetal death. A full coagulation screen should be performed before regional analgesia or delivery.

The loss of a twin at any stage of pregnancy is devastating for parents. The psychological issues related to grieving for the lost twin while preparing for the birth of the surviving twin may be profound. The thought of still carrying the retained dead twin and the uncertainty regarding long-term outcome compound the stress of losing a twin. Extensive counselling is often required.

Dichorionic diamniotic twins

Delivery should be delayed until at least 34 weeks gestation, provided there is no obvious continuing pathology that may cause demise of the surviving co-twin. Careful monitoring with serial ultrasound assessments of growth and Doppler blood flow studies as well as regular cardiotocography should be undertaken.

Monochorionic diamniotic twins

When fetal death has been identified in one of an MC twin pair, the neurological injury has already been inflicted. If the fetus has survived that insult, delivery should be delayed as long as possible. This will give the greatest chance of detecting any intracranial pathology. Weekly ultrasounds should be performed, looking for evidence of the changes detailed above. Fetal magnetic resonance imaging (MRI) has improved detection of these changes. An MRI three weeks after the fetal death is diagnosed is recommended. If intracranial pathology is detected, further neonatal paediatric consultation should be arranged. Many parents will then opt for late feticide when the option is legally available. Some reassurance can be offered to parents if the fetal MRI and serial ultrasounds remain normal for many weeks after the fetal death, but a guarded prognosis is strongly advised.

Doppler assessment of the fetal middle cerebral arteries may indicate anaemia in the surviving co-twin, particularly if it has been performed close to the time of fetal demise. The presence of fetal anaemia in the surviving co-twin is, not surprisingly, associated with a significantly poorer prognosis. The use of a 'rescue' fetal blood transfusion has been attempted in several centres, with varying results. It could be considered if fetal demise is of very recent origin and fetal anaemia is evident in the co-twin, but it is unlikely to be of any great value given the timing of causation of these neurological injuries.

Monochorionic monoamniotic twins

The majority of deaths in MCMA twins involve the death of both twins. Occasionally a single MCMA twin may survive the death of its co-twin. The rarity of this circumstance makes it difficult to offer specific advice, but it must be noted that the rate of neurological sequelae in these survivors is extremely high. It may be appropriate, if the death occurred at a very preterm gestation, to delay delivery to allow administration of steroids and magnesium sulphate. Delivery by 28 weeks gestation would be reasonable in these circumstances, although it may be too early at that stage to detect intracranial pathology.

Conclusion

The management of single fetal death in a twin pregnancy can be difficult for any obstetrician. Identification of the cause, monitoring the surviving co-twin, deciding the appropriate time and mode of delivery and counselling in potentially very difficult circumstances can be challenging. Knowledge of the chorionicity is essential to any decision-making process and almost entirely determines the outcome.

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Journal Club

Had time to read the latest journals? Catch up on some recent O and G research by reading these mini-reviews by Dr Brett Daniels.

Bone health in anorexia

The acquisition of bone mass during adolescence is vital to the development of normal bone density later in life. Adolescent girls with anorexia nervosa have low bone mineral density (BMD) secondary to decreased lean body mass, hypogonadism, decreased insulin like growth factor-1 (IGF-1) and other hormonal factors. The first of these two articles reviews the current knowledge concerning this issue. It has previously been demonstrated that women who had anorexia nervosa as adolescents have a lower BMD later in life, when compared to women in whom anorexia did not occur until adulthood, even if the total duration of amenorrhoea was the same. Gynaecologists may encounter these girls as part of assessment and treatment of amenorrhea. It is reported that if weight is gained and menses return then there is an increase of BMD of 1.4 per cent at the spine after one year, compared with an decrease of 0.3 per cent girls who remain amenorrhoeic and a three per cent increase in normal weight controls.

Treatment of anorexia nervosa can be extremely difficult and some women will remain amenorrhoeic for a number of years despite treatment. Some researchers have investigated the effect of oestrogen replacement on BMD in adolescents with anorexia nervosa. In the second article Misra et al. report the results of physiological levels of oestrogen replacement on BMD in adolescent girls with anorexia nervosa. In a placebo controlled trial of over 100 girls aged between 12 and 18 with anorexia nervosa, the authors compared placebo to low-dose 'physiological' oral ethinyl-oestradiol in girls who had not yet reached bone maturity and higher dose transdermal 17β-ooestradiol (with cyclic progesterone) in girls who had reached bone maturity. In both age groups the girls receiving oestrogen showed an increase in BMD after 18 months of treatment compared to the placebo groups. Interestingly, previous research cited by the authors found that oral oestrogen replacement given as the combined oestrogen-progestin oral contraceptive pill did not increase BMD in girls with anorexia nervosa, possibly due to suppression of IGF-1 by the pill. It should, however, be noted that oestrogen replacement alone will not return BMD to normal levels in these girls, due to the multifactorial mechanism of BMD reduction in anorexia nervosa.

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Misra, M, Katzmann, D et al. 2011. Physiologic estrogen replacement increases bone density in adolescent girls with anorexia nervosa. *Journal of Bone and Mineral Research*, 26: 2430-2438.

Ultrasound and β-hCG in early pregnancy

A relatively common situation in early pregnancy arises when a woman presents with a quantitative β-hCG result and an ultrasound, with the question of whether her pregnancy is likely to be ongoing. It is a commonly held belief that if the β-hCG is greater than the discriminatory level of 1500-2000mIU/mL, then evidence of an intrauterine pregnancy should be visible on transvaginal ultrasound. This recent American paper reports the pregnancy outcomes on over 200 women who had both a β-hCG and transvaginal ultrasound performed on the same day without finding an intrauterine fluid collection suggestive of a gestational sac and in whom a live intrauterine pregnancy was later documented. The results showed that over ten per cent of these women had an initial β-hCG level of >1500mIU/mL. The highest initial β-hCG level in which a live term baby was later delivered after there being no ultrasound evidence of an intrauterine pregnancy was 4336mIU/mL. The authors reasonably conclude that: 'The hCG discriminatory level should not be used to determine the management of a haemodynamically stable patient with suspected ectopic pregnancy, if sonography demonstrates no findings of intrauterine or ectopic pregnancy.'

Doubilet, PM, Benson, CB. 2011. Further evidence against the reliability of the human chorionic gonadotropin discriminatory level. *Journal of Ultrasound in Medicine*. 30: 1637-42.

Ulipristal for fibroids

Ulipristal is an oral selective progesterone receptor modulator that is not currently available in Australia or New Zealand. It is available in some European countries and in the USA. Initially used primarily for emergency contraception, two recent European studies report on the efficacy of ulipristal in the treatment of fibroids.

In the first study the authors randomly assigned 194 women with symptomatic fibroids and anaemia to receive 13 weeks of either daily oral ulipristal or placebo. The results after 13 weeks showed control of uterine bleeding in over 90 per cent of women receiving ulipristal, compared to 19 per cent in women receiving placebo, with amenorrhea in over 70 per cent of women receiving ulipristal compared to six per cent in women receiving placebo. The ulipristal group also showed a significantly greater reduction in uterine volume compared with the placebo group.

A second study by the same group was a randomised double-blind non-inferiority trial comparing 13 weeks of oral ulipristal to 13 weeks of leuprolide (delivered as monthly intramuscular injections of 3.75 mg each). The authors concluded that oral ulipristal was non-inferior to intramuscular leuprolide in controlling uterine bleeding and significantly less likely to cause hot flashes. While this treatment option is not currently available in Australia or New Zealand, these studies suggest it may become an additional medical treatment option for fibroids at a later date.

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The Frank Forster Library
Book Sale

The Library will be publishing a list of titles for a book sale in the next issue of *O&G Magazine*.

Titles will include O&G textbooks as well as biographies, pamphlets and facsimile editions based on great obstetrical and midwifery manuscripts

Authors include – Donald, Smellie, Te Linde, Bonney, Wachtel, Schlink, Mayes and Eden.

Q&a

Q&a attempts to provide balanced answers to those curly-yet-common questions in obstetrics and gynaecology for the broader *O&G Magazine* readership, including Diplomates, Trainees, medical students and other health professionals.

Q *The use of antenatal and postnatal RhD immunoglobulin prophylaxis has successfully reduced the incidence of maternal alloimmunisation to the RhD antigen to less than 1.5 per cent. However, since assessment of an adequate dose of RhDIg is critical to the success of these programs, should fetal maternal haemorrhage screening be widely practised?*

Mr Ken Davis
CSci, FIBMS, ARCPA, FFSc(RCPA)

a Fetal maternal haemorrhage (FMH) screening is the recommended standard of care post-delivery in RhD negative women delivering an RhD positive baby. The test is undertaken to ensure that the correct dose of RhD immunoglobulin (RhDIg) is administered following delivery. The standard post-delivery dose is 625 IU, sufficient to protect against 6.25ml of fetal red cells.

However, in up to three per cent of deliveries the FMH will be greater, hence the importance of the routine use of this screening test as recommended by the RANZCOG College Statement on Anti-D[1] administration in obstetrics.

This case described below highlights the importance of compliance with the national standard of testing for FMH immediately post-delivery, or indeed at any other stage of pregnancy.

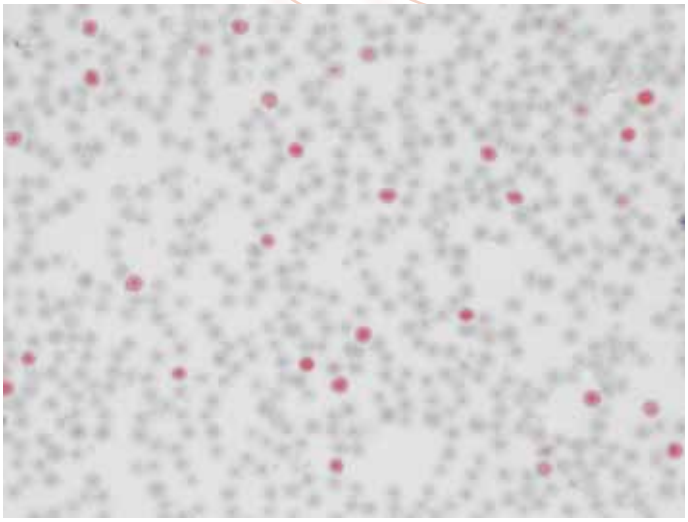
Case report

AG, a 29-year-old woman, delivered an apparently non-anaemic RhD positive baby by lower segment caesarean section two days before a request for a crossmatch of two units of red cells for postpartum anaemia. Her blood group was already known to be O RhD negative and she had already received the standard 625 IU RhDIg dose immediately after delivery.

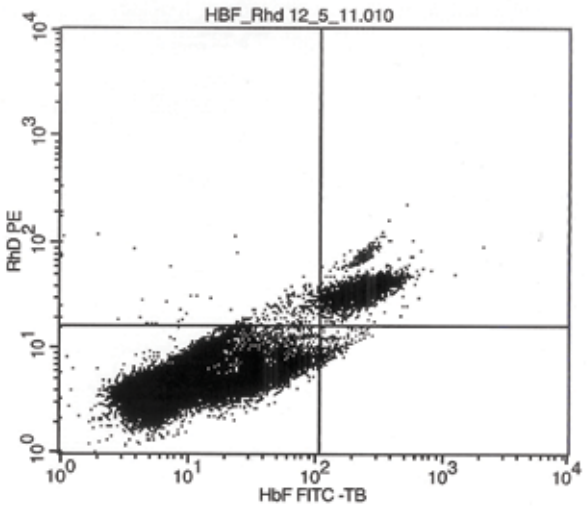
The testing at the laboratory performing the crossmatch request (on a sample collected two days after delivery) gave a weak result in the RhD group, which was an unexpected finding. This was confirmed by further testing. Consideration of this result and the fact that the maternal antibody screen failed to detect any trace of the RhDIg given two days earlier led the laboratory to recommend that an FMH screen be performed urgently, given that the 72 hour anti-D administration window was quickly closing. The cord Hb was reported as 118g/l (normal range 136–196g/l), which could be considered as a further marker to suspect a large FMH.

The FMH screen was performed using both Kleihauer-Betke and flow cytometric techniques and returned a result of more than three per cent fetal red cells.

Using the recommended formula it was estimated that an FMH of >70ml had occurred. For haemorrhages greater than 6ml, the recommended dose is 100 IU per ml RhD positive red blood cells. Where large volumes of RhD-Ig need to be administered or the patient has a specific contraindication to intramuscular injections, an intravenous (IV) RhD-Ig preparation should be considered. In discussion with her treating physician a further dose of 13 vials of WinRho RhDIg was recommended to be given intravenously. The



Kleihauer-Betke film showing prominent numbers of RhD positive maternal cells.



Flow cytometry scan of results showing upper right-hand quadrant HbF / RhD positive cells = 3.19 per cent.

Council meeting report

The November RANZCOG Council meeting was held at College House in Melbourne.

President's report; Board recommendations to Council
The President spoke to his report, drawing Councillors' attention to: matters associated with AOFOG; the new College website; the Melbourne Annual Scientific Meeting; meetings with other colleges involved in maternity care, particularly the ACM, RACGP and ACCRM; and regional committee elections. Councillors were asked to continue their efforts in encouraging regional participation in College activities.

FIGO: Nomination of Dr Kenneth Clark for President
Council noted that the College would be supporting Dr Kenneth Clark in his bid to be elected FIGO President-Elect.

Acting CEO report
The Acting CEO referred Councillors to her report and highlighted the following items:

- The preparations for the AMC accreditation process that will be happening during 2013.
- The advent of the Workforce Committee. Councillors were asked to encourage their colleagues to fill in the Practice Profile.
- The bid for joint meeting with the RCOG in 2015.

The Acting CEO thanked the President, Board, Councillors, Directors of Education and Training and Corporate Services and the staff in the Office of the CEO for their support during her time as Acting CEO. Council formally noted its appreciation of Ms Jenkins' contribution as Acting CEO.

Treasurer's report, finance report, balance sheet
Prof Rane presented the Treasurer's Report, drawing Councillors' attention to the investments portfolio and the profit and loss statements. Prof Rane and Dr Ngan Kee, Chair of the Finance Advisory Committee, briefed Councillors on the investment advice that the College regularly receives and acts upon.

Training and Accreditation Committee
The report from the Training and Accreditation Committee was noted and Dr Ritossa advised that for the last 18 months the Committee had focused significantly on the new ITP Selection Process. The reports of the 2011 Australian and New Zealand selection processes have now been received. Dr Ritossa reported that the new process had gone smoothly and outlined minor changes planned for next year.

Continuing Professional Development Committee
The report from the Continuing Professional Development Committee was noted; Dr Pecoraro highlighted the following issues:

- The rationale for changes as a result of a review of how surplus funds are distributed after the regional scientific meetings.
- CPD Committee efforts to source and offer innovative ways for Fellows to meet their CPD requirements continue.
- Dr Pecoraro also spoke about the Committee's work on surveys.

Education and Assessment Committee
The report of the Education and Assessment Committee was noted and Prof Symonds outlined the following items:

- A/Prof Stephen Robson shall be convenor of the MRANZCOG Oral Examination, a role he will share with Dr Celia Devenish;
- feedback provided to examinations candidates;
- standard setting;
- subspecialty assessment reviews; and
- online support of trainees.

An examination preparation workshop is to be developed for international medical graduates (IMGs).

Specialist IMG Assessment Committee
The report of the Specialist IMG Assessment Committee was noted and Dr Tout outlined the items within it, including recommendations to the Board relating to Specialist IMG interviews, applications for Fellowships and appointment of assessors. Other issues under consideration by the Committee include:

- The Australian and New Zealand process for assessing Specialist IMGs have been assimilated, though some differences necessarily remain.
- The Council of Medical Colleges in New Zealand is looking into the issue of the Medical Council of New Zealand observance of specialist medical college recommendations regarding the suitability of Specialist IMGs.
- Involvement of local TACs – guidelines are being developed.

Subspecialties Committee
The report of the Subspecialties Committee and the individual Subspecialty Committees was noted and A/Prof Robson outlined the major issues under consideration, including:

- Continued work in relation to assessment processes.
- Recruitment to the subspecialties.
- Amendments to the Terms of Reference to ensure that Chairs have some association with Trainees.

Conjoint Committee for the Diploma of O and G
The report was noted and Prof Rane outlined the major items of business being addressed, including Grandfathering of Diploma holders until December 2013 (for Diplomates who are required to have a Diploma Advanced for credentialling purposes). Prof Rane urged Councillors to encourage PGY2 and above candidates to consider undertaking the Certificate of Women's Health.

GP Obstetrics Advisory Committee
The GP Obstetrics Advisory Committee report was noted and Dr Taylor highlighted the following item:

- Diplomate recertification numbers.

Fellowship Review Committee
The report of the Fellowship Review Committee was noted.
Dr Weaver reported that the Fellowship Review Committee is recommending to the Board that the College change its re-entry guidelines so that they are congruent with those of the Medical Board of Australia, which had just changed its guidelines for re-entry into practice.

Provincial Fellows Committee
The report of the Provincial Fellows Committee was noted and Dr Geraghty outlined the main items, including:

- The Rural Health Continuing Education program is funding a number of projects for Provincial Fellows, such as the laparoscopy audit and perinatal audits.
- SOLS – funding for this program will now be ongoing.
- Developments in telehealth; Dr Geraghty will report further on this at March Council.

The President reported that PROMPT negotiations are nearing successful completion and that the program will be rolled out in regional areas.

Trainees Committee
Dr Milford reported that the main issue currently under consideration by the Trainees Committee is the development of policy for flexible training, and he anticipates that it will go before the Training Accreditation Committee for consideration in March 2012.

Dr Milford advised that the Trainees Committee had been involved in the formulation of the Workforce Committee Trainee survey, and that Trainee representative had been asked to encourage their Trainee groups to complete the survey

Workforce Committee
The Workforce Committee report was noted and Prof Permezel outlined the main item under consideration:

- Trainee survey – the Workforce Committee sees Provincial Specialists, Academic Practice, Subspecialist Practice and the influx of practitioners from New Zealand to Australia as the principal issues to be addressed. Prof Permezel urged Councillors to encourage their Trainees to complete the survey.

The President encouraged Fellows to do their own Practice Profile and to encourage others to do so as well.

Asia-Pacific ASM scholarships

Carmel Walker
Senior Coordinator,
Asia Pacific Services

There was an exciting opportunity for networking, education and collegial support for Pacific O and G Trainees and specialists at the RANZCOG Annual Scientific Meeting.

RANZCOG welcomed five Pacific O and G specialists and Trainees to the 2011 Annual Scientific Meeting, held at the Melbourne Convention Centre, 27–30 November 2011. The RANZCOG Regional and New Zealand Committee ASM Scholarships initiative aims to provide collegial support and professional development as part of capacity building in the O and G workforce in the region. The inaugural Regional Committee RANZCOG ASM Scholarship, provided by the Queensland Regional Committee, allowed Dr Leeanne Panisi, Honiara, Solomon Islands, to attend the 2011 ASM.

This was the first scholarship provided under the new College initiative. The Queensland Regional Committee is to be congratulated on taking it up in such an enthusiastic way, as has the New Zealand Committee, whose scholarship will apply to the New Zealand ASM in 2012. The College hopes the program will expand, with more regional committees providing a scholarship so that young Pacific O and Gs can have the opportunity to attend College ASMs.

Dr Panisi said, 'Attending the RANZCOG ASM was an exciting and worthwhile experience. Working as a consultant at the National Referral Hospital, in the Solomon Islands, with limited support, mentoring and resources, the new information from the ASM was very helpful for me, my continuing education and for my work generally. Meeting specialists is important for networking and possible future discussion of cases by email. I want to thank the Queensland Regional Committee for sponsoring me to attend the RANZCOG ASM. Continuous support for the Pacific Islands in these forms makes a difference to our practices in maternal health in our various countries. After the ASM, I was fortunate to be invited to spend a day observing at the Royal Women's Hospital with Dr Kirsten Connan and this was an interesting and useful day for me too.'

The selection process for ASM scholarship awardees has been developed by the RANZCOG Asia-Pacific Committee, in collaboration with the departments of O and G at the medical schools attached to the University of Papua New Guinea (UPNG) and the Fiji National University, and liaison with the Pacific Society for Reproductive Health. Guidelines for the scholarship process and interaction with the Regional and New Zealand Committees have been approved by the RANZCOG Board, and will allow for individual Committees' interest and levels of involvement with the scholarship awardees. If the initiative is successful it may, in time, be extended if the College educational program expands to other medical schools in the Asia/Pacific region in a formal way.

Drs Julia Singh, Angela Seginami, Sylvester Tati, Leeanne Panisi and Frank Apamumu at RANZCOG ASM Melbourne.

The RANZCOG Regional and New Zealand Committee's RANZCOG ASM Scholarships initiative adds to the existing scholarships provided by the College for Pacific O and G Trainees and specialists to attend the ASMs. The Pacific O and G specialists scholarship awardee for 2011 funded by RANZCOG was Dr Angela Seginami, consultant O and G at Alotau General Hospital, Milne Bay Province, PNG. Angela gained her specialist qualification, the Master of Medicine (O and G), at the UPNG in 2008, and was admitted as an Associate Member by the College Council in November 2011. As well as attending the meeting, Angela was delighted to receive her Associate Membership certificate from President Dr Rupert Sherwood.

Angela said, 'Associate Membership has been a wonderful boost in supporting me in my career as an isolated O and G in Alotau. The opportunity to attend the Anatomy of Complications workshop recently, and now the RANZCOG ASM, provided me with exposure as to how I can manage pelvic surgical complications alone. As a young gynaecologist working alone, the only help I can access is a phone call to Prof Mola or Prof Amoa at the Port Moresby General Hospital. The practical sessions at the Anatomy of Complications workshop gave me good insight into how I can do procedures such as identifying and repairing an injured ureter or a blood vessel. This is a very useful course for gynaecologist practising in the Pacific as we do come across these sorts of complications.

'Attending the ASM was very interesting too, especially the latest research findings to improve the management of our patients. The latest research on premature births and gynaecological cancers, stem cell therapy and medical management of ectopic pregnancies was amazing. I was particularly fascinated by the fact that ovarian cancers originate from the fimbrial end of the tube. If I identify women who have a strong family history of ovarian cancer and are requesting tubal ligation, I will advise them to have bilateral salpingectomy. Although a lot of new scientific research may not be practical in my current hospital setting, it is excellent knowledge to impart to the Trainee registrars. I have two Trainees with me and I have passed CDs and journal articles to them to read. I am privileged and honoured to have been given scholarships to attend the ASM and the Anatomy of Complications Workshop and I would like to thank RANZCOG for recognising the need to invest in the young doctors of the Pacific.'

ASM Scholarships for Pacific O and G Trainees have been offered by the College since 1992, a number of recipients have gone on

to provide specialist O and G services and many have become Associate Members of RANZCOG over the past two years. Dr Julia Singh, who recently completed her Masters in O and G from Fiji National University, was the nominated O and G Trainee from Fiji and, when her specialist registration is formalised in Fiji, she will be awarded Associate Membership of RANZCOG.

Dr Frank Apamumu and Dr Sylvester Tati, final year O and G Trainees from the UPNG currently working for a year at Sunshine Hospital, Melbourne, also attended the ASM. Dr Apamumu said, 'We were privileged to attend the 2011 RANZCOG ASM, where the most recent papers on evidence-based medicine were presented. This was a very good learning experience and also gave us the opportunity to see how international conferences are organised. Thanks to the RANZCOG Asia Pacific Scholarship program, which enables my Pacific Islands colleagues and I to attend this conference. I am also very thankful to RANZCOG for the support that enabled me to obtain my registration with AHPRA, allowing me to practise O and G at Sunshine Hospital, for the last ten months. This period has been a great educational and professional development experience for me. All these experiences combined, will, I feel, equip me to be a good clinician in O and G in PNG, working to improve women's health services and put into practice skills I've learned in Australia with the resources we have available. We really appreciate everything the RANZCOG Asia Pacific Program is doing to help O and G training in the Pacific Islands to improve women's health and we look forward to continued support from RANZCOG.'

Dr Angela Seginami receiving her Associate Membership certificate from RANZCOG President Dr Rupert Sherwood.

The RANZCOG Shan S Ratnam Young Gynaecologist Award

Dr Ngaire Anderson
RANZCOG Trainee

The RANZCOG Young Gynaecologist Award is available to members of the College who are under 40 years of age.

I wish to thank the Asia and Oceania Federation of Obstetrics and Gynecology (AOFOG) and RANZCOG for the 2011 New Zealand Shan S Ratnam Young Gynaecologist Award (YGA). As part of this award, I was given financial assistance to allow me to present a poster titled 'The impact of ethnicity and body mass index on pre-eclampsia in a multiethnic New Zealand population' at the XXII Asian and Oceanic Congress of Obstetrics and Gynecology (AOCOG). AOCOG was held from 23–27 September 2011 in Taipei, Taiwan and was attended by delegates from throughout the Asia-Pacific Region as well as from the USA and UK. This conference brought together practitioners from very disparate healthcare resource settings with the program highlighting the contrasts in challenges facing developed and developing countries throughout the Asia-Pacific region. The broad array of topics ranged from providing safe termination of pregnancy services to robotic gynaecologic surgery, obstetric fistula repair and fetal endoscopic surgery.

All YGAs were presented with their awards at the President's Night, which was a great opportunity to meet other awardees as well as introduce ourselves to the AOFOG Committee members from around the region. We were able to discuss our own regional practice and the difficulties our respective countries were facing with regards to meeting women's healthcare needs, at the same time as enjoying an exotic banquet. Later in the week, we were also treated to the Delegate Banquet, held in the opulent Grand Hotel, which allowed for further informal networking. This night showcased local Taiwanese cultural performances and some took the opportunity to indulge in a touch of karaoke.

AOCOG was an enjoyable conference that provided me with valuable insights into the issues facing women and healthcare around the Asia-Pacific region. Once again, I thank AOFOG and RANZCOG for this award.

Australian to lead ISUOG

A/Prof Lachlan de Crespigny
FRANZCOG

Dr Andrew Ngu FRACOG, COGU, has been appointed President-Elect of the International Society of Ultrasound in Obstetrics and Gynecology.

Although the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) has existed since 1991, in 2014 when Andrew Ngu's term of presidency commences, he will be the first president to come from outside Europe and the USA. Andrew's appointment is the culmination of an extraordinary career of contribution to O and G generally, and ultrasound in particular, both in Australia and internationally. His presidency is seen by his fellow ISUOG board members as an opportunity for ISUOG to develop extensive education programs in developing-world countries, particularly in Asia, thanks to Andrew's extensive international ties and friendships.

Andrew has surmounted extraordinary obstacles to reach where he is today. Born on 15 August 1952, in Kuching, Sarawak in Malaysia, he comes from a close and loving family. His parents had little formal education, but in 1970 they accompanied him to Singapore, before, aged 17, Andrew flew alone to Melbourne where he completed his matriculation (years 11 and 12). When he arrived, Andrew did not speak English.

Andrew completed his education at McKinnon High School in Melbourne. He initially stayed at the Flinders Hotel in the city, but with the assistance of the school he found accommodation with a very kind war widow, Mrs Marrow, who became his Australian mother. He overcame his inability to speak English and achieved Dux of McKinnon High School, including winning the prize in English. Andrew was the first Malaysian boy to become Dux of the school and had his photo taken in the local paper to acknowledge this achievement. Mrs Marrow bought many copies and told everyone how proud she was of her son. Andrew had a passion to do medicine and was accepted into Monash University, commencing in 1971. Later, when working at the Royal Women's Hospital as a registrar, he was mentored by Dr Hugh Robinson and this led to his interest in pursuing a career in O and G ultrasound.

Throughout his career, Andrew has generously donated his time to professional organisations. He is currently Honorary Secretary of ISUOG. He has been on the Australasian Society for Ultrasound in Medicine (ASUM) Council for 14 years (few have served longer) and has been on the Executive Council for most of this time. He has held many senior ASUM positions, including the presidency. Andrew has served on the Board of Examiners for the Diploma of Diagnostic Ultrasound continuously since 1998, and was on the RANZCOG Board of Examiners for COGU between 2000 and 2008.

Unusually for an ultrasonologist, Andrew remains a practicing clinical O and G, based at the Northern Hospital, Epping, and is currently the Chair of the Division of O and G. He has his own ultrasound practice in East Melbourne.

Few obstetricians have done as much as Andrew to produce continuing education programs. He has led large numbers of national and international meetings, including:

- ISUOG Congress 2001;
- ASUM Annual Scientific meetings 1992, 1998, 2006 and 2010;
- ASUM Ultrasound Multidisciplinary Workshops in 2005 and 2008;
- Ultrasound workshops in Melbourne in 2006, 2007 and 2008;
- GP Obstetric Shared Care Programme in 2005, 2006 and 2009;
- Fetus as a Patient in 2009; and
- Fetal MRI meeting in 2012 in Whistler, USA.

Dr Andrew Ngu will commence his term as President of ISUOG in 2014.

He has also been an active member of the organising committees of many other meetings.

In collaboration with ASUM, Andrew established the Vision College in 2003, in Malaysia, and 120 certified sonographers have graduated since its inception. This is Malaysia's only ultrasound training school. He chaired the Obstetric Update Ultrasound Course in Penang in October 2011.

During a life of overcoming special obstacles, Andrew has been a unique contributor in his field. Few have done as much to provide opportunities for continuing education to their colleagues – and through them enhancing women's health – as he has. He will see his new appointment as an opportunity to do even more to improve obstetric and gynaecologic healthcare.

Acknowledgement
Thanks are due to Wendy Ngu, Andrew's wife, for providing biographical detail and the photo.

Staff news

Left to right: Damian Waters, Judy Walker, Sarah Lofts, Debra O'Brien, Deborah James, Annie Holdsworth and Shamila Kumar.

New appointments

Annie Holdsworth joined RANZCOG as senior education coordinator in the education and training department. She brings a wealth of experience to the role, having worked at Melbourne, La Trobe, Deakin, James Cook, RMIT and Victoria Universities as a lecturer, associate dean – teaching and learning, education consultant, workshop facilitator and postgraduate supervisor.

Deborah James came to RANZCOG in February as an administrative officer in corporate services. In this role, Deborah supports RANZCOG's committees and Council. She has over 20 years of experience in administration/executive assistant roles across a range of industries.

Shamila Kumar joined RANZCOG as women's health administrative officer, covering Nola Jackson's maternity leave. She previously worked at the Princess Margaret Hospital for Children in the Patient Safety Unit, WA. Before that, she worked with the WA Cervical Cancer Prevention Program and in Aboriginal health promotion. Shamila holds a BSc of health science with honours in pharmacology and public health.

Sarah Lofts, as continuing professional development officer, joined RANZCOG in November. She previously worked at Monash University in the Research and Commercialisation Department, and, before that, as a team assistant/administrative officer at GWA Ltd. Sarah holds a degree in psychology from La Trobe University.

Debra O'Brien started in November in a part-time role, funded by the UroGynaecological Society of Australasia (UGSA), that involves both being the UGSA administrator and co-ordinating ultrasound workshops. Having come from AMA Victoria, Debra has a good understanding of the health system and health-sector events.

Judy Walker came to RANZCOG in November as rural services administration officer; a part-time role primarily to assist on SOLS. She previously worked with RACGP in the Quality Care Unit and before that with Relationships Australia Victoria in executive support.

Damian Waters joined RANZCOG as director of finance and infrastructure, after holding similar roles in state government authorities and the University of Tasmania. Damian is a Fellow of CPA Australia and holds a MBA specialising in strategy and planning.

Departures

Kate Lawrey left the College to concentrate on her MBA course. We wish her all the best with her studies.

Bob Kelly retired in January. We hope he enjoys his well-earned rest and relaxation.

Australia Day Honours Awards

The following RANZCOG Fellows and members recently received Australian and New Zealand Honours awards:

- Dr Grahame Robert Deane, Gunnedah, New South Wales. Awarded Member of the Order of Australia. For service to medicine in the Gunnedah region and to professional associations, particularly the Australian Divisions of General Practice.
- Dr Thomas Victor Roberts, Ballarat, Victoria. Awarded Medal of the Order of Australia. For service to the community of Ballarat, particularly through the Royal Australian Air Force Association and to medicine.
- Dr Brian Peter Wheatley, Collinswood, South Australia. Awarded Medal of the Order of Australia. For service to medicine in the field of obstetrics and gynaecology, and to medical education.
- Dr Leslie Arthur Woollard, Moree, New South Wales. Awarded Medal of the Order of Australia. For service to medicine in rural and remote areas of New South Wales.

Letters to the editor

O&G ***Magazine*** **Vol 13 No 4 Homebirth**

I read with interest the recent homebirth issue with its varying views and international experiences. I was prompted to reflect on my own homebirth experiences as an O and G Diplomate working in remote Kimberley region of West Australia, based in Broome in the 1980s and 90s.

My first experience was of a couple, newly arrived in town and with few supports, that covertly arranged a homebirth with no contact with mainstream medicine. The pregnancy ended in a stillbirth after a long labour. This prompted me to proactively seek contact between homebirthers and mainstream services in the future. When another couple engaged a homebirth practitioner I actively encouraged them to have an ongoing dialogue and a shared-care approach, but suspicions prevailed. This pregnancy ended in a prolonged labour in a remote farmhouse and a mother with a third-degree tear presenting the next day. A few years later, a couple insisted on a homebirth. This time I reluctantly resolved to be more actively involved. So, when called, I found myself a few miles from town in large tree house with an entourage of supporters, but no clinicians and a mother in a pool of blood with a retained placenta. Having put up a drip by torchlight and staunched the bleeding, the best I could do was persuade the mother to attend the hospital the next day where the haemoglobin was found to be seven. She left hospital straight after the transfusion.

An ongoing problem was persuading pregnant Aboriginal women to come into town to stay for the last weeks of their pregnancy to avoid remote births. Sometimes our efforts were in vain as homesick women would return home before confinement, ending in a homebirth or an urgent retrieval by the Royal Flying Doctor Service. As our ultrasound skills improved and our dating became more accurate, we were better able to plan the late pregnancy transfers to avoid bush births.

On one occasion, while doing a routine remote fly-in community clinic, I delivered a 30 week infant who survived, despite the dust and the cold. Luckily, I happened to have a city-based paediatrician with me that day.

My final homebirth experience was happily closer to home. My wife's fourth labour was particularly brief so I found myself delivering my daughter in our own home. It was quite wonderful. When it was over, and a friend had came over to care for the other children, my wife insisted on going to hospital for a few days' rest and lying-in.

While my experience cannot condone homebirth, I can see its attraction. Mainstream services have an obligation to engage with responsible and reputable homebirth providers in a non-judgmental manner, while providing the best-quality information to prospective parents, to ensure the best outcomes for mothers and babies.

Dr Stuart Garrow
MBBS MPH DRANZCOG FRACGP

As a retired obstetrician who for some 30 years has taken an interest in the topic of homebirth in Australia, I would like to comment on your coverage of the subject.

Firstly, I congratulate on your general presentation of the topic. Your articles were well selected for balance of views of the subject and geo-political variation. All participants in the issue were covered, including consumers.

You fairly presented the respective views of those participants who value safety (in their perception) above all other considerations in contrast with those who, to varying degrees, allow other considerations to have their input.

A woman not only has the right to put her baby at risk, she also has an obligation to do so. All stages of life have their risks, even putting the child to bed risks its death from SIDS. Every time she crosses the road with her baby in its stroller she risks its life. A number of children are born by precipitate labour on the journey to hospital: this is usually only the subject of a happy news story, but there can be a serious outcome.

I would emphasise the part that the medical profession, and its obstetric discipline, is expected to fulfil in the management of pregnancy and childbirth extends way beyond their remit in terms of the diagnosis and treatment of disease. Childbirth is an important and very sensitive part of the culture in any society and needs to be treated in a way that does not regard it as a disease cured by a surgical procedure. Doctors are only fulfilling their proper role when they treat abnormalities of pregnancy or labour and should not be involved in normal childbirth, but should leave it to midwives, who are quite adequately trained to detect abnormalities.

The features presented in your survey make it quite clear that, for pregnancies screened as normal, homebirth is quite reasonable. If there is an increased risk in homebirth, it is of a small degree and does not justify any pressure from the medical profession that makes it difficult or impossible for the mother to exercise a perfectly reasonable option. If we tolerate a woman having a caesarean section on demand, we must extend the same sympathy to a woman wanting to give birth with a midwife who she has got to know well and at a location of her choosing.

We, the medical profession and obstetricians, have domination of the management of childbirth in our culture by the acceptance of our authority and advice by the community and media outlets and by the bureaucracy that administers financial health benefits. We have to be sure that we honour this trust and that our advice is fully in accordance with our properly researched professional knowledge.

Dr Ralph Hickling
FRCOG DDU

O&G ***Magazine*** **Vol 13 No 4 Treating vulvodynia**

In their article titled Treating vulvodynia, Pagano and Tran[1] have presented one side of a current controversy in gynaecology. Many of us support the notion that 'vulvodynia' (that is vulval pain) is merely a description of a symptom, in the same way that menorrhagia describes heavy menstrual bleeding, but is not a diagnosis. To talk about 'treating vulvodynia' is therefore to advocate empirical treatment. An alternative approach to vulval pain was published in *O&G Magazine* in 2006[2], and we do not believe that there has been any significant change.

Good clinical practice starts with accurate diagnosis, that is, a careful history and examination and appropriate investigation. The cause (or causes) for genital pain can almost always be found, if not at the initial consultation, then over the ensuing months. The Vulva and Vagina Manual[3] lists 58 causes of female genital pain. The Vulva: a Clinician's Practical Handbook[4] includes a diagnostic algorithm for the patient who presents with vulval pain. Our opinion is that most vulval pain has a primarily physical origin, but is often multifactorial by the time the patient presents. Although there are women whose vulval pain is mainly psychosexual, it is essential that any physical causes for the patient's pain are identified and treated.

Heroic surgical treatments, such as vestibulectomy, may not be required when accurate diagnosis leads to rational and effective treatment. This is analogous to hysterectomy for menorrhagia, which increasingly has been replaced by effective and less-destructive treatments that target the specific diagnosis.

The last thing we would want would be our Trainees thinking that the management described in Pagano and Tran's article is standard.

Dr Jenny Bradford
FRANZCOG

Dr Graeme Dennerstein
FRANZCOG

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2 Dennerstein G. Vulval Pain. *O&G Magazine* 2006:8;3;54-55 http://www.ranzcog.edu.au/publications/oandg-magazine/doc_download/423-vol-08-no-3-spring-2006-complete-issue.html .
3 Dennerstein G, Scurry J, Brenan J et al. The Vulva and Vagina Manual. Melbourne: Gynederm Publishing: 2005.
4 Fischer G, Bradford J. The Vulva: a Clinician's Practical Guide. http://www.fpnsw.org/products/The-Vulva%2C-A-Clinician's-Practical-Handbook.html .

Notice of Deceased Fellows

The College was saddened to learn of the death of the following Fellows and Honorary Fellow:

Dr Robert Austin Kenihan, SA, on 3 February 2012
Dr John Greenwell, Vic, on 6 January 2012
Rt Hon Sir Zelman Cowen, Vic, on 8 December 2011

Author Index

Volume 13 2011
Volume numbers will appear first in index entries, issue numbers in brackets afterwards and page numbers following: , e.g. 10(1): 18 = Vol 10, No 1, page 18
Articles A, In and The are ignored in filing entries

The following abbreviations have been used:
O and G = obstetrics and gynaecology

Series names and editorials have been placed in square brackets [ ]
Eg. Cervical cancer, postcoital bleeding [Q&a] 11(3): 54
[Q&a] refers to an article from the Q&a series.

Subject Index

Volume 13 2011

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Articles A, In and The are ignored in filing entries.

The following abbreviations have been used:
O and G = obstetrics and gynaecology.

*Articles written about working in overseas countries, have been indexed under the place name eg Ethiopia 12(2): 63–65.

RANZCOG RESEARCH FOUNDATION

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RANZCOG trainees, clinical researchers and other interested individuals are warmly welcomed. Membership fees are tax deductible.

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The RANZCOG Research Foundation supports research in the fields of obstetrics, gynaecology, women's health and the reproductive sciences through the awarding of various scholarships, fellowships and grants.

The RANZCOG Research Foundation works closely with the RANZCOG Board, Council and College Committees to further the needs for research and research training in the broad fields of obstetrics, gynaecology, women's health and the reproductive sciences.

Our Scholars

The Foundation proudly supports promising young Fellows, clinical researchers and scientists undertaking high quality, innovative research and research training at an early stage in their career.

Scholars supported by the RANZCOG Research Foundation have a strong record of subsequent achievement in research and in academic careers in Australia and overseas.

Grants and Scholarships

Each year, approximately $120,000 is disbursed helping to support early career researchers in their work.

The Foundation continues to expand its program of grants, scholarships and other awards. Recent initiatives include Collaborative Bachelor of Medical Science Research Scholarships, Project Grants to assist RANZCOG trainees in undertaking their research project and the *Mary Elizabeth Courier Research Scholarship*, introduced following a bequest to the Foundation by her late husband, Australian lithographic artist, Jack Courier.

Further Information

Further information about the work of the Foundation is available on the website at: www.ranzcog.edu.au/research

Any questions should be directed to the RANZCOG Research Foundation Coordinator:

Ms Georgina Anderson:
t: +61 3 9417 1699
e: ganderson@ranzcog.edu.au

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