Magazine

Vol 12 No 3 Spring 2010



The Royal Australian and New Zealand/College of Obstetricians and Gynaecologists



Available online at: www.ranzcog.edu.au/publications/oandg

O&G Magazine Advisory Group

Prof Caroline de Costa Council Rep, QLD Dr Sarah Tout Council Rep, New Zealand A/Prof Stephen Robson Fellows Rep, ACT Dr John Schibeci Diplomates Rep, NSW Dr Brett Daniels Trainee Rep, TAS

O&G **Magazine Editors**

Penelope Griffiths Julia Serafin Peter White Rachel Corkery

Designer and Production Editor Rachel Corkery

Editorial Communications

O&G Magazine Advisory Group, RANZCOG 254-260 Albert Street EAST MELBOURNE, VIC 3002 Australia (t) +61 3 9417 1699 (f) +61 3 9419 0672 (e) ranzcog@ranzcog.edu.au

Advertising Sales

Bill Minnis Director Minnis Journals (t) +61 3 9824 5241 (f) +61 3 9824 5247 (e) billm@minnisjournals.com.au

Printer

Fineline Printing Australia Pty Ltd (t) +61 3 8791 4200 (f) +61 3 8971 4277

O&G Magazine authorised by Dr Peter White © 2010 The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG). All rights reserved. No part of this publication may be reproduced or copied in any form or by any means without the written permission of the publisher. The submission of articles, news items and letters is encouraged.

> For further information about contributing to O&G Magazine visit: www.ranzcog.edu.au/publications/oandg

The statements and opinions expressed in articles, letters and advertisements in $O\dot{c}G$ Magazine are those of the authors and, unless specifically stated, are not necessarily the views of the RANZCOG.

Although all advertising material is expected to conform to ethical and legal standards, acceptance does not imply endorsement by the College. ISSN 1442-5319

Cover image ©Shutterstock_Tim Bird

Fertility

- 13 Editorial: When it rains... Stephen Robson and Caroline de Costa
- 14 Demographics of infertility Phillip McChesney
- 16 Age and women's fertility John Chenoweth
- 20 The future of assisted reproduction Peter Illingworth
- 22 Protection and preservation of fertility for young women with cancer Kate Stern
- 26 Difficulties in providing fertility treatment for rural women **Robert Miller**
- 28 The infertile couple a GP's perspective Sally Lyttleton
- 32 Fertility-enhancing effects of Lipiodol and the IVF-LUBE Study Shelley Reilly and Neil Johnson
- 34 Endometriosis and infertility Luk Rombauts
- 36 Lifestyle, periconception and fertility problems in men and women Anne Clark
- 38 An overview of surrogacy in Australia Bronwyn Devine
- 40 Uterine and related structural anomalies Kim Matthews and Peter Benny
- 55 The long barren years of Catherine de Medicis a gynaecologist's view of history Caroline de Costa

Women's Health

- 47 Trainee pullout: Male fertility Stephen Robson
- 54 Journal Club Brett Daniels
- 58 Review: Syntocinon dosages at caesarean section Louise Ellard
- 60 Obstetric Management Update: Epilepsy in pregnancy Sandra Lowe
- 62 Gynaecological Management Update: Primary amenorrhoea Sonia Grover

RANZCOG Regional Committees

66 *Qċa*: Management of delivery of woman following seven years of IVF treatment **David Molloy and Sue Jacobs**

- 68 ACSQHC OSSIE Guide to Clinical Handover Improvement
- 69 Clinical handover from project to policy Sara Hatten-Masterson
- 71 Safe Motherhood for All: Part of the Global White Ribbon Alliance
- 86 Women's health in India a personal journey Ajay Rane
- 88 Alleviating suffering in Sudan Médecins Sans Frontières
 Alan Hughes and Katie Butt
- 89 Queen's Birthday Honours List

Medico-legal

64 Case study: how many embryos? Andrew Took

The College

- 5 From the President Ted Weaver
- 9 From the CEO Peter White
- 43 Meetings Calendar Spring 2010
- 72 College Statements Update July 2010 Michael Permezel
- 84 Fetal Surveillance: A Practical Guide Reviewed by Anthony Marren and Jonathan Hyett
- 84 News from the Frank Forster Library
- 90 RANZCOG Research Foundation Collaborative Bachelor of Medical Science Research Scholarships David Healy
- 92 Council Meeting Report July 2010 Penelope Griffiths
- 94 Staff News
- **95** RANZCOG Pacific Midwifery Leaders Program Brian Spurrett Foundation **Carmel Walker**
- 96 Obituaries

New Zealand Dr John Tait Chair Kate Bell Executive Officer Level 3, Alan Burns Insurances House 69 Boulcott Street/PO Box 10 611 WELLINGTON, NEW ZEALAND +64 4 472 4608 (f) +64 4 472 4609 (f) kate.bell@ranzcog.org.nz (e)

Australian Capital Territory

Dr Andrew Foote Chair Deakin Gynaecology Centre 39 Grey Street DEAKIN, ACT 2600 +61 2 6273 3102 (t) +61 2 6273 3002 (f) muttons@dynamite.com.au (e)

New South Wales

Professor Alec Welsh Chair Lee Dawson Executive Officer Suite 4, Level 5, 69 Christie Street ST LEONARDS, NSW 2065 +61 2 9436 1688 (t) +61 2 9436 4166 (f) admin@ranzcog.nsw.edu.au (e)

Queensland

Dr Paul Howat Chair Lee-Anne Harris Executive Officer Unit 22, Level 3, 17 Bowen Bridge Road HERSTON, QLD 4006 +61 7 3252 3073 (t) +61 7 3257 2370 (f) Iharris@ranzcog.edu.au (e)

South Australia/Northern Territory

Dr Preeti Khillan Chair Tania Back Executive Officer 1-54 Palmer Place/PO Box 767 NORTH ADELAIDE, SA 5000 +61 8 8267 4377 (t) +61 8 8267 5700 (f) ranzcog.sa.nt@internode.on.net (e)

Tasmania

Dr Stephen Raymond Chair Hobart Urogynae & Incontinence Clinic 4/44 Argyle Street HOBART, TAS 7008 +61 3 6223 1596 (t) +61 3 6223 5281 (f) rfullert@tassie.net.au (e)

Victoria

Dr Elizabeth Uren Chair Fran Watson Executive Officer 8 Latrobe Street MELBOURNE, VIC 3000 + 61 3 9663 5606 (t) + 61 3 9662 3908 (f) vsc@ranzcog.edu.au (e)

Western Australia

Dr Tamara Walters Chair Janet Davidson Executive Officer Level 1, 44 Kings Park Road WEST PERTH, WA 6005/PO Box 6258 EAST PERTH, WA 6892 +61 8 9322 1051 (†) +61 8 6263 4432 (†) ranzcogwa@westnet.com.au (e)

The Royal Australian and New Zealand College of Obstetricians



and Gynaecologists College House 254-260 Albert Street EAST MELBOURNE, VIC 3002 +61 3 9417 1699 (t) +61 3 9417 0672 (f) ranzcog@ranzcog.edu.au (e) www.ranzcog.edu.au (w)

> President Dr Ted Weaver Vice Presidents Prof Michael Permezel Dr Rupert Sherwood Dr Digby Ngan Kee Honorary Secretary Dr Gino Pecoraro Honorary Treasurer Dr Bernadette White Chief Executive Officer Dr Peter White

From the President



Dr Ted Weaver President

t gives me great pleasure to introduce the latest issue of O&G Magazine, entitled 'Fertility'. Spring seems an appropriate time for this issue's title, as we are all made aware at this time of the fecundity of the Earth, with new life bursting forth after winter, as nature renews itself. Following the short days and cold, dark nights of winter, there could be few sights that gladden the eye more than fruit trees in blossom, or the fresh green of newly sprouted deciduous trees. This issue also reminds us of the pivotal role that our specialty plays in the management of pregnancy and the safe arrival of new life. In this issue, a number

of authors consider aspects of infertility from different perspectives, including history, demographics, emerging technology and lifestyle. It is sobering, yet not surprising, to reflect that infertility is on the rise in both Australia and New Zealand, contributed to by many women delaying childbearing until well into their 30s, the average age of first maternity being around 30 years. Given that infertility affects ten to 15 per cent of the women that we care for, this issue is timely.

'This issue also reminds us of the pivotal role that our specialty plays in the management of pregnancy and the safe arrival of new life.'

This is the final column I will write for *O&G Magazine* as President of the College. At the last Council meeting which was held in mid-July, elections were held for the new RANZCOG Board. I am happy to announce that the new College Vice-Presidents will be Professor Michael Permezel and Dr Louise Farrell representing Australia and Dr Digby Ngan Kee representing New Zealand. The College Treasurer will be Professor Ajay Rane and the two other RANZCOG Board members will be Dr Gino Pecoraro and Associate Professor Steve Robson. I would like to congratulate these Fellows on their successful election to the inaugural RANZCOG Board, where they will serve under the presidency of Dr Rupert Sherwood. I would like to wish the Board well in its capacity as the executive arm of RANZCOG and hope that the new governance structure developed over the last few years serves RANZCOG well. Elections for the Seventh RANZCOG Council took place in August.

RANZCOG, as the body representing obstetricians and gynaecologists in Australia and New Zealand, has a number of international affiliations. One of these is with the International Federation of Gynecology and Obstetrics (FIGO), based in London. The President-elect of FIGO is an Honorary Fellow of RANZCOG, Professor Sir Sabaratnam Arulkumaran, and he is due to take office in two years' time. The presidency of FIGO is awarded on a regional basis and after Sir Arul's presidency, it will be the turn of the Asia Oceania region to provide a president. Dr Ken Clark from Palmerston North, New Zealand, a previous President of RANZCOG, has indicated that he is interested in putting forward his candidacy for the FIGO presidency. This will be a huge undertaking by Dr Clark. He has discussed his intentions with the RANZCOG Executive and Council and has received our support. It would be an enormous honour for him and a great benefit to the women of Australia and New Zealand and the women in the Pacific were Dr Clark to succeed in being elected as FIGO President. It would also raise the profile of our specialty regionally for the three years of his presidency. Thus, the College has committed to supporting Dr Clark in as many ways as it can, including financially, to try to achieve this goal. I would be grateful if you could also support Dr Clark in any way that you can, as I think he would be a worthy President of FIGO, bringing the virtues of vision, humanity, humility and common sense to the role.

As RANZCOG President, I have been overseas representing the College at both the Society of Obstetricians and Gynaecologists of Canada (SOGC) meeting in Montreal and the Royal College of Obstetricians and Gynaecologists (RCOG) meeting in Belfast, and have had discussions with both presidents, and other office bearers, of those organisations about fostering further links with them. The Executive Committee has had a discussion about our international relations and it will be now a standing item on the Board agenda to try to improve those links, for the benefit of RANZCOG and its members.

The College conducts its business in an increasingly difficult medico-political environment. The President's role is often taken up with negotiating with many government bodies about their policies in a number of areas, including maternity services, rural health, workforce training and assessment. Our policies are often in conflict with government initiatives and other health professional bodies. Because of this, the College is aware that we are often not portrayed in the media as favourably as we might like.

To try to develop a more positive media profile and to try to ensure that RANZCOG's position on various issues in both Australia and New Zealand is portrayed accurately in the media, RANZCOG Council has decided to enter into an agreement with Porter Novelli, a media company based in Melbourne, to further these aims. This is a new area of College business which will involve extra expenditure. This has been accounted for in this year's budget. The Executive Committee has since held extensive discussions with Porter Novelli to discern the main issues of concern and to develop a plan of action. I hope Fellows will notice an enhanced media profile for the College which will be of benefit to us.

Professor David Ellwood has resigned from his role as Editor in Chief of the Australian and New Zealand Journal of Obstetrics and Gynaecology (ANZJOG), due to other work commitments. Professor Ellwood has done a great job in developing the journal as a regional publication and has also been integral in improving the journal's impact factor. I would like to thank him for his efforts and wish him well in his future endeavours. A number of candidates applied for the position of Editor-in-Chief, and I am pleased to announce the appointment of Professor Jan Dickinson to the position. Jan is a materno-fetal medicine specialist from Perth, Western Australia. I am sure Jan will acquit herself well in the role and look forward to the journal's further evolution as a quality publication. It is important that the College does have an Australian and New Zealand journal to showcase developments in our specialty in this region and I would ask Fellows, should they have research articles of interest, to consider publishing them in our journal rather than in alternative journals here or overseas.

Continued on page 6.

The Maternity Services Reform agenda continues, though its progress maybe interrupted, pending the outcomes of the Australian Federal election. From previously enacted legislation, 'eligible' midwives are due to enter practice on 1 November 2010 provided that they are engaged in collaborative systems of care with doctors. At the last Maternity Services Advisory Group meeting held in Canberra in early July, it was apparent that there was still much work to be done before the 1 November. Indemnity provisions for midwives are now available through the Medical Insurance Group Australia (MIGA), and also in a limited way through MEDIPROTECT, but as yet the Government has not released anything like a collaborative agreement. It seems these agreements will have to be worked up outside a Government framework and advice from the College will be forthcoming about this.

'RANZCOG is eager to move the debate on maternity away from those around place of birth and choice of carer to one about responsible labour management and better outcomes for mothers and babies.'

In New Zealand, the Health Minister, the Hon Tony Ryall, has identified four areas of review for maternity services there and the New Zealand Committee is actively engaged in this work. The National Health and Medical Research Council (NHMRC) has recently endorsed the guidance document for collaborative care which has been developed with the input of RANZCOG Fellows and others. This document is available on the NHMRC website. I suggest that you read it to familiarise yourself with the theoretical basis for collaborative care and to consider adopting the principles contained within it for your own practice.

I recently attended the Breathing New Life into Maternity Care conference which was held in Alice Springs. This was a joint conference convened by RANZCOG, the Australian College of Midwives (ACM) and the Australian College of Rural and Remote Medicine (ACRRM). RANZCOG has co-badged these meetings twice previously and they have been held every two years.

One of the recommendations that arose from the conference was that the College should re-constitute the Joint Committee on Maternity Services (JCMS). This was a joint College committee, containing representatives from both RANZCOG and ACM, but its meetings lapsed for a variety of reasons. ACM is very keen to re-activate this committee as a forum to address issues pertinent to maternity care. The RANZCOG Executive has discussed this matter and has suggested that the committee should include representatives from ACM, the Royal Australian College of General Practitioners (RACGP), ACRRM, consumers, and possibly a representative from the Australian and New Zealand College of Anaesthetists (ANZCA), who practises obstetric anaesthesia, and a practitioner to represent neonatologists. At present, it is envisaged the JCMS will not have New Zealand representation, as the New Zealand Committee does not consider it would be necessary at this stage. Having all these health professionals involved will produce, in Executive's opinion, a more complete discussion and more informed decisions about maternity care in the future. This matter will be progressed during the lifespan of the next Council. RANZCOG is eager to move the debate on maternity away from those around

place of birth and choice of carer to one about responsible labour management and better outcomes for mothers and babies.

As my two years of presidency draws to a close, I would like to briefly reflect on that role and on RANZCOG's position as a training and standards body and as an advocate for excellence in women's healthcare.

There is no question that obstetricians are the best-trained health professionals in maternity care. Clearly, we are not the only practitioners involved in this space, but we have a duty to advocate for the best care for the women under our charge. That care should be evidence-based, safe, acceptable to women and should be regularly audited in a multi-disciplinary way to ensure it is effective. Care based on out-dated ideology or practice has no place in modern maternity care. I think it is imperative that we, as obstetricians, take the lead in critically auditing our own and our unit's practice, and maternal and neonatal outcomes in the women under our care. One of the hallmarks of an effective medical professional is their engagement with other providers of care and their willingness to design systems for, and speak out for, safe care. Given the a number of different groups involved in maternity care and as the best-trained group, I think it is our responsibility to ensure that a high standard of care is maintained in Australia and New Zealand.

Thus, a strong College is essential. I have been constantly surprised how many Fellows have a rather nearsighted, sometimes unfavourable view of the College, its role and its policies. Every Fellow is a member of RANZCOG and the whole is only as good as the sum of its parts. It is important that the Fellows, Members, Trainees, Diplomates and Affiliates of RANZCOG feel a part of the organisation. The College would fail without the pro bono efforts of numbers of College members. The College training system has worked well and will continue to work well if supported. I view the training of future O and G specialists being undertaken by others as potentially bringing about a huge blowout in the cost of training, with little additional benefit. A strong, relatively independent College, producing well-trained doctors in our specialty and providing quality continuing professional development, is our best safeguard against this. The College is our professional organisation and, as such, we should all be interested in its effective functioning and its long-term viability.

I would ask you to consider what role you could have in helping the College to function effectively. This could range from becoming involved in training our Diplomates or Trainees, becoming an examiner, a training supervisor, a regional committee member, a Councillor, or even a Board member. In my experience, doing these things is interesting, enriching professionally, and adds a different dimension to one's practice. Your contribution and involvement, however small, will help to maintain the vibrancy and relevance of the College, and I would urge you to consider it.

Finally, I would like to pay tribute to the Executive Committee and Councillors of the Sixth RANZCOG Council, who have worked very hard to progress the work of the College. I would also like to thank the College CEO, Dr Peter White, and College House staff for the huge amount of work they do and their loyalty and dedication. It has been my privilege to work with you all.

From the CEO



Dr Peter White Chief Executive Officer

have written in recent times of the evolution and maturing of RANZCOG as an organisation. Again, I am reminded of this as the seasons turn and RANZCOG looks toward the Annual General Meeting in November that will see the inaugural Board and associated Council declared elected under the revised Governance arrangements approved earlier this year. Under the leadership of Dr Rupert Sherwood, the new governing body has the responsibility of stewarding the College through the next stage of its evolution and I congratulate all involved on their election to the Board, as well as those elected to the underpinning Council.

The willingness of individuals to commit to the task of serving on the Board and Council is demonstration of commitment to the organisation in a tangible manner, and I, along with the College staff as a whole, will do what we can to assist both the Board and the Council to continue the evolution of the College.

For a college of this size, the current and likely future agendas of RANZCOG can perhaps be considered ambitious; a characteristic that may have helped to shape and may continue to help shape the organisation and its standing. Indeed, in relation to what is traditionally considered the 'core' business of the College, there is much afoot in the area of education, training and continuing professional development (CPD). For example, working parties are progressing reviews of the FRANZCOG Training Program and the assessment methodologies employed to determine the comparability of Specialist International Medical Graduates and Overseas Trained Specialists to that of specialists trained by RANZCOG, while the trial of a framework to align the RANZCOG CPD program with the FRANZCOG Curriculum framework continues.

Of major significance is the development of revised curricula for the Diploma and Diploma Advanced qualifications, as well as a third qualification, the Certificate of Women's Health, that will underpin this suite of qualifications for non-specialists working in the areas of women's healthcare delivery. As I write this column, the core components of the curriculum are in place, with work in progress to develop the underlying administrative structures necessary to operationalise the three programs so that they may be opened to new enrolments in early 2011.

Also under development are the necessary educational resources to assist participants to assimilate the knowledge and skills necessary to satisfactorily complete the requirements of the three programs. This activity is yet another example of the contributions College members make to the work of the College, as well as to improving healthcare standards for the women for whom this organisation advocates. There are currently some 50 individuals involved in developing online educational materials to support the three qualifications, as well as another 20 or so involved in the development of other online education initiatives for use with the FRANZCOG Training Program and CPD activities. The College is extremely grateful for these contributions and is cognisant of the pro-bono manner in which they are provided. As with other areas of College activity, the increase in the number and range of educational materials being produced and made available by the College brings with it an increased awareness of aspects related to such matters that may not have been fully appreciated or addressed until recently. One of these aspects is the issue of Intellectual Property (IP). To this end, the College Executive has recently endorsed a College IP Policy, the central purpose of which is to clarify aspects of IP associated with materials that are created for the College and ensure that any materials incorporated do not infringe the IP rights of any third parties. The policy, along with an accompanying Deed that all contributors to College materials will be asked to enter into, is not intended to enable the College to procure IP rights to materials to which it is not entitled. However, the College, as an organisation, must heed the legal advice it is given and ensure that all involved with such College activities have a clear understanding of the purposes for which such materials are being created and are protected as much as possible.

Also of importance as the College moves forward and continues to mature is the ability for the specialist colleges such as RANZCOG to engage with the jurisdictions in relation to our core business element of training, particularly in relation to the traditional areas of tension articulated through the standards and workforce considerations. Increasingly, organisations such as the specialist colleges are expected to proactively engage with relevant jurisdictional entities (see, for example, the Australian Medical Council Accreditation Standards for the specialist colleges) and the burgeoning interest of individual jurisdictions with promoting a skilled, non-specialist, procedural medical workforce bears testament to the importance of the need to be aware of developments in this area. To this end, it is perhaps incumbent upon us to consider how best to systematically achieve effective engagement with such bodies in order to ensure that we are both seen to be meeting this expectation, as well as actually doing so and sending the message to all involved that we do have something to offer in respect to the increasing debates to be had in the realm of medical workforce, with the advent of groups such as Health Workforce Australia and Health Workforce New Zealand.

For organisations such as RANZCOG, it is clear that a significant determinant of what such an organisation can ultimately deliver for its stakeholders is the financial resources available to it. In the case of RANZCOG, even though we have consistently been in receipt of some grant monies from the Commonwealth Government in the recent past to undertake targeted projects that are able to value add to the traditional core business, the majority of income is still obtained through membership subscriptions (Fellows, Diplomates, Members, Associate Members, Educational Affiliates), as well as training fees.

From this income, activities as diverse as the development and production of quality learning materials to support training (including trainees and trainers), accreditation of training sites to ensure consistent, high-quality training experiences, production of quality materials for the information and guidance of College members and the public, the running of infrastructure, and the advocacy activities of the College must be resourced.

The College aims to run an operating budget that is, essentially, balanced, therefore, the activities which represent the core business of the organisation that apply to the overall membership should be able to be financed from income on a year-to-year

Continued on page 10.

basis. Additionally, funds also need to be able to be accumulated so as to enable the organisation to be confident of its reserves moving forward, as well being able to finance activities that may require some significant capital input, such as those relating to the development of more efficient and effective information and communication technology, including new database and finance packages, as well as e-portfolio technology for Trainees.

To this end, the College has recently undertaken an analysis of all activity that has an allocated budget cost centre (some 100 individual cost centres) by apportioning activity (either wholly or on a proportional basis) to member/user groups.

The analysis has resulted in membership subscriptions being held to the relevant CPI for the 2010-2011 financial year, with training fees for RANZCOG specialty/subspecialty trainees being subject to an increase markedly higher than CPI for the 2011 calendar year. Diploma training fees and other College fees (for example, examination fees) will also rise only by CPI. These decisions have been taken in order to ensure that the financial outlays associated with College activities are equitably distributed across users.

With regard to the work currently being undertaken through external funding from the Australian Government, the College has recently commenced work in relation to two new projects, both of which reflect the funding priorities of the Government, as well as the manner in which the Commonwealth is wishing to divest the administrative components associated with distributing funds associated with these priorities.

The first involves the College undertaking selection of successful applicants for support grants for general practitioners located in rural and remote areas to assist them in completing the DRANZCOG Advanced. Over the financial years 2009-2010 to 2012-2013, the Government has committed some five million dollars to assist general practitioners in rural and remote areas to undertake procedural training in obstetrics or anaesthetics by offering support grants of A\$40,000. The College will facilitate the applications, selection process and payments of these grants. In conjunction with interest from specific jurisdictions from a workforce perspective, it is anticipated that this will stimulate interest in the DRANZCOG Advanced at a time when new Diploma curricula are getting close to being realised.

Along similar lines, the College has entered into an arrangement with the Australian Government for 2010 in relation to funding associated with the Specialist Training Program (STP), the program that came into being as a result of the consolidation of a range of programs previously offered by the Commonwealth, most notably the Expanded Settings Training Program (ESTP). The agreement has three components, which reflect different priority aspects of the STP: development of infrastructure and processes to enable the College to manage the funding contracts between the Commonwealth and successful applicants for expanded setting posts in 2012; educational project funding to enable development of online modules for supervisors of trainees in expanded settings; and the provision of up-skilling opportunities for overseas trained specialists working toward RANZCOG Fellowship.

Indications are that the STP is anticipated to represent some 460 fulltime equivalent (FTE) specialist training posts in 'expanded' settings in 2011, rising each year through to 2014. When it is considered that each FTE post represents an outlay by the Commonwealth of some A\$100,000, there are clearly large sums being committed to this initiative. Expanded settings training represents a relatively modest component of training relative to some other specialist colleges. However, the interest in applying

for funds under the STP has increased and it is incumbent on the College to consider what part training in settings outside the traditional public hospital sites can play in ensuring that our trainees are as well trained as possible, with access to appropriately supervised clinical experience. The involvement of the specialist colleges and individual jurisdictions in considering STP applications ensures consideration of both workforce and educational imperatives to proposed expanded settings training placements.

By the time this edition of O&G Magazine is published, the guidelines and application processes associated with the Rural Health Continuing Education (RHCE) program, another program formed from the consolidation of previously funded Commonwealth programs, one of which is the Support Scheme for Rural Specialists (SSRS), will have been finalised and promulgated. While not a direct replacement of SSRS, the RHCE program still has at the core of one of its funding streams the provision of funding to enable education opportunities to be accessed by medical specialists in rural and remote areas of Australia. Current understanding is that funding will be offered over a period to 2012-2013 and be available on a competitive basis for educational opportunities that enable support to be afforded to rural and remote medical specialists to engage in multidisciplinary team-based educational activities at their location, as well as individual educational (CPD) opportunities. The possibility of funding for projects over a multi-year timeframe addresses what was generally considered a major drawback of the SSRS scheme.

Since the previous edition of O&G Magazine, I have attended a meeting of organisational stakeholders held subsequent to the release of the report of the New Zealand Parliamentarians' Group on Population and Development into maternal health in the Pacific. Coordination of work in the Pacific region is clearly of importance to many stakeholders, heightened perhaps by the Millennium Development Goals (MDGs), in particular MDGs 4 and 5. In conjunction with the Pacific Society for Reproductive Health (PSRH), and others, the College clearly has a role to play and much to offer. This is, however, a space that appears to be occupied by many 'players'. A clear pathway with specific aims and desired outcomes and targets in relation to offerings that we can make is something that we must ensure we can articulate, particularly if we are to convince other stakeholders that we, along with PSRH, are organisations that can produce value-adding benefits in partnership.

In Australia, the National Registration and Accreditation Scheme (NRAS) is now up and running in all States and Territories, with the exception of Western Australia. The most recent advice received from the Medical Board of Western Australia at the time of writing is that the date for the relevant 'National Law' to be operational in order for Western Australia to participate in NRAS is 18 October 2010 (pending legislation). Until Western Australia is able to participate, medical practitioners registered with the Medical Board of Western Australia will need to obtain registration with the Medical Board of Australia in order to practise in all others States and Territories of Australia.

I take this opportunity to remind readers that information relating to NRAS may be found on the AHPRA website (www.ahpra.gov.au) with a link to the website of the MBA (www.medicalboard.gov.au) also available.

By the time of publication, the College's Annual Report to the Australian Medical Council (AMC) will have been compiled and submitted. The report represents a summary of activities since the preceding Annual Report, submitted in May 2009, against the AMC Accreditation Standards for Specialist Colleges. It is worthy of note that the AMC is moving to streamline the reporting requirements of colleges, including a clearer indication of recommendations from accreditation reports that can either be considered to have been addressed and closed, or which may have been modified as a result of activities since the time of accreditation. In the case of RANZCOG, the accreditation report and associated recommendations now dates back to 2003 and much has occurred since that time.

In closing, I thank all Councillors for their contributions to the College during the term of this Council and congratulate all those who have been elected to positions on the inaugural RANZCOG Board. We are all aware of the dependence of organisations such as RANZCOG on the efforts of those who give their time for the advancement of the profession and thank all those Councillors who are not seeking re-election to the Council for their contributions to the work of the College over time.

In particular, as it draws to a close, I would acknowledge the contributions to the College of Dr Ted Weaver in his time as President of RANZCOG. It has been an absolute privilege to have worked alongside Ted during this time and I continue to be in awe of the commitment and sacrifice inherent in occupying the position of RANZCOG President. All members can be thankful and proud of the job Ted has done during his period, leading the College in what has been a particularly demanding time, with both internal and external issues to be grappled with and progressed. I have been grateful also for the immense support that Ted has shown me and, on behalf of the entire RANZCOG staff, I thank him and wish him well as he prepares to be the first President to sit as Immediate Past-President on a RANZCOG Council. I look forward to working with the next Board and Council under the leadership of Dr Rupert Sherwood and, as always, assure all members of the absolute support of College staff to the continued work of RANZCOG.

When it rains...

A/Prof Stephen Robson FRANZCOG 'Spring has returned. The earth is like a child that knows poems.' Rainer Maria Rilke

Prof Caroline de Costa FRANZCOG

Many young children have grown up in Australia not having ever seen rain! What a wonderful winter has just passed for them, then. We have finally bid a cheerful goodbye to El Niño and welcomed the arrival of the delightfully wetter La Niña. This Spring brings with it a bountiful promise, with even dreary brown Melbourne donning a proud coat of green.

With the rain and returning warmth of Spring, the earth really does seem like a child with poetry in her heart. We selected the introductory quote not because of the sly connection with its author, a man with 'rain' in his name, but because of the Australian connection. Rainer's protégé was the celebrated Australian musician Alma Templeton Moodie, the foremost violinist of 1920s Europe. Ms Moodie succumbed to thrombo-embolism during the Second World War, however, her life has recently been celebrated in a magnificent concert series in Melbourne.

 $O \mathscr{C} G$ Magazine has retained a relatively static format for the last five years. With Spring comes the opportunity to revitalise and regenerate the publication. We are pleased to announce a few changes in $O \mathscr{C} G$ Magazine as we 'move forward' into the new decade.

We are well aware that $O \not C Magazine$ is now one of the most popular educational initiatives of the College. To further enhance this role and to ensure the quality of the material published, we are working towards instituting a formal peer review process for selected articles. Papers that have been formally peer-reviewed will have a boxed 'P' in the top right corner. We will be looking to introduce this in coming issues. We are planning to invite Diplomates and senior Trainees to become peer reviewers with us; we anticipate initially teaming Trainees with experienced reviewers.

Readers will also notice the first in our new series, 'Review', specially-commissioned papers appearing in each issue that will deal with important topics impacting on our specialty. The first concerns the thorny issue of syntocinon doses at caesarean section (page 58). We intend to bring you timely updates on 'hot issues' in obstetric anaesthesia and neonatal paediatrics in particular. Ideas for future 'Reviews' are keenly sought from our readership.

As such a delightful Spring blooms across Australia and New Zealand, it seems only appropriate to lead with an issue devoted to fertility. The team behind O c G Magazine have never been shy of cliché! We have aimed to put together an issue that will interest and inform Fellows, Diplomates and Trainees and indeed subspecialists. As always, our sincere thanks go to all of our contributors. This issue is definitely best enjoyed with a cool drink in a shady Spring garden.

Also, in keeping with the season and the theme of our issue, we must announce the imminent departure on maternity leave of our wonderful Production Editor, Rachel Corkery. We wish Rachel a completely uncomplicated pregnancy and birth, and look forward to her return to Ocord Magazine in mid 2011.

Demographics of infertility



Dr Phillip McChesney MRANZCOG CREI Trainee

The vast majority of people (approximately 95 per cent in parenting surveys) express the desire to have children at some point in their lives.¹ However, not all couples who desire pregnancy will achieve one spontaneously and some will require medical or lifestyle interventions to assist them towards their goal.

From 2007 data, it can be estimated that 3.1 per cent of babies born in Australia and 1.8 per cent of babies born in New Zealand are the result of assisted reproductive technology (ART) treatment.^{2,3,4} The term 'infertility' is usually defined as the failure to conceive after one year of unprotected intercourse, however, it is a clinical continuum rather than an absolute or irreversible condition.

An international study by Boivin and colleagues in 2007⁵ found the prevalence of current infertility in 'more developed' countries to range from 3.5 per cent to 16.7 per cent, with a median figure of nine per cent in women aged 20 to 44 years. They also found the prevalence of lifetime infertility ranged from 6.6 per cent to 26.4 per cent, highlighting the fact that many couples' delay in conception is not absolute. Interestingly, their findings relating to 'less developed' countries were very similar in numbers, although they speculated that the type of infertility and the mechanisms thereof may be quite different.⁵ For example, Cates *et al* in 1985 reported that most cases of infertility in Africa were due to treatable infection, a cause which is not common in the developed world. Conversely, the steady rise in age-related infertility is just not seen in less developed countries as it is in Australasia and other first world nations.^{4,5,6}

Closer to home, a study of Australian couples found that approximately one in six experience a delay of greater than 12 months to achieve a planned pregnancy during their reproductive life.⁷

It is commonly estimated that only half of couples that experience infertility seek medical treatment and those who do are frequently older, Caucasian, married women with higher levels of education and income. Less than half the couples who seek medical advice actually receive any specialist infertility treatment. These estimates appear to hold true both in countries that provide generous access to treatment such as Denmark and countries in which access is very restricted, like Gambia.^{5,8}

The European Society of Human Reproduction and Embryology (ESHRE) Capri Workshop Group has estimated that at least 1500 IVF cycles per million people are needed to meet demands.⁸ Denmark has been reported to have the highest IVF treatment ratios, with 1251 IVF cycles per 100,000 women of reproductive age, while Australia ranked third with 954 cycles per 100,000 women of reproductive age. New Zealand was amongst the lowest at 328 per 100,000, while the United Kingdom had 396 per 100,000 and interestingly, the United States had the lowest IVF treatment ratios with only 237 cycles per 100,000 women of reproductive age.⁹

A study in the US found that both IVF utilisation and availability was positively correlated with the median state income, percentage of individuals 25 years of age or older with a bachelor's degree, percentage of single persons, percentage of childless households, percentage urbanisation and presence of IVF insurance coverage.⁸ Unpublished data from Fertility Associates in New Zealand reveals similar trends to those found in the US study. In New Zealand, education appears to be a better indicator of demand than income, however, both are positively correlated with uptake of fertility services. Individual motivation and GP referral behaviour may actually be better indicators suggesting that general community awareness regarding infertility issues still needs to be improved.

'It is important that infertility is considered a medical condition rather than a socially constructed need to ensure appropriate availability and delivery of treatment to those who require it.'

Looking again at local data, in 2007 there were 56,817 ART treatment cycles (including fresh and thawed cycles) in Australasia, 92 per cent from Australia and eight per cent from New Zealand. This reflects an increase of approximately 40,000 cycles per year since 1991. In Australia, there were 11.7 cycles per 1000 women of reproductive age (15 to 44 years old) compared to 4.9 cycles per 1000 women of reproductive age.⁴ In New Zealand, access to publicly funded ART is much more restricted than in Australia, with a maximum of two cycles of IVF funded providing that certain criteria are met, including a BMI restriction of 32 and age restriction of 39 years or less. Any treatment outside of this must be totally privately funded with costs generally upwards of NZ\$9000. In contrast, Australia has an unrestricted approach to public funding of ART, with patients paying a part charge for each cycle with the Medicare Plus Safety Net picking up approximately 75 per cent of medical expenses once an individual's or family's threshold is reached (although the actual calculations are somewhat more complicated than this).

Based on the Australian and New Zealand Assisted Reproduction Database (ANZARD) 2007 data, the proportional representation of the four major groups of infertility treated by IVF or intrauterine insemination (IUI) in Australasia were: 33.6 per cent only female infertility; 27.7 per cent only male infertility; 21.8 per cent unexplained infertility; and 14.3 per cent combined male and female factors.⁴ The major change seen over the past 20 years has been a doubling in the proportion of unexplained infertility, halving the proportion of tubal infertility and a gradual increase in male and combined factors.¹⁰

It appears likely that there will be an increase in the incidence of infertility over the next decade. Contributing to this is the increasing obesity epidemic which is associated with anovulation (as well as increased miscarriage and poorer pregnancy outcomes), the falling mean sperm count and the increase in prevalence of sexually transmitted diseases in young women (although this does not seem to have made the dramatic increase in tubal infertility once predicted).

There has also been an obvious trend over the past 50 years throughout the western world for delaying childbirth. In New Zealand, for example, the average age at first birth has increased from 23.9 years in 1962 to 30.5 years in 2009.¹¹ The reasons for this are many and varied but may include financial pressures, the pressure of time spent in higher education and climbing the employment ladder to a point which is safe to take time away from work, and the frivolity and freedom that can be enjoyed by the relatively wealthy DINKYs (double income, no kids yet).¹² In contrast to this European view, however, in 2006 the National Fertility Study in Australia found that the first priorities for having children were a stable relationship and good income, while female career was further down the list. They also found that one in three women in their late twenties and early thirties were not in a stable relationship.⁷ A significant consequence of this delay in childbearing is an increase in unexplained infertility related to the natural decline in monthly fecundity with age from approximately 25 per cent at age 25 years to 16 per cent at 35 years and six per cent at 40 years.¹³ Unfortunately, there still appears to be some belief in the community that ART will negate the effects of age, however, IVF live birth rate declines with age in a similar way to natural fecundity.

At Fertility Associates, Auckland, the mean age at first private consultation has increased over the past ten years from 35 years to over 36.5 years. Over a 20-year timeframe, the average age at which a privately funded IVF cycle is initiated has risen from approximately 34.5 years to 38 years, with women aged 40 years or older now making up about one third of cycles compared to less than ten per cent in the late 1980s.¹³ The average age for all women undergoing ART in Australasia in 2007 was 35.7 years, with over one in five cycles undertaken by women aged 40 years and older. For women using their own oocytes, the average age was 35.5 years (0.5 years older than recorded in 2003), while the average age of women using donated oocytes was five years older at 40.5 years.⁴

Demographic data suggest that infertility is a significant issue throughout the world. It is important that infertility is considered a medical condition rather than a socially constructed need to ensure appropriate availability and delivery of treatment to those who require it. Ongoing community education regarding determinants of natural fertility will be important in minimising the impact of infertility into the future.

Acknowledgement

I would like to thank Dr Richard Fisher, Dr Freddie Graham and Alex Price of Fertility Associates for their contribution and editorial assistance with this article.

References

 Lampic C, Svanberg AS, Karlstrom P, et al. Fertility awareness, intentions concerning childbearing and attitudes towards parenthood among female and male academics. Hum Reprod. 2006; 21:285-91.

- Lawes PJ, Abeywardana S, Walker J, Sullivan E, 2008. Australia's mothers and babies 2006. *Perinatal Statistics Series* no.22. AIHW cat. no. PER 46. Sydney: AIHW National Perinatal Statistics Unit. Viewed 20/06/10.
- Statistics New Zealand 2008. Births and Deaths: December 2007 quarter. Web: www.stats.govt.nz. Viewed 20/06/10.
- Wang YA, Chambers GM, Dieng M, Sullivan EA, 2009. Assisted reproductive technology in Australia and New Zealand 2007. Assisted Reproduction Technology Series no. 13 Cat. no. PER 47. Canberra: AIHW.
- Boivin J, Bunting L, Collins J, Nygren K. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. *Hum Reprod.* 2007; 22(6):1506-12.
- 6. Cates W, Farley T, Rowe P. Worldwide patterns of infertility: is Africa different? *Lancet* 1985; 2:596-8.
- Clark A. National Fertility Study 2006. Australians' experience and knowledge of fertility issues. Viewed 29 June 2010. Web: www. fertilitysociety.com.au/wp-content/uploads/preservation-of-fertilitypresentation-2006.ppt#1.
- Hammoud A, Gibson M, Stanford J, White G, Carrell D, Peterson M. In vitro fertilization availability and utilization in the United States: a study of demographics, social, and economic factors. *Fertility and Sterility* 2009; 91 (5):1630-35.
- Lancaster P. Worldwide variations in the use of ART services [abstract]. Hum Reprod. 2006; 21(Suppl 1):i23.
- Lancaster P, Shafir E, Huang J. Assisted Conception, Australian and New Zealand, 1992 and 1993. Sydney: AIHW National Perinatal Statistics Unit, 1995 (Assisted Conception Series no. 1).
- Median and average age of mother. Statistics New Zealand 2009. Web: www.stats.govt.nz. Viewed 20/06/10.
- 12. WL Ledger. Demographics of infertility. *Reprod BioMed Online* 2009; 18 Suppl 2:11-14.
- 13. Unpublished data. Fertility Associates.

Age and women's fertility



Dr John Chenoweth FRANZCOG Deputy Director Wesley Monash IVF Unit

Few practitioners would be unaware of the impact of sweeping social trends on our working and personal lives. One such trend of particular relevance to our specialty is the phenomenon of delaying starting a family that has resulted from the use of effective contraception. Women and couples have the ability to give childbearing a lower priority than other individual goals.

Fertility rates have halved since 1961. Forty years ago, the rate was 3.83 children per woman, whereas now it is only 1.81. Over the same period, the proportion of mothers aged 30 years or over has increased from 31.5 per cent to 46.4 per cent, with remarkable consequences for the prevalence and pattern of infertility. Statistics from the Wesley Monash IVF Unit, like other assisted reproduction technology (ART) units

in Australia, have revealed an increase in the proportion of women over the age of 37 attending our unit over the last decade. Last year, one-third of our fertility patients were in this age group.

The biological clock

Despite some groups looking for evidence of oocyte regeneration from non-ovarian progenitor cells¹, it is widely accepted that females lose the capacity for germ cell regeneration. At menarche, girls have approximately 250,000 primordial folllicles in their ovaries. Apoptosis and the cohorts of primordial follicles that contribute to ovulation steadily reduce follicle numbers each month, until the count drops to about 25,000 in a woman's late 30s. Thereafter, accelerated losses occur until the menopause, when only a few remain. This latter period is associated with declining gamete competency and can predate menopause by more than a decade.² In ART practice, the decline in female fertility is seen as starting from age 32 and most in vitro fertilisation (IVF) units will not perform IVF on women using their own eggs from age 45 older, since the chance of a live birth is so low. Accelerated loss of ovarian reserve is seen in patients who have undergone chemotherapy or radiotherapy, those who carry a genetic predisposition and smokers.

What is the physiological basis underlying this reduction in count and quality of follicles that we call the 'biological clock'? Declining numbers may be due to impaired follicular microcirculation, hormonal disturbances and disrupted perifollicular somatic cell function from stromal senescence³, with underlying degradation of cohesins associated with chromatid disaggregation at metaphase 1.⁴ Two separate events may explain the poorer quality of the oocyte of the older woman: reduced formation of chiasmata during fetal oogenesis; and chromatin insult secondary to reactive oxygen species damage sustained before ovulation.⁵

Investigations to establish a woman's ovarian reserve

For the clinician the more important question is: How much time is left on my patient's clock? What is a woman's ovarian reserve? Over the past two decades a number of tests of ovarian reserve have been studied in the context of IVF treatment, with the outcome measures of oocyte yield and occurrence of pregnancy. Broekman's systematic review concluded that these tests have modest predictive properties for poor ovarian response to hyperstimulation and very limited ability to predict successful pregnancy.⁶ Sills review published last year reached similar conclusions, but added that such tests may be useful as a screening tool and I list them below as an indication for earlier referral to an ART unit.⁷

Age

Age is still one of the best indicators of reduced number and quality of oocytes. Infertility has been defined as the inability to fall pregnant after 12 months trying for a pregnancy. In women 35 years of age or more, most ART units would encourage referral after six months of trying. This is because there is little remaining time for investigation and potential treatment, especially if more than one child is desired.

Antral follicle count (AFC)

Ovarian imaging by transvaginal ultrasound shows a reduced number of smaller antral follicles available for gonadotropin recruitment as ovarian reserve declines. The number of antral follicles with a diameter of 2 to 10 mm measured on day one or day two of the period is readily counted and this measure is widely used, formally or informally, in ART units. Other studies have counted follicles up to 6 mm. A count of less than five follicles has been linked with inability to achieve pregnancy.⁸ Prognostic usefulness is reduced by problems that include intercycle variation in results, and inter-observer differences. A meta-analysis concluded that the AFC had limited use in prediction of non-conception.⁶

Anti-mullerian hormone (AMH)

AMH is one of the intra-ovarian growth factors regulating primordial follicle recruitment and FSH-sensitivity of growing follicles in an inhibitory manner. AMH is secreted by granulosa cells, from primary, pre-antral and antral follicles up to 6 mm in size. The serum levels are unaffected by use of the oral contraceptive pill or by pregnancy. Levels are mildly reduced in obese patients and a small brief drop occurs after ovulation or IVF hyperstimulation, but inter- and intracycle variability is low enough to permit random timing of AMH measurement during the menstrual cycle.⁹ AMH is believed to be the earliest marker to change with advancing maternal age. The cost of AMH testing to the patient in Brisbane is A\$60 and a result of less than 14 pmol/L is suggestive of failing ovarian reserve, while a level of greater than 30 pmol/L indicates the possibilities of polycystic ovarian syndrome (PCOS), with increased risk of ovarian hyperstimulation syndrome in a stimulated cycle, or in postmenopausal females, a granulosa cell tumour.

While AMH and antral follicle count are regarded as 'the best' of the tests of ovarian reserve, many IVF units may use these tests to work out starting dose of gonadotropins, but would rarely use them to refuse IVF treatment without a trial IVF cycle first.

Early follicular phase FSH levels

Elevated serum follicle-stimulating hormone (FSH) is a direct pituitary compensation for the older and less responsive ovary.

Continued on page 18.

Reduced follicle numbers and estradiol levels attenuate the negative feedback loop on the hypothalamo-pituitary secretion of FSH. Timing of collection is important and levels vary considerably between cycles. Values above 20 mIU/ml are associated with a pronounced decline in conceptions.¹⁰ Another study suggests that a level over 10 mIU/ml warrants earlier referral.⁷

Elevated estradiol levels

Basal levels of estradiol measured on days two or three of menstruation correlate inversely with ovarian response to gonadotrophins in patients undergoing IVF. Levels over 275 pmol/L are unfavourable.⁷ Overall, this test has low predictive value for poor response and for non-pregnancy. Other tests of ovarian reserve that have been evaluated, including the clomiphene citrate challenge test, GnRH-agonist stimulation test and ovarian biopsy, but these have not become part of standard practice.

It can be summarised that while we can predict the number of oocytes retrieved in an IVF cycle, we are still unable to test for the quality of those oocytes and the consequent pregnancy rate.

Age is still the most clinically useful measure. In a woman aged under 36, an AFC of less than 10, or an AMH level of less than 14 pmol/L, or a day two FSH of greater than 10 mlU/ml, are all suggestive of reduced ovarian reserve, with the consequent need for earlier referral. It is worth stating too that these tests have no additive effect. In essence, they are measuring the same thing, so using different tests adds little new information.

Management of age-related fertility delay

Controlled ovarian hyperstimulation and IVF does not treat the underlying problem of age, the reduced number and poor quality of oocytes. It does, however, allow the search for the 'good' embryo to be accelerated and many months of 'trying' to be sped up. Thus, IVF is currently the commonest treatment for age-related infertility. The only ART treatment that really addresses the problem of age is the use of oocytes donated from younger known or unknown, altruistic, or paid (overseas) donors.

Oocyte freezing

The advent of rapid freezing vitrification of oocytes has opened the door to more widespread oocyte freezing for the 'social' indication of reduced ovarian reserve. Good freeze-thaw rates of over 90 per cent, fertilisation rates of 75 to 90 per cent and pregnancy rates of 32 to 65 per cent have been reported.¹¹ Women need to be informed, however, that this technique is still experimental and the cost is considerable as Medicare funding is not applicable.

Conclusions

Inexorable social changes mean that more women are delaying childbearing. This has been a burden for IVF units and a major shock for women. Various tests are available to 'predict' ovarian reserve but none are perfect. At present, there is no treatment that effectively overcomes the deleterious effect of age on a woman's fertility. The best advice is to have children young.

References

 Bukovsky A, Caudle MR, Svetlikova M, Upadhyaya NB. Origin of germ cells and formation of new primary follicles in adult human ovaries. *Reprod Biol Endocrinol.* 2004; 2:20.

- Faddy MJ, Gosden RG, Gougeon A, Richardson SJ, Nelson JF. Accelerated disappearance of ovarian follicles in midlife: implications for forecasting menopause. *Hum Reprod.* 1992; 7:1342-6.
- Johnson NP, Bagrie EM, Coomarasamy A, et al. Ovarian reserve tests for predicting fertility outcomes for assisted reproductive technology: the International Systematic Collaboration of Ovarian Reserve Evaluation protocol for a systematic review of ovarian reserve test accuracy. BJOG 2006;113:1472-80.
- 4. Coccia ME, Rizzello F. Ovarian reserve. Ann NY Acad Sci. 2008; 1127:27-30.
- 5. Keefe DL, Marquard K, Liu L. The Telomere theory of reproductive senescence in women. *Curr Opin Obstet Gynecol.* 2006; 18:280-5.
- Broekmans FJ, Kwee DJ, Hendriks DJ, Mol BW, Lambalk CB. A systematic review of tests predicting ovarian reserve and IVF outcome. Human Reproduction Update 2006; 12(6):685-718.
- Sills ES, Alper MA, Walsh APH. Ovarian screening in infertility: Practical applications and theoretical directions for future research. European Journal of Obsterics and Gynecology and Reproductive Biology 2009; 146:30-36.
- Chang MY, Chiang CH, Chiu TH, Hsieh TT, Soong YK. The antral follicle count predicts the outcome of pregnancy in a controlled ovarian hyperstimulation/intrauterine insemination program. J Assist Reprod Genet. 1998; 15:12-7.
- La Marca A, Sighinolfi G, Radi D, Argento C, Baraldi E, Carducci Artensio A, Stabile G, Volpe A. Anti-Mullerian hormone as a predictive marker in assisted reproductive technology. *Human Reproduction Update* 2010; 16:113-130.
- Muasher SJ, Oehninger S, SimonettiS, et al. The value of basal and/ or stimulated serum gonadotropin levels in prediction of stimulation response and in vitro fertilisation outcome. *Fertil Steril.* 1988; 50:298-307.
- Homburg R, van der Veen F, Silber S. Oocyte vitrification women's emancipation set in stone. *Fertil Steril.* 2009; 91:1319-1320.



Have you completed a Practice Profile in **2010**?

Fellows: Already filled in a Practice Profile in 2009?

Review your details on the profile to ensure the information we have is correct, and respond to several new questions.

Fellows & Diplomates: Is this your first time?

Follow the online instructions to complete your profile.

Last year's results for Fellows are available on our website.

Log in to your Practice Profile via our website:

FELLOWS:

www.ranzcog.edu.au/fellows/PracticeProfile.shtml

DIPLOMATES:

www.ranzcog.edu.au/diplomates/PracticeProfile.shtml

Did you know

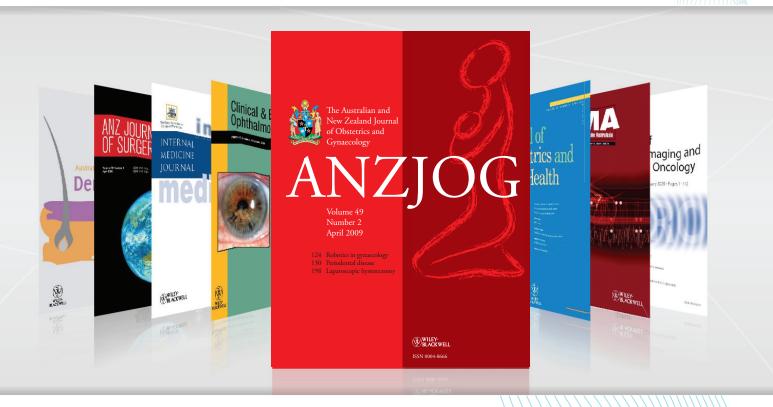
you can access *The Australian and New Zealand Journal of Obstetrics & Gynaecology* online through the Royal Australian and New Zealand College of Obstetricians and Gynaecologists' website?

Go to www.ranzcog.edu.au

- Log in using your college username and password
- = FREE access to all ANZJOG current and digitised backfile content from volume one, 1961!

Wiley-Blackwell is proud to publish in partnership with a majority of medical colleges in Australia and New Zealand.

Did you also know that in accessing your journal via your secure members' site you also have access to these college titles published by Wiley-Blackwell:



Access your college journal online

WILEY-BLACKWELL



The future of assisted reproduction



A/Prof Peter Illingworth FRANZCOG CREI Medical Director IVF Australia

2010 is the 30th birthday of Candice Reed, Australia's first in vitro fertilisation (IVF) baby. The first 30 years of IVF have been revolutionary times. In the early days, pregnancies were few and far between and every baby born was a cause for celebration.

In the 30 years since, there has been a steady increase in our understanding of the growth needs of early embryos, we have refined ovarian stimulation regimes and, in the major breakthrough of the 1990s, developed intracytoplasmic sperm injection (ICSI) as a treatment for male factor infertility. We have now reached the point where IVF treatment is

commonplace and one in thirty babies in Australia is born from assisted reproduction. So what does the future hold now for ART?

Developments in cryobiology

There have been some striking developments in cryobiology. Alan Trounson's team in Melbourne were pioneers in achieving pregnancies from cryopreserved embryos and this approach has since become a central part of any modern ART program, contributing to 34 per cent of the births from ART in Australia and New Zealand in 2007.¹ By comparison, the freezing of unfertilised oocytes was considered, until recently, to have only a very low prospect of success. However, in the past few years, a number of centres around the world have applied the emerging technology of vitrification to the freezing of oocytes and have reported success rates that are only slightly lower than those for cryopreserved embryos.²

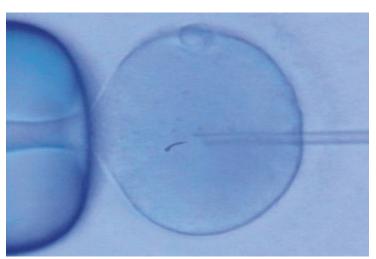


Figure 1. Intracytoplasmic sperm injection (ICSI) is one of the major breakthroughs in ART in the early nineties.

If these success rates can be reproduced in Australia, the ability to store oocytes prior to fertilisation could make a significant contribution to addressing one of the big ethical concerns of ART, the gradual accumulation of large numbers of early human embryos in storage. In addition, this development has great importance for single women who may seek some form of 'reproductive insurance' prior to undergoing cancer treatment. However, the role of 'social' oocyte freezing in women with age-related fertility decline is less clear. It is important to note that success rates from oocyte freezing around the world have been exceptionally variable.² In addition, experience of thawing (as opposed to freezing) of unfertilised oocytes in Australia remains limited and one cannot extrapolate from large overseas egg-freezing programs, using young egg donors, to the anticipated outcome for a 38-year-old woman in Australia.

Refinements in stimulation regimes

A major focus of clinicians in Australia will be to continue to strive to make IVF easier for women going through it. The development, in the past decade, of pen-style injection systems, the use of lower follicle-stimulating hormone (FSH) dosages and, critically, the move towards greater uptake of gonadotropin-releasing hormone (GnRH) antagonist down-regulation protocols, have all served to make an IVF cycle significantly less of an ordeal than before.

Looking into the near future, it is likely the trend towards lower dosages and greater uptake of antagonists will continue. Recombinant long-acting FSH combines the FSH molecule with the beta-chain extension of human chorionic gonadotrophin (hCG) to give a form of FSH with an action lasting for a full seven days.³ There remain significant concerns about the potential for such a molecule to increase the risk of ovarian hyperstimulation syndrome. However, there is no doubt that, for carefully selected patients, one single FSH injection instead of seven daily injections will be attractive.

Egg and embryo selection

In the late 90s and early 2000s, there was a dramatic increase in the success rates of IVF in association with greater understanding of the nutritional and environmental needs of the early embryo. In the past few years, this rise has plateaued¹ as we have come up against the unavoidable fact of the biological variation in embryonic genotype.

Further improvements in success rates may only arise through better understanding of embryo quality and thus more rapid identification of the right embryo for transfer. A number of approaches are currently being explored for this:

• The use of metabolomic techniques to study the waste products of developing embryos and predict the likelihood of successful implantation.

- The use of new imaging techniques to study the unfertilised egg, particularly its spindle and the morphologic features of the developing embryo.
- The use of more sophisticated genetic techniques, possibly involving microchips, to predict the genetic makeup of embryos.

Embryonic stem cells

Ten years ago, embryonic stem cells were thought to foreshadow a massive advance in medical technology, creating the possibility of being able to generate medical spare parts for diseased or damaged organs. While there have been enormous advances in stem cell biology in the last decade, these have not yet translated into clinical developments. It now seems that the role of embryonic stem cells, as opposed to adult stem cells, will be very limited.

Improving the health of children conceived from ART

As clinicians, we have continually had concern for the future health of children conceived through IVF. Australia has led the way in preventing the biggest health risk of fertility treatment, multiple pregnancy, through the transfer of one embryo at a time. Interestingly, recent studies of perinatal mortality following IVF now indicate that the excess perinatal mortality, associated with even singleton ART births, can be returned to baseline through single embryo transfer.⁴

There is growing awareness of the small increase in congenital anomalies associated with ART conception.⁵ Recent research suggests that couples who need to use ART to conceive may already be at greater risk of congenital anomalies⁶ and that it may be this rather than anything inherent to the IVF process that explains the difference. However, more detailed research is needed to understand the aetiology of this problem and this research is likely to give us clearer insights over the next few years.

Finally, in the course of the last 30 years, we have come to understand the importance to the child conceived from donated gametes of understanding more about their genetic parentage. Over the next 30 years, gamete donation will be much more open with donor registers, including voluntary retrospective registers, being established in every Australian state.

Developments in sperm biology

This is, in my view, the most likely area for significant advance. Half the genetic material in an embryo comes from the spermatozoa and

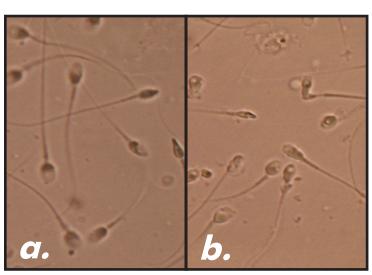


Figure 2. Two images of sperm under high resolution microscopy illustrating the difference between (a) healthy sperm and (b) sperm with abnormal DNA, raising the possibility that novel microscopy techniques such as these may allow better selection of sperm for ART.

there have been enormous advances in our understanding of sperm biology over the past decade; advances that are yet to translate into benefits in clinical practice. A woman doing IVF will present with eight to nine eggs while her partner will provide 80 million sperm cells. There is thus far greater potential for effective gamete selection through better understanding of sperm biology and it is highly likely that developments in this area will significantly change clinical practice in the next few years.

Pre-implantation genetic diagnosis

Developments in IVF have been paralleled by exponential advances in molecular biology over the same time period. We are now able to use polymerase chain reaction technology to study expression of single genes in human embryos. Techniques for studying the whole genome, such as comparative genomic hybridisation⁷, are emerging. At present, these still pose serious methodologic problems. However, the development of more rapid and sophisticated microchip technology is likely to make this very much easier in the next few years and we will be able to have a more sophisticated understanding of the future health of each embryo in the laboratory.

Clearly, there will need to be public discussion of the important ethical issues involved in handling all this information over the next few years. However, in the past, we have been able to responsibly resolve the ethical issues raised by developments in reproductive medicine in a manner that Australian and New Zealand society has accepted and we can achieve this again.

And when Candice Reed is 60?

So, finally, to stick my neck out, how do I think IVF will look in 30 years time, when Candice Reed is celebrating her 60th birthday? We will be using low dosage single injection FSH regimes based on short antagonist protocols. We will have access to a range of microchips for easy and rapid pre-implantation diagnosis. We will have a better understanding of the role of the sperm in ART, with new tools for sperm diagnosis and selection for ICSI. We will have much more sophisticated techniques for assessing early human embryos (although these may not significantly improve IVF success rates). Embryonic stem cell lines will have been supplanted by new ranges of adult stem cell lines with the same potential for future tissue generation. Younger women will be able to use these techniques to identify the right embryo and conceive a little more quickly than at present, but things will still be very difficult for older women trying to conceive.

References

- Wang YA, Chambers GM, Dieng M, Sullivan EA. Assisted reproductive technology in Australia and New Zealand 2007. Assisted Reproduction Technology Series no. 13. Cat. no. PER 47. 2009. Canberra: AIHW.
- Nagy ZP, Chang CC, Shapiro DB, Bernal DP, Kort HI, Vajta G. The efficacy and safety of human oocyte vitrification. *Semin Reprod Med.* 2009:450-5.
- Fauser BC, Mannaerts BM, Devroey P, Leader A, Boime I, Baird DT. Advances in recombinant DNA technology: corifollitropin alfa, a hybrid molecule with sustained follicle-stimulating activity and reduced injection frequency. *Hum Reprod Update*. 2009 15(3):309-21.
- Wang YA, Kovacs G, Sullivan EA. Transfer of a selected single blastocyst optimizes the chance of a healthy term baby: a retrospective population based study in Australia 2004-2007. *Hum Reprod.* Advance Access June 2010.
- Hansen M, Bower C, Milne E, de Klerk N, Kurinczuk JJ. Assisted reproductive technologies and the risk of birth defects – a systematic review. *Hum Reprod.* 2005 Feb; 20(2):328-38.
- Davies M. Comparative risk of birth defects across ART treatment modalities and spontaneous pregnancies within a population cohort. O-136. (AQbstract) ESHRE Annual Meeting, Rome 2010.
- Wilton L. Preimplantation genetic diagnosis and chromosome analysis of blastomeres using comparative genomic hybridization. *Hum Reprod Update* 2005 Jan-Feb;11(1):33-41.

Protection and preservation of fertility for young women with cancer



Cancer treatments have improved dramatically over the past few decades, such that the majority of young women diagnosed with the commonest forms of cancer can expect to be cured.¹ The concern of treating physicians now is not just provision of a 'disease-free state', but also the preservation of an optimum 'quality of life' following chemotherapy treatment.

This has resulted, fortunately, in greater awareness and recognition of the importance of the long-term effects of cancer treatment.

Dr Kate Stern FRANZCOG CREI

Rising cancer survival rates have also led to an increased interest in trying to reduce the risk of premature menopause in affected patients, without compromising the efficacy

of chemotherapy.^{2,3} In particular, it is recognised that certain chemotherapy treatment regimens, especially those including highdose alkylating agents, can lead to reduced fertility. This is a serious side effect for young women who would otherwise expect to lead a normal life after surviving cancer, including raising a family of their own.⁴

The diagnosis of a potentially life-threatening malignancy, requiring toxic chemotherapy, is an extremely traumatic and shattering experience for young women and their families. Discussion of further evaluation, therapeutic choices and the short and longer term implications of these, as well as discussion of prognosis, is extremely challenging for oncologists and their teams. Figure 1 lists some of the issues which need to be considered when making decisions about fertility preservation. Counselling often requires several consultations, despite the pressure of time for commencement of treatment. Incorporation of discussion about threats to future fertility and options to preserve and protect fertility, can potentially add an extra layer of complexity and often confusion to an already fraught interaction. However, patients and their families invariably welcome the information imparted regarding future fertility. This information, and perhaps most importantly, the referral for fertility discussion, can give young women and their families optimism about future survival and quality of life. It can also provide an opportunity for them to feel more in control of their situation and to make choices which suit their individual life situation. Counselling is of paramount importance, as many young people will choose not to avail themselves of any interventionist options, but will appreciate being informed of both the implications of their cancer and its treatment on future fertility and the choices available. This helps them to feel more in control of their reproductive future. For those who wish to be more active regarding future fertility, we can now offer the various options with increasing confidence and optimism.

How big is the problem? Cancer risk for young women in Australia

Cancer prevalence increases with age, but data from the Australian Institute for Health and Welfare (AIHW) suggest that the risk of

cancer in young women is not insignificant. Over 770 women less than 40 years of age were diagnosed with cancer in Victoria alone in 2004 (CCV 2005). Although survival and prognoses are gradually improving, the incidence of cancer is not diminishing. In 2010, it is expected that over 70/100,000 girls less than 20 years of age and over 380/100,000 young women aged 20 to 39 years will be diagnosed with cancer (www.aihw.gov.au/publications/can/ cipa02-11/cipa02-11.pdf). Figure 2 shows the incidence of the common cancers in young Australian women in 2005.

Figure 1. Factors to consider in decision-making for fertility preservation.

Balance of risk

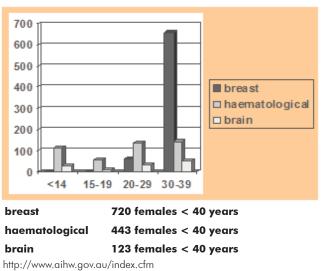
Risk to patient from doing procedure:

- Delay in commencement of cancer treatment
- Medical risks of procedure
- Potential risks of hormones
- Suboptimal response to fertility-preserving treatment
- Risk of false hope/insurance for future fertility

Risk to patient from not doing procedure:

- Reduced fertility/sterility
- Potential childlessness
- Lack of confidence in survival

Figure 2. Common cancers in Australian females, 2005.



Risk of damage from cancer treatment

Chemotherapy is commonly associated with a temporary cessation of menstrual and ovulatory function, with hot flushes and amenorrhoea.^{5,6,7} This may persist into more 'permanent' ovarian failure and premature menopause, or may resolve over six to 18 months and thus be diagnosed as 'temporary' only in retrospect. Sometimes ovarian function may appear to persist normally, as evaluated by clinical or hormonal measures.

Although many young women continue to menstruate regularly after chemotherapy, or resume menses after a period of amenorrhoea, morphological and ultrasound assessments usually demonstrate reduced follicle numbers, and endocrine assessment commonly reveals alterations in levels of follicle-stimulating hormone (FSH), anti-Mullerian hormone (AMH), inhibin B (InhB) and luteinising hormone (LH), indicating persistent vulnerability to premature ovarian failure.^{8,9} Thus, resumption of 'normal' menstrual cycles after cancer treatment may unwittingly, but inaccurately, reassure physicians and their patients, with potentially serious long-term fertility consequences.

Many anti-cancer drugs exert their actions predominantly on dividing cells. The toxic effects of chemotherapy treatments may include inhibition of cell division and adverse effects on DNA function within the dividing granulosa and theca cells of the ovary, as well as the oocytes contained within the follicle.

It has been confirmed that exposure to various alkylating agents during chemotherapy treatment (in particular cyclophosphamide and procarbazine), with resultant effects on the ovaries, are agedependent.⁷ As the number of oocytes declines with advancing age, the ovaries of older individuals become more vulnerable to gonadal toxins relative to the ovaries of younger women and girls. An individual young woman's chance of developing both acute and permanent ovarian failure is related to increasing age, diagnosis and the specific treatment modalities used. Radiotherapy and chemotherapy, with the use of alkylating agents in particular, all increase risk.^{7,10} Radiotherapy to the pelvis can also cause serious damage to the uterus, particularly the endometrium and the myometrium. Cranial radiation may affect pituitary hormone production and release.

Table 1 illustrates the range of fertility risks associated with treatment of the commonest cancers.¹⁰ However, given the scarcity of data regarding rates of infertility following most cancer treatments, oncologists may have difficulty in providing specific and accurate data to patients about their particular risks for infertility.

Table 1. Representative rates of ovarian failure after treatment of common childhood and young adult cancers.¹⁰

Disease	Likelihood of premature ovarian failure		
Breast cancer: Age < 30 Age 30–40	< 10% 20 - 40%		
Sarcoma	< 10 - 40%		
Hodgkin's lymphoma	< 10% unless intensive therapy		
Non-Hodgkin's lymphoma	10 – 40%		
Leukaemia (early stage)	< 10%		
High-dose therapy and stem-cell transplantation	> 90 - 95%		

Options for fertility preservation and protection

Given the potentially toxic effects of chemotherapy agents on the ovary, with the resultant risk of temporary and more permanent ovarian failure, the availability of options to preserve and protect fertility is of great importance to these young women and their families. Current options to preserve fertility in this patient population of women who undergo chemotherapy treatment are limited, but include preservation of embryos, oocytes or ovarian tissue prior to cancer treatment, and ovarian protection with the use of gonadotrophin-releasing hormone (GnRH) analogues throughout the duration of treatment.¹¹

Protection of the ovaries during chemotherapy

GnRH analogues may be agonists or antagonists, inducing their effects by either down-regulation or competitive inhibition respectively. In women, they induce a temporary and reversible medical state of hypo-oestrogenism by decreasing pituitary FSH and LH. GnRH analogues are commonly used in the treatment of endometriosis, in some infertility treatments to prevent the LH surge, and as adjuncts to chemotherapy in hormonally sensitive breast and prostate cancers. In children, they have also been utilised in the treatment of central precocious puberty.

Recently, GnRH analogues have been shown to protect the ovary from damage during chemotherapy in some animal models.^{12,13} The mechanism of this protective effect is poorly understood, particularly as the early phases of follicle development are thought to be gonadotrophin-independent.¹⁴ Possibly, the protective effect could be mediated either by reduction of blood flow to the ovary or through modulation of AMH activity.

Most human studies of GnRH analogues to date involving cancer patients have been uncontrolled and/or retrospective. There is thus little prospective data specifically addressing the issues for those women of reproductive age who are at highest risk of infertility from chemotherapy. However, despite the above limitations, there is now increasing evidence from clinical studies to suggest a therapeutic benefit from GnRH agonists for ovarian protection.

The recent publication of a randomised trial¹⁵, together with several reviews^{16,17}, provide support for the role of GnRH analogues for ovarian protection. They also lay the groundwork for further prospective studies. Other medications, including immunomodulators, are also being trialled as ovarian protectors in animal models. It is important to note, however, the 'chemoprotection' of the ovaries should still be considered experimental. Patients should be counselled accordingly, especially about the lack of large studies currently available, and where possible they should be enrolled in clinical trials.

Embryo freezing

Cryopreservation of embryos in an IVF cycle prior to the onset of cytotoxic treatment offers the best chance of a subsequent pregnancy, should a woman subsequently become infertile after chemotherapy. This is an established technology whereby the ovaries are stimulated with gonadotrophins to produce mature oocytes. These are then harvested and fertilised with the partner's (or, occasionally, donor) sperm. Resultant embryos are then frozen and stored until required. The survival rate of embryos after freezing and thawing is in the range of 75 to 90 per cent, and implantation rates (clinical pregnancy rate for each individual embryo transferred) are between 18 and 30 per cent (currently 25 to 30 per cent in women under 37 years of age), approximating spontaneous fertility.¹⁸ If multiple embryos are available, the cumulative pregnancy rate can be more than 60 per cent.

Continued on page 24.

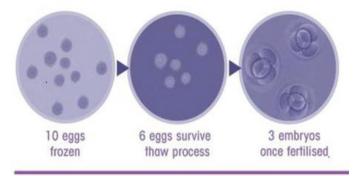
Unfortunately, there are sometimes barriers to the use of this technique in the oncology setting. Often, commencement of chemotherapy is required forthwith after diagnosis, so there is not enough time for the ten to 16 days required to initiate and complete an IVF cycle. Additionally, younger women or adolescents may not have a stable partner and for young women it may not be appropriate to consider donor sperm. In some jurisdictions, if a relationship subsequently dissolves, the woman may not be able to utilise the embryos if her ex-partner refuses to give permission. In addition, many women with a malignancy do not respond well to standard ovarian stimulation regimens, perhaps because of intense physical and psychological stress associated with the cancer diagnosis, such that the numbers and/or quality of oocytes obtained may not be optimal. Finally, there are theoretical concerns that the endocrine stimulation required to produce suitable oocytes may have an adverse effect on hormonally sensitive tumours such as breast or endometrial cancer.⁷

Oocyte freezing

An alternative to embryo freezing is to freeze mature oocytes after ovarian stimulation. This maintains autonomy, as there is no requirement for a partner or sperm donor. Freezing of mature oocytes has been practised for well over a decade¹⁹, but for many years the fragility of the oocyte, compared with the embryo, hampered success rates with viability after thawing. Recent improvements in freeze-thaw protocols, however, make this a much more reliable option with reports of over 60 per cent of mature oocytes surviving the thaw, and subsequent fertilisation rates now approximate those for fresh oocytes during IVE¹⁹

Over 930 births have now been reported from oocyte freezing (including several in Australia), with no major increase in complication rates such as miscarriage or congenital abnormalities.²⁰ Like embryo freezing, however, the requirement for hormonal stimulation and time may preclude the use of oocyte freezing for some young women about to embark on chemotherapy.

Figure 3. The survival of oocytes after freezing.



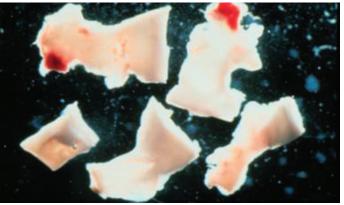
Ovarian tissue freezing and grafting

In some centres, patients may be offered the opportunity to harvest and freeze ovarian tissue prior to the commencement of cancer treatment. The tissue is obtained laparoscopically, with the surgeon usually taking up to one-third of one ovary, or a whole ovary if highdose chemotherapy or pelvic radiotherapy is planned for cancer treatment.

This option has an advantage in that there is no requirement for stimulation, meaning that it can be undertaken rapidly. However, it exposes the patient to the risk of laparoscopy, which carries approximately a 0.5 to two per cent chance of conversion to open laparotomy and a one in 12,000 chance of death.²¹ At the time of the European Society for Human Reproduction and Embryology (ESHRE) meeting in Rome this year, there have only been 14 live births reported worldwide following the re-implantation of thawed ovarian tissue. Follicular development from grafted ovarian tissue does not always follow typical cyclical patterns, making spontaneous fertility and IVF more difficult than in the conventional setting.²² Although the harvested tissue is rigorously and repeatedly tested by histological and other immunohistochemical and molecular techniques, concerns have been expressed that small ovarian vessels, or even the ovarian tissue itself, has the potential to harbour malignant cells, particularly in acute leukaemia.²³

It is hoped that further improvements in freeze-thaw technology may allow frozen ovarian tissue to be a more dependable form of fertility preservation in the near future. This field is rapidly evolving, so patients should be counselled that while this technique is currently highly experimental, there is the potential to preserve a large number of follicles within the tissue, and the results to date are very encouraging. Again, this procedure should only be performed in the setting of a properly-conducted clinical trial.

Figure 4. Thin slices of ovarian tissue prepared for freezing.



Conclusion

It is now acknowledged that discussion of future fertility options should be considered an essential part of the treatment plan for young women having gonadotoxic therapy. Increasing research and clinical collaboration and cooperation between reproductive medicine specialists and oncological teams will allow us to provide our patients with information which can help them to have more control over their reproductive future.

References

- 1. Jemal A, Murray T, Samuels A, Ghafoor A, Ward E and Thun MJ. Cancer Statistics, 2003. *CA Cancer J Clin.* 2003; 53: 5-26.
- Chen WY, Manson JE. Premature ovarian failure in cancer survivors: new insights, looming concerns. J Natl Cancer Inst. 2006; 98: 880-881.
- Royal College of Physicians, Royal College of Radiologists, Royal College of Obstetricians and Gynaecologists. The effects of cancer treatment on reproductive functions: Guidance on management. Report of a Working Party. London: RCP, 2007.
- Schover LR. The cancer experience and motivation for biological and social parenthood. Parenthood after Cancer Conference. Texas: MD Anderson Cancer Center, 2004.
- Warne GT, Fairley KF, Hobbs JB, Martin FI. Cyclophosphamide induced ovarian failure. N Eng J Med. 1973: 289-1159.
- Nicosia SV, Matus-Ridley M, Meadows AT. Gonadal effects of cancer therapy in girls. *Cancer.* 1985; 55: 2364.
- Meirow D. Ovarian injury and modern options to preserve fertility in female cancer patients treated with high dose radio-chemotherapy for hemato-oncological neoplasias and other cancers. *Leuk Lymphoma*. 1999; 33: 65-76.
- Anderson RA, Themmen AP, Al-Qahtani A, Groome NP and Cameron DA. The effects of chemotherapy and long-term gonadotrophin suppression on the ovarian reserve in premenopausal women with breast cancer. *Hum Reprod.* 2006; 21: 2583-92.

- 9. Sklar CA. Reproductive physiology and treatment related loss of sex hormone production. *Med Pediatr Oncol.* 1999; 33: 2-8.
- Stern CJ, Toledo MG, Gook DA, Seymour JF. Fertility preservation in female oncology patients. ANZJOG 2006; 46: 15-23.
- Levine J, Canada A, Stern CJ. Fertility reservation in adolescents and young adults with cancer. Early release, published online May 10 2010. J Clin Oncol. 10.1200/JCO.2009.22.8312.
- Ataya K, Rao LV, Lawrence E, Kimmel R. Luteinising hormone-releasing hormone agonist inhibits cyclophosphamide-induced ovarian follicular depletion in rhesus monkeys. *Biol Reprod.* 1995; 52: 365-372.
- Meirow D, Assad G, Dor J, Rabinovici J. The GnRH antagonist cetrorelix reduces cyclophosphamide-induced ovarian follicular destruction in mice. *Hum Reprod.* 2004; 19: 1294-1299.
- McNatty KP, Smith P, Moore LG, Reader K, Lun S, Hanrahan JP, et al. Oocyte-expressed genes affecting ovulation rate. *Mol Cell Endocrinol.* 2005; 234: 57-66.
- Badawy A, Elnashar A, El-Ashry M, Shahat M. Gonadotropin-releasing hormone agonists for prevention of chemotherapy-induced ovarian damage: Prospective randomized study. *Fertil Steril.* 2009; 91: 694-697.
- Beck-Fruchter R, Weiss A, Shalev E. GnRH agonist therapy as ovarian protectants in female patients undergoing chemotherapy: a review of the clinical data. *Hum Reprod Update* 2008; 14: 553-561.
- Blumenfeld Z, von Wolff M. GnRH-analogues and oral contraceptives for fertility preservation in women during chemotherapy. *Hum Reprod Update* 2008; 14: 543-552.
- Jansen RP. The effect of female age on the likelihood of a live birth from one in-vitro fertilisation treatment. *Med J Aust.* 2003; 178: 258-261.
- Gook DA, Edgar DH. Human oocyte cryopreservation. Hum Reprod Update 2007; 13: 591-605.
- Noyes N, Porcu E, Borini A. Over 900 oocyte cryopreservation babies born with no apparent increase in congenital anomalies. *Reprod Biomed Online* 2009; 18: 769-776.
- Jansen FW, Kapiteyn K, Trimbos-Kemper T, Hermans J, Trimbos JB. Complications of laparoscopy: a prospective multicentre observational study. Br J Obstet Gynaecol. 1997; 104: 595-600.
- 22. Demeestere I, Simon P, Emiliani S, Delbaere A and Englert Y. Orthotopic and heterotopic ovarian tissue transplantation. Hum Reprod Update 2009; 15: 649-665.
- Seshadri T, Gook D, Lade S, Spencer A, Grigg A, Tiedemann K, et al. Lack of evidence of disease contamination in ovarian tissue harvested for cryopreservation from patients with Hodgkin lymphoma and analysis of factors predictive of oocyte yield. Br J Cancer. 2006; 94: 1007-1010.

Want to locum in rural Australia?

Do you want to: Help your rural colleagues? Keep up your obstetric skills? Experience rural Australia?



SOLS needs RANZCOG Fellows and DRANZCOG holders to fill obstetric locum placements in rural and remote Australia.

For more information: www.ranzcog.edu.au/sols/index.shtml (03) 9412 2912 | sols@ranzcog.edu.au

Specialist Obstetrician Locum Scheme

Anatomy of Complications Workshops 2011, Perth

Dates:

18-19 February 2011 6-7 May 2011 24-25 June 2011 7-8 October 2011

For queries and registrations please contact:

Wendy Rutherford

(e) Wendy.Rutherford@health.wa.gov.au (t) +61 8 9340 1393 (f) +61 8 9340 1063

CPD Self-Education Activities

Have you been involved in developing or reviewing guidelines and protocols?

Did you know you can claim CPD points in the self-education category?



Download a form from the College website at: www.ranzcog.edu.au/fellows/cpdselfeducation.shtml

If you have been further involved with the implementation and audit of the effectiveness of the guideline/protocol, you can claim this time spent in the PR&CRM category at the rate of one point per hour.

Difficulties in providing fertility treatment for rural women



Dr Robert Miller FRANZCOG

Australia is a vast continent. There are three regional hospitals with a wide range of specialist referral services across north and north eastern Australia: Darwin, Cairns and Townsville.

Smaller regional hospitals and Outreach clinics, provided by those Base Hospitals, in conjunction with the Royal Flying Doctor Service, seek to fill in the gaps. Obviously, such clinics have to prioritise and triage their care. Understandably, infertility advice and treatment comes low on that list.

Also, the vagaries and variability of a woman's menstrual cycle seem to rarely correspond with a scheduled fly-in fly-out clinic.

So much of infertility care and monitoring revolves around flexible visits, specialised laboratory procedures and ready access to pelvic ultrasound monitoring, both for diagnosis and treament. For example, same day gonadotrophin assays. Patients need ready access to a 'helpline' with a nurse coordinator.

Infertility is not really a one-stop visit, although couples often have that expectation, especially when just to get to Cairns is a four to 12-hour round trip or a plane flight away. The cyclone and wet season can derail the best laid plans!

It takes two to tango. The partner may not be able to attend, at least the first visit, and certainly would rather be somewhere else. Society still tends to think infertility is the woman's problem and there is no shortage of this sentiment in the 'men of the bush', whereas we know that five per cent of men have sub-optimal sperm (Laureate Professor John Aitken, the University of Newcastle). Also, the men have their fair share of lifestyle problems and don't always take kindly to advice in regard to changing their ways.

Getting the man organised for a formal seminal analysis and basic screening can be a challenge. Those with busy lifestyles may be crewing a prawn boat in the Gulf, running cattle stations, teaching or policing up the Cape, in the navy, or fly-in fly-out miners on a ten-day out-four-day home roster. In fact, constantly absent partners may be a relevant infertility factor, I think!

While ovulation induction with low-dose clomiphene is relatively straightforward and can be managed at a distance for a few cycles, coordinating and monitoring for timed intrauterine insemination is a different kettle of fish. The partner is often trying to juggle staying at work as long as possible, while having to be ready to drop everything and rush to Cairns in order to play his part. One has to be careful that couples don't drop out of view and continue with self-monitored repeat scripts of clomiphene, or get put off by negative and fragmented care. They need to be given a clear 'road map' and timetable of how their management will progress if there is no quick result. That plan should include the important place assisted reproduction has in helping to achieve a result.

Ovulation induction with gonadotrophins is fraught with difficulties. Even with the low-dose step-up regime, high order pregnancy is a concern and the treatment length is unpredictable. It can tend to drag on, to everybody's frustration, with the woman 'camped 'in Cairns, while her partner works at home on 'stand-by'.

Quite honestly, I think the best option for many couples in such situations is to opt for in vitro fertilisation (IVF), as they can plan ahead, arrange their affairs around a fairly fixed set of dates, and a single embryo can be transferred. 'Bushies' tend to be more resourceful and accepting of the tyranny of distance.

However, like their compatriots in the city, when trying to conceive, they tend to leave it too long and too late. Also, their management tends to be more spread out over time due to their and their partner's dislocation.

I'm afraid, we now have a generation of women who have had the benefit of such effective contraception that they have 'mis(sed)'conception. Society's idea of planning for a family seems to be to start trying at age 32 to 38. This is a recipe for disappointment and leads to failure to fulfil their desires for the hoped for number of children to complete their family unit, even when successful the first time. We need to redouble our efforts to explain the benefits of experiencing chilbirth in the 'twenties'. Many infertility problems would then just fade away.

Another product of modern society is the 'post vasectomy', 'I'm ready to go again, Doc' phenomenon. Often the man is in his fifties and is showing the effects of a few decades of poor lifestyle. Occasionally, they are quite young men who haven't even experienced fatherhood yet. Maybe the bush attracts such types, I don't know. It seems that all the safeguards built into the informed consent process required for female sterilisation go out of the window where men are concerned.

Patients can be left 'in limbo', losing precious time, when measures short of assisted reproduction fail. While assisted reproduction technology is the last option, it is the 'end game'. Take-up of this resource is limited by logistical and financial considerations. From where I sit in Far North Queensland, I know that a lot of rural women are in need of such treatment, are not aware that they would benefit from such treatment and/or are not being given the opportunity or help with facilitating access to such treatment.

Also, myths continue, even in medical circles, as to the actual 'out of pocket' costs in regard to IVF cycles. Informed financial consent is readily available if patients are encouraged to make direct contact.

The Australian bush contains a cross-section of society. If Australia has a two-tier economy, this is also seen in the bush. There are those in well-paid jobs, those that are struggling to stay comfortable, and many disadvantaged groups. A lot of people are missing out.

All units carry out some 'pro bono' work for disadvantaged patients. For example, Queensland Fertility Group (QFG) has done 'prechemo' sperm freezes for years, and more latterly, egg freezing and other fertility preservation options, again pre-cancer treatment. The recent passing of legislation allowing surrogacy is a new challenge, mainly explaining to those that haven't yet accepted closure why it doesn't apply to them!

QFG also now dedicates about 30 IVF-stimulated cycles a year to disadvantaged people. Of course, this is a drop in the ocean compared to potential demand. However, running such units is very expensive. For example, our small unit in Cairns costs approximately A\$10,000 a week, especially as we don't have the economy of scale of the bigger units.

I guess a public-private facility is the best option, but there is no sign of such an arrangement in Queensland in the foreseeable future. The next option is for a certain number of cases to be contracted out to the private sector, as in the Surgery Connect program. Again, there are much higher priorities than this for Queensland Health.

An observation, based on experience from working in both the public and private sectors, is that a co-payment quickly sorts out those with the right intent and attitude. One cannot organise a stimulated cycle in a safe and successful manner if the patient is not compliant with treatment.

Nor can the patient be 'lost' to the bush post egg pick-up and embryo transfer. Most complications arise then: ovarian hyperstimulation syndrome (OHSS); the risk of deep vein thrombosis; pelvic infection; and complications of early pregnancy, including ectopic pregnancy. Those pesky embryos can drift anywhere before they implant! I have even had to remove a cornual ectopic after a previous total salpingectomy. This was a heterotopic pregnancy and the intrauterine pregnancy continued.

Single embryo transfer is obviously safer for the isolated patient for all stages of pregnancy. Contact must be maintained during this time by the treating unit and this applies to capital city units that often treat patients from all points north and west.

'Bushies' can be very stoical. They may shrug off early symptoms of complications. Some women will even hide their symptoms if they can, as they want it to succeed. The unit must have someone prepared to talk to concerned regional medical staff at any time, to help triage. OHSS patients should be transferred to a major centre. It is a condition that has too many idiosyncracies. Thankfully, the more recent antagonist protocols and trend to lower gonadotrophin dosage, have served to reduce the incidence and severity of this condition, but can't claim to have eliminated this dreaded complication. While assisted reproduction is expensive care, there are novel ideas for cheap, effective treatment in the developing world, such as intra-vaginal incubators. However, I can't see this being practical in Australia, where we have to conform to strict guidelines and quality assurance. Incidentally, complying with paperwork, such as the latest ISO standard in Australia, is a significant on-cost to ARTaccredited clinics – a necessary evil.

Outreach clinics can only do so much and the health dollar can only be stretched, and has been, so far. May I suggest that the referral process could be streamlined somewhat. The satellite clinic does the initial assessment. The details are passed onto the base hospital team, that includes a dedicated subspecialty clinic, clinician, registrar and nurse coordinator. All the appointments and necessary investigations are set up, including laparoscopy and hysteroscopy if indicated, so that when the couple come to town, they are done in an efficient and timely manner, the results reviewed, and further management discussed and planned. By the time the couple return home, they have clear timelines as to how their management will unfold, if the initial lines of treatment are unsuccessful.

Good fertility care can be cost-effective for a nation that needs youngsters to look after us ageing ob/gynae baby boomers! The women of 'the bush' need the same chance and opportunity to access the full range of reproductive care as urban and urbane women.



Bob Miller with IVF mums, enjoying their membership of 'Muddies' baby playgroup, Cairns, Queensland.

The infertile couple A GP's perspective

Dr Sally Lyttleton DRANZCOG

In 2006, the Fertility Society of Australia commissioned a large survey of how fertility problems affect Australians. Some of the findings are quite surprising in terms of how little general knowledge is held in the community about fertility.¹ As general practitioners, we are ideally placed to highlight these fertility issues for our patients.

Infertility is defined as failure to conceive after 12 months of regular unprotected intercourse. The majority of couples matching this definition will have subfertility, with true sterility estimated at only one per cent. It is helpful to bear in mind that 50 to 60 per cent of 'infertile' couples will conceive in the second year of trying, if no reason for subfertility is found. It is important to counsel these couples to be hopeful of eventual success if age is on their side.² However, once three years of trying to conceive have passed, the chances of success are much less and intervention is recommended (if wanted and not already pursued).

'Having a good understanding of what might be influencing a couple's fertility means we can get a good amount of the groundwork established prior to their first appointment with the fertility clinic.'

Extent of the issue

Fertility problems affect one in six Australian couples and this has been constant over the past several decades.¹ What has changed, however, is the time at which couples start to try for pregnancy, now much later, when age-related fertility decline is starting to have an impact. Consequently, couples don't have as long in their reproductive lives to either continue trying for spontaneous conception, or give themselves the best chance with assisted reproductive technologies (ART).

It is a problem for the couple together, with an estimated 30 per cent female factors, 30 per cent male factors, 30 per cent combined factors and ten per cent unexplained.

Over the last five years, the number of ART procedures has increased on average by over ten per cent per year in Australia and New Zealand. Latest estimates indicate that 3.1 per cent of babies born in Australia are conceived as a result of ART treatment.⁷

Lifestyle factors that influence fertility

A lot of emphasis is put on medical causes and interventions for fertility. In fact, lifestyle factors play a significant role and are perhaps underestimated in general practice and certainly in mainstream media.

Age

Female fertility starts to drop off after the age of 31 and the rate of decline increases as a woman approaches her 40s.

The percentage of infertility is estimated at:

- Eight per cent for women aged 19 to 26 years;
- 13 to 14 per cent for women aged 27 to 34 years; and
- 18 per cent for women aged 35 to 39 years, therefore, twice the rate from age 25 to late 30s.²

Another way of looking at it is by spontaneous conception rates (see Table 1).

Table	1.	Spontaneous	conception	rates.
-------	----	--------------------	------------	--------

Age	Spontaneous conception rates		
Early 20s	25% per cycle		
Early 30s	19% per cycle		
35 years	15% per cycle		
39 years	8% per cycle		
45 years	1% per cycle		

The message is not getting through

Despite stating they knew fertility declines with age, a surprising 42 per cent of Australian women aged 40 to 49 years thought they could have a child without any problems.¹ Pregnancy for an older woman also presents a higher risk for an array of complications, the discussion of which is beyond the scope of this article.

So what about men? Not one person, either male or female, in a Fertility Society of Australia (FSA) survey realised that a man's age might be a reason for needing IVF treatment.

Although not as dramatic, it is now clear male age does affect conception rates. Specific sperm parameters have been shown to change with age, in particular, motility rates deteriorate, and observed conception rates fall from the late 30s onwards.^{2,3} If a woman is 35 years of age, the risk of infertility increases from 18 per cent if the male partner is 35 years old to 28 per cent if he is 40 years old.²

It is also documented that with advancing paternal age there is a small increased risk of autism, schizophrenia and some types of malformations in offspring. Up to seven per cent of Down's syndrome cases can originate from the paternal side.^{5,6}

As GPs, we should take every opportunity to bring up the issues around delayed parenting with our patients.

Continued on page 30.

Free Copies of Sexual Assault Module

Would your hospital or practice use a free copy of *Medical responses to* adults who have experienced sexual assault: an interactive educational module for doctors?

RANZCOG has a limited number of copies of this Sexual Assault Module and for only the cost of a postage and handling fee, we will send you a copy.

Sexual Assault Module Order Form	The Royal Australian and New Zealand College of Obstetricians and Gynaecologists ABN 34 100 268 969
Please send me free copies of Medical responses to adults who have experienced sexual assault: an interactive educational module for doctors.	
Postage Include the following postage amounts with your order: AustraliaA\$10.00 New ZealandA\$20.00 For delivery to all other countries or to order more than one copy, please contact on (t) +61 3 9417 1699 to discuss postage.	College House
Delivery name: address: address: suburb/town: country: phone:	
Payment details credit card: Visa Mastercard card name: expiry date: card number:	
cheque Please make payable to RANZCOG.	
signature: total amount due in AUD\$	
Send a completed form to: Reception, College House 254-260 Albert St East Melbourne Vic 3002, Aust (t) +61 3 9417 1699 (f) +61 3 9419 0672 (e) ranzcog@ranzcog.edu.au	tralia

Smoking

39 per cent of women and 36 per cent of men experiencing fertility problems smoke.¹ The smoking community know it is unhealthy, but perhaps don't understand the possible implications for fertility. *Smoking and reproductive life* is a detailed report published by the British Medical Association which documents all the usual information, with concise and highlighted boxed summaries.⁶ I find picking some of these boxes out from the pdf copy can be a useful visual tool when talking to couples. For example:

Key messages: Smoking and fertility

- Men who smoke have a lower sperm count and a higher proportion of malformed sperm.
- Women who smoke take longer to conceive.
- Women who smoke are twice as likely to be infertile as nonsmokers.
- Men and women who smoke have a poorer response to fertility treatment.
- Women who have stopped smoking take no longer to become pregnant than women who have never smoked.
- Stopping smoking improves sperm count and quality.

There is also evidence that if a man has been smoking for five years or more prior to conception, his child is four times more likely to develop childhood cancer before the age of five years.

There is a careful line to tread, I find, when giving negative information without being punitive or judgemental, especially if the male partner is not a regular attendee and has been dragged along by his partner, already feeling inadequate about not achieving pregnancy. If one partner is a smoker but the other is not, I try to see them separately for smoking cessation counselling.

Alcohol

30 per cent of men and 19 per cent of women affected by fertility problems report they drink more than 14 alcoholic drinks per week and that is probably underreported.¹ Even moderate alcohol intake is related to delayed conception. The evidence quantifying the effects (therefore, how much is safe, if any) is not entirely conclusive and is difficult to control for confounding factors.¹⁴ The National Health and Medical Research Council (NHMRC) recommendation for women who are pregnant or planning a pregnancy is that abstinence from alcohol is the safest option to reduce the risk of harm to the developing fetus.

Weight

Fertility for women declines with increasing weight, miscarriages are more likely, and pregnancy and perinatal complications are higher. In one large study, after adjusting for other lifestyle variables, age and menstrual pattern, women with a body mass index (BMI) of more than 25 (or less than 20) were at twice the risk of infertility compared to women with a normal BMI.⁴ Male BMI of less than 20 or more than 25 has also been associated with a reduction in sperm quality.⁴

There is good evidence that modest weight reduction and increased exercise can improve fertility, especially in very obese women. Some fertility clinics now offer lifestyle programs in conjunction with, or prior to, treatments to improve outcomes.

Further history and investigations

Causes of subfertility

• Tubal factors with incomplete blockage (for example, pelvic inflammatory disease, endometriosis, adhesions).

- Endometriosis.
- Ovulation factors irregular or infrequent (for example, PCOS).
- Uterine abnormalities fibroids, septum.
- Lifestyle factors.
- Abnormal sperm.

Causes of complete infertility

- Complete tubal occlusion.
- Azoospermia.
- Absence of ovulation and menstrual cycle:
 - Temporary (for example, amenorrhoea, hyperprolactinaemia, hypothalamic suppression from stress).
- Permanent (for example, congenital malformation, genetic abnormality).

The female partner

- Ensure adequate folate (400 mcg daily) supplements, adequate iodine intake/supplements (150 mcg daily), vitamin D intake (sun and supplements 10 mcg daily). Most prenatal vitamin mixes will cover this, but it is helpful to check.
- A Pap smear and pelvic examination.
- Hormone levels on day 2 and day 21 of the cycle.
- Gynaecological ultrasound.
- HyCoSy/hysterosalpingogram.

With a history of painful periods, especially beyond the first day or two, spotting premenstrually, pain with sex, or pelvic pain between periods, endometriosis should be considered.

If endometriosis is detected by scans showing endometriomas, or with a high index of suspicion, then laparoscopy with a surgeon experienced in excision of all visible spots of endometriosis is the best treatment option for subsequent fertility outcomes and early referral is recommended. Laparoscopy is also indicated in asymptomatic women with failure to conceive, as endometriosis is found in a significant proportion of asymptomatic infertile women.

There is fascinating new research being done whereby an endometrial sample taken in the office can diagnose endometriosis based on abnormal changes within the eutopic endometrium.⁸ If we can confidently rule out endometriosis without invasive surgery, it is a huge advantage. This treatment is not widely available yet.

Although the number of women having IVF for tubal occlusion due to pelvic inflammatory disease is significantly less than it used to be, the chlamydia notification rates are increasing in young people. We need to be vigilant in screening young women. For anyone with delayed fertility, it is useful to rule out current infection with an endocervical swab or first void urine for PCR testing.

Testing hormones

Measuring day 2 follicle-stimulating hormone (FSH), estradiol (E2), prolactin and thyroid-stimulating hormone (TSH) is a reasonable minimum. It is good to use this opportunity to check rubella and chicken pox immunity; blood group and infectious screen of HIV; hepatitis B and C; and Venereal Disease Research Laboratory (VDRL) tests. It is considered unnecessary in regular menstrual cycles, but luteal phase progesterone (seven days prior to the next expected period) can be reassuring.

Anti-Mullerian hormone

Anti-Mullerian hormone (AMH) is produced by the granulosa cells and regulates growth and development of follicles. It correlates highly with antralfollicle count and age, decreasing over time. AMH is stable throughout the cycle and between cycles, which makes it a useful marker of reduced ovarian reserve.¹⁰ We can also measure it when a woman is still on the contraceptive pill. In an older woman, AMH is likely to be low commensurate with her age and therefore adds no new information about her chances of conception. It can a useful test in younger women, because if an unexpected low level is found, it would prompt early referral. On the other hand, if a higher than expected level was found in an older woman, while it is good news, don't delay referral on that basis alone. AMH levels can help to predict response to stimulation in ART.

In the presence of oligomenorrhoea, acne problems, hirsutism, alopecia and weight gain, polycystic ovary syndrome (PCOS) is easily suspected, and I would include androgen hormone testing in the follicular phase with free androgen index, dehydroepiandrosterone sulfate (DHEAS) and androstenedione. The extent of PCOS is generally under-recognised and has significant repercussions for general health and for obstetric health when pregnancy is achieved.¹ I would consider measuring androgens and order a pelvic ultrasound in all patients presenting with infertility, even with regular cycles. It is possible to find polycystic ovaries with chemical hyperandrogenism in women with regular cycles and a normal BMI.

Insulin resistance is an important part of the pathophysiology of PCOS and when documented indicates a better response to metformin.¹⁰ Metformin has been shown to be safe periconceptually and throughout pregnancy⁹, in some studies improving conception rates and reducing miscarriage rates in women with PCOS.^{9,10}

Discussing and initiating metformin use with women diagnosed with PCOS, while undergoing lifestyle measures, is something GPs can do in conjunction with endocrine/fertility specialist assessment, particularly if waiting for those specialists to be available.

Clomiphene is the drug of choice for women with infrequent or absent ovulation. GPs with an interest in managing infertility can initiate clomiphene treatment if comfortable doing so and if they have fully informed patients of the rare but possible side effect of hyperstimulation. We need to have a plan in place for investigating and managing this, should hyperstimulation occur.

Hysterosalpingogram or HyCoSy?

Imaging the patency of the tubes and uterine lining is valuable. HyCoSy (hysterosalpingo contrast sonography) is done with ultrasound while contrast is passed into the uterus and observed to pass out the end of the tubes. HyCoSy will only be available in ultrasound facilities with a skilled and experienced operator. The best way to determine if this test is available in smaller centres is to ask your local fertility specialist or fertility clinic. If HyCoSy is not available, then a hysterosalpingogram is a better choice, done at hospital radiology departments and some private practices. Both tests require a catheter to be inserted through the cervix, which can be uncomfortable, and taking pain relief an hour before the procedure is usually recommended.

The male partner

Enquire about history of testicular surgery, sexually transmitted diseases, medications taken and illicit androgen use, which will depress spermatogenesis.

Semen analysis is mandatory, even if a female factor is present, and must be performed by an experienced laboratory. The sample should be examined within an hour of being produced, so if distance from home is an issue, encourage men to go to the collecting room at the laboratory. Instructions on collection and abstinence requirements are provided by the laboratory and it is important the patient knows these details. As an initial test, basic analysis and sperm antibodies is sufficient and may cost up to A\$110. If any of the parameters (sperm count, motility and morphology) are low, it is worth repeating the test. If the parameters remain low, particularly if there are additional female contributing factors, it may be worth testing for sperm DNA integrity (sperm chromatin structure assay [SCSA]). This is an expensive test (approximately A\$250) and one can manage couples well without it until invasive technologies are planned. If semen parameters are abnormal, it is indeed possible there may also be some reduced DNA integrity, but the advice remains the same: be a non-smoker; drink alcohol moderately or abstain completely; ejaculate regularly; include plenty of antioxidants in the diet; and consider antioxidant supplements for which there is some evidence of effectiveness. For a low sperm count and/or if erectile dysfunction is present, measure testosterone, luteinising hormone (LH) and follicle-stimulating hormone (FSH). Do a general medical check up for blood pressure, BMI, fasting lipids and blood suger level (BSL) (if not already known). Hypoandrogenism needs to be treated for general health and for fertility purposes will need specialist treatment, with possible testicular biopsy. A karyotype is advisable if a very low count is found

When to refer

The rule of thumb is to refer couples to a specialist after 12 months of trying to conceive, or six months if the woman is over 35 years of age. Having a good understanding of what might be influencing a couple's fertility means we can get a good amount of the groundwork established prior to a couple's first appointment with the fertility clinic.

If no abnormality is found and the couple are under 35 years of age, then depending on their desires and urgency to intervene, it is reasonable to advise them their chances of conceiving without treatment are good. If the woman is over 35 years and they have been trying for six months or longer, it is appropriate to initiate referral, while encouraging the couple to continue trying to conceive, as they too have a good chance of requiring no intervention to get pregnant. With any combination of factors present, or a past history of infertility, early referral is appropriate.

References

- 1. National Fertility Study 2006, Fertility Society of Australia. Access at: www.fertilitysociety.com.au (go to news menu).
- 2. Dunson D, Baird D, Colombo B. Increased infertility with age in men and women. *Obstetrics and Gynaecology*, January 2004; 103(1).
- 3. Dunson, et al. Impact of male age on chance of natural conception. Hum Reproduction 2002; 17:1399-4033.
- Homan G, Davies M, Norman R. The impact of lifestyle factors on reproductive performance in the general population and those undergoing infertility treatment: a review. *Human Reproduction Update* 2007; 13(3): 209-223.
- Yang Q, Wen S, Leader A, Chen X, Lipson J, Walker M. Paternal age and birth defects: how strong is the association? *Human Reproduction* 2007; 22(3): 696-701.
- Smoking and reproductive life. The British Medical Association. Access at: www.bma.org.uk/health_promotion_ethics/tobacco/ smokingreproductivelife.jsp.
- Wang Y, Chambers G, Dieng M, Sullivan E. Assisted reproductive technology in Australia and New Zealand 2007. 2009. AIHW.
- Al-Jefout M, Dezarnaulds G, Cooper M, Tokushige N, Luscombe G, Markham R, Fraser I. Diagnosis of endometriosis by detection of nerve fibres in an endometrial biopsy: a double blind study. *Hum Reprod. Advance Access* published online 18 August 2009.
- Glueck C, Wang P. Metformin before and during pregnancy and lactation in polycystic ovary syndrome. *Expert Opin Drug Saf.* 2007 Mar; 6(2):191-8.
- Palomba S, Falbo A, Zullo F, Orio F. Evidence-based and potential benefits of metformin in the polycystic ovary syndrome: a comprehensive review. *Endocr. Rev.* 2009; 30:1-50.
- Nawroth F, Ludwig M. What can we expect if we measure hormones in eumenorrhoeic infertile patients? *Reproductive BioMedicine Online* 2008; 16(5): 621-626.

Fertility-enhancing effects of Lipiodol and the IVF-LUBE Study

A multi-centre randomised trial



Dr Shelley Reilly FRANZCOG CREI Trainee



A/Prof Neil Johnson FRANZCOG CREI Medical Director Fertility Plus, Auckland

The oil-based contrast media Lipiodol, an iodised poppy seed oil, can be administered straightforwardly in a hysterosalpingogram. The FLUSH Trial¹ showed enhanced spontaneous pregnancy rates in couples with unexplained infertility and especially in women with mild endometriosis-related infertility following Lipiodol administration.

A related new study is currently underway, the IVF-LUBE Trial, aiming to determine whether these positive effects exist for those undergoing in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) in women with a diagnosis of either recurrent implantation failure or endometriosis.

Consistent with the FLUSH Trial findings, it has been long perceived that there is a possible therapeutic effect associated with diagnostic tubal patency testing. This is supported by Weir and Weir.² In 1951, they noted a possible increased pregnancy rate following hysterosalpingogram (HSG) with oil-based media. The first metaanalysis of tubal flushing³ suggested that oil-based contrast media has a greater fertility-enhancing effect than water-based media and that the effect is most pronounced in couples with unexplained infertility.

Current practice for tubal patency testing has moved away from the use of oil-based to water-based contrast media. The reasons for this include lower cost, finer imaging, lower viscosity, and reduced adverse effects such as intravasation, allergic reactions and lipogranuloma formation. However, with the advent of fluroscopic screening, oil-based media have become safe to use.

How Lipiodol works

Several theories exist on how Lipiodol is thought to enhance pregnancy rates, including flushing of non-occlusive but pregnancy-hindering debris from fallopian tubes³; positively influencing the intraperitoneal environment; improving either the environment in which eggs mature or the sperm-egg interaction^{4,5,6}; or by enhancing implantation through a direct effect on the endometrium.¹ Evidence does exist to support a uterine bathing effect of Lipiodol on the endometrium in a murine model⁷, where changes in uterine antigen-presenting dendritic cells may make the endometrium more receptive to implantation of an embryo.

The FLUSH Trial

The FLUSH Trial – Flushing with Lipiodol for Unexplained (and Endometriosis-related) Subfertility by Hysterosalpingography: a randomised trial ¹ randomised 158 couples to receive either Lipiodol tubal flushing by HSG with fluoroscopic screening or no intervention. Ninety-six of the couples had 'pure' unexplained infertility and 62 women had mild endometriosis in the context of otherwise unexplained infertility.

Follow-up occurred over the subsequent six months. Results revealed that in the purely unexplained infertility group, the pregnancy rates were 33.3 per cent for women who received Lipiodol and 20.8 per cent in the no intervention group. However, this result did not reach statistical significance, though when the data was meta-analysed with a very similar published trial⁸, the pooled results did show a significant beneficial effect from having Lipiodol (pregnancy RR 2.05, 95% Cl 1.07-3.93). At two years follow-up, a beneficial effect lasting longer than six months was found in this group.⁹

What was more interesting was that in the mild endometriosis group the pregnancy rate at six months was 48.0 per cent following Lipiodol compared to only 10.8 per cent in the no intervention group (pregnancy RR 4.44, 95% Cl 1.41-12.21, p=0.001), showing a highly significant beneficial effect of Lipiodol.

The FLUSH Trial has created speculation on its possible role in enhancing pregnancy rates in those undergoing an IVF or ICSI cycle. We have seen success rates for IVF/ICSI treatment continuing to improve, but we are aware that the point at which treatment fails is usually after embryo transfer. Previous studies examining treatments for IVF/ICSI implantation failure have failed to identify a solution. Any treatment shown to improve outcomes for women with recurrent implantation failure would be a key advance in IVF/ICSI fertility treatment, and Lipiodol, which may exert a positive effect in this situation, has not yet been examined in this context, leading onto the initiation of the IVF-LUBE Trial.

The IVF-LUBE Trial

This trial aims to examine the possible benefits of Lipiodol in relation to IVF/ICSI in two sub-populations in which Lipiodol would be expected to provide the most benefit in improving IVF/ICSI outcomes, that being women with recurrent implantation failure⁷ and women with endometriosis¹.

The trial is currently recruiting and randomising women. Eligibility to enter the study consists of a woman being scheduled to undergo an IVF/ICSI cycle with a diagnosis of either or both recurrent implantation failure, defined as having three consecutive previous embryo replacements of good quality embryos without a resultant pregnancy, or any stage of endometriosis which has been diagnosed laparoscopically. A woman must be aged 39 years or under, have infertility for a duration of 12 months or more, or an absolute cause for infertility and have both fallopian tubes confirmed as patent. Women participating in the study are randomised approximately four to five weeks before commencing their IVF/ICSI cycle to either having the cycle as well as Lipiodol or the cycle alone. The primary outcome measured will be live birth, with secondary outcomes recorded including biochemical/clinical/viable/ongoing/ectopic and multiple pregnancies, as well as miscarriage and any adverse events.

The study is an open parallel randomised controlled trial of multicentre design, with Auckland acting as the coordinating centre. The pilot study, which will randomise 84 women, is being undertaken as a CREI subspecialty training research project, and 27 women have been randomised so far from clinics around New Zealand. The interim results gained from this study will provide a useful foundation for the complete study that aims to recruit 350 women. To accelerate the recruitment process, overseas centres based in Australia, the United Kingdom and India have been approached to consider participating on a multi-centre basis.

If you would like further information on the the IVF-LUBE Trial, please contact me. I would appreciate further assistance both in terms of recruitment and funding opportunities.

Dr Shelley Reilly Principal Investigator

The IVF-LUBE Trial (e) sreilly@adhb.govt.nz

Dedication

I have recently given birth to twins. I take this opportunity to thank my obstetrician, Dr Tony Baird, my midwife Gail Stockwell, and the medical and midwifery staff working in the high dependency unit and on Ward 96 at Auckland City Hospital for their amazing care and support, especially through my 'rocky' initial postpartum period.

References

- Johnson NP, Farquhar CM, Hadden WE, Suckling J, Yu Y, Sadler L. The FLUSH Trial – Flushing with Lipiodol for Unexplained (and Endometriosis-related) Subfertility by Hysterosalpingography: a randomised trial. *Hum Reprod* 2004; in press.
- Weir WC, Weir DR. Therapeutic value of salpingograms in infertility. *Fertil Steril.* 1951; 2:514-522.
- Watson A, Vandekerckhove P, Lilford R, Vail A, Brosens I, Hughes E. A meta-analysis of the therapeutic role of oil soluble contrast media at hysterosalpingography: a surprising result? *Fertil Steril*. 1994; 61: 470-7.
- Johnson J, Montoya I, Olive D. Ethiodol oil contrast medium inhibits macrophage phagocytosis and adherence by altering membrane electronegativity and microviscosity. *Fertil Steril.* 1992; 58:511-7.
- Sawatari Y, Hori T, Hoshiai H. Oily contrast medium as a therapeutic agent for infertility because of mild endometriosis. *Fertil Steril.* 1993;59:907-11.
- Mikulska D, Kurzawa R, Rozewicka L. Morphology of in vitro sperm phagocytosis by rat peritoneal macrophages under influence of oily contrast medium (Lipiodol). *Acta Europaea Fertilitatis* 1994; 25:203-6.
- Johnson NP, Bhattu S, Wagner A, Blake DA, Chamley LW. Lipiodol alters murine uterine dendritic cell populations: a potential mechanism for the fertility enhancing effect of Lipiodol. *Fertil Steril.* 2005; 83:1814-21.
- Nugent D, Watson AJ, Killick SR, Balen AH, Rutherford AJ. A randomised controlled trial of tubal flushing with Lipiodol for unexplained infertility. *Fertil Steril.* 2002; 77:173-175.
- Johnson NP, Kwok R, Stewart AW, Saththianathan M, Hadden WE, Chamley LW. Lipiodol fertility enhancement: Two-year follow-up of a randomized trial suggesting a transient benefit in endometriosis, but a sustained benefit in unexplained infertility. *Hum Reprod.* 2007; 22:2857-2862.





Trainee Connect



Online Training Resources for RANZCOG Trainees

http://online.ranzcog.edu.au

Have you changed your address or email account recently?

Have you notified the College of these changes?

If not, please update your contact details via the RANZCOG website (www.ranzcog. edu.au) and follow the link to 'Update contact details' or call 03 9417 1699 to notify the College of your changed contact details.

Endometriosis and infertility

Same old, same old?



Dr Luk Rombauts FRANZCOG CREI

When attending endoscopic conferences you could be forgiven for thinking that little has changed in the management of endometriosis: 'When you see it, you treat it – surgically.'

While that advice may be reasonable enough when dealing with severe disease causing debilitating pain, things are a little more complicated for endometriosis-related infertility.

The link between infertility and endometriosis

First of all, the link between infertility and endometriosis has not always been accepted as naturally evident. Nobody guestions that connection in severe

cases where the tubo-ovarian anatomy is critically altered through adhesion formation and fibrosis. But even in the recent past, some considered the presence of minimal and mild endometriosis inconsequential. The prevalence of endometriosis is increased in subfertile women (estimates vary between 30 to 50 per cent), but it was argued that this is mostly an epiphenomenon. Endometriosis happens to be more common in women with infertility, but one doesn't cause the other.

However, those views are slowly changing. There is increasing evidence for a causal link. To begin with, genomic and proteomic studies have clearly shown that the uterine epithelium in women with endometriosis is functionally different from that in women without endometriosis.^{1,2,3}

From observational studies in women with minimal or mild endometriosis we know the monthly fecundity rate (MFR) is reduced following intrauterine insemination (IUI), both with autologous or donor sperm.⁴ A meta-analysis⁵ showed that pregnancy outcomes in IVF also worsen with the severity of the disease.

Perhaps the most convincing evidence supporting a causative link comes from a study in baboons confirming that the MFR in baboons with experimentally induced mild to severe endometriosis is reduced, compared with those with no or minimal endometriosis.⁶

Pain and infertility

The question then obviously arises how to treat the disease to improve a patient's fertility. Ideally, such decisions should be informed by high quality evidence. Despite the difficulties undertaking such trials, it is pleasing to see there is a steadily growing body of such evidence, guiding us with the surgical treatment of endometriosis for both pelvic pain and infertility.

Patients with severe pain deserve the best surgery they have access to. Randomised controlled trials (RCTs) have clearly shown that endoscopic surgery for endometriosis is effective in reducing pain levels⁷, even though the recurrence rates are higher than we would like, estimated at 20 per cent after two years and 40 to 50 per cent after five years.⁸ In patients with co-existing infertility, such surgery obviously needs to be conservative.

Although surgery is justifiable for pain reduction, it is unclear to what extent the surgery also restores normal fertility. No RCTs have been done in infertile women with moderate to severe disease. The only evidence which is available is retrospective and thus potentially biased in favour of surgery, but it suggests that the cumulative pregnancy rate (CPR) in this patient group is increased by ten per cent to 25 per cent following surgery.⁹ Until better studies are performed, the case for surgery in patients with severe disease but no significant pain (they do exist!) is not overwhelmingly convincing. It is for the surgeon to carefully assess whether laparoscopic procedures in such patients will result in a positive benefit/risk ratio.

Treating women with minimal or mild disease

RCTs don't always provide the full answer to our clinical questions. An example may illustrate the point. Does laparoscopic treatment of mild or minimal endometriosis improve a patient's fertility? A meta-analysis is available to answer that question.¹⁰ It summarises the results of two RCTs, one showing no effect and the other larger one showing a favourable effect. When live birth rate and ongoing pregnancy after 20 weeks were combined, the odds ratio (OR) was 1.64 (95% confidence interval [CI] 1.05 to 2.57) in favour of laparoscopic surgery compared to a diagnostic laparoscopy.

Albeit statistically significant, this effect is relatively small. You need to dig a little deeper to find out that the number needed to treat is 12, which means that one extra live birth is achieved for every 12 women undergoing surgery for minimal or mild endometriosis. And it gets worse: if we assume a 25 per cent prevalence rate of minimal or mild endometriosis, almost 50 laparoscopies need to be performed to find those 12 women. Whether these statistics make it a worthwhile intervention depends on other factors. There may be additional reasons to perform the laparoscopy, such as the need for a tubal patency check or the co-existence of significant pain symptoms. The financial cost to the patient and the community needs to be taken into consideration too, as well as the risk of the intervention.

'A good surgeon knows how to operate. A better surgeon knows when to operate. The best surgeon knows when not to operate.'

The search for a non-invasive diagnostic test

Part of the problem with the ongoing debate is that it is flawed with circular reasoning: if a woman suspected of having endometriosis doesn't have a laparoscopy, we won't know whether she needs one. This explains the feverish search for a non-invasive diagnostic test pursued by many teams, including some in Australia. Our own approach has been to look for a characteristic proteomic 'fingerprint' in the endometrium³, others are investigating siRNAs¹¹ and nerve fibers¹². Although it is unlikely that any such test will be perfect, it may improve patient selection and ultimately reduce the number of unnecessary laparoscopies. Conversely, Somialiana and colleagues¹³ have raised concerns that the number of unnecessary interventions might actually increase should the test be used as a screening tool. In their highly recommended paper, the authors warn of the real risk of 'disease mongering', a process that turns healthy people into patients, adds iatrogenic harm and wastes precious resources.

Used as a screening tool, the test would 'diagnose' endometriosis in a large number of asymptomatic women. It is uncertain to what extent the presence of non-symptomatic endometriosis presents a significant health concern. It is also important to draw attention here to the observation from two randomised placebo-controlled studies that endometrial deposits spontaneously disappear in up to a third of patients.^{14,15}

To laparoscope or not to laparoscope?

As yet, such a non-invasive diagnostic test does not exist and the question therefore remains: to laparoscope or not to laparoscope? That choice will eventually be influenced by the potential downstream need for in vitro fertilisation (IVF) treatment. On the one hand, Barnhart's meta-analysis of 22 observational studies⁵ demonstrated that the chance of achieving pregnancy with IVF is lower in endometriosis patients (OR 0.56; 95% CI, 0.44–0.70). Furthermore, pregnancy rates for women with severe disease are much lower than for women with mild endometriosis (OR 0.60, 95% CI 0.42–0.87).

So, at first glance this provides a strong argument in favour of surgery even when IVF is contemplated. Unfortunately, we desperately need evidence to show that ablation/excision of endometriosis prior to IVF actually restores pregnancy rates to those of women without endometriosis. Without such evidence, it can be argued that a laparoscopy only delays and drains money away from IVF treatment without a proven benefit. This would be particularly true for example in older women and couples where there is a serious male factor problem. On the other hand, a laparoscopy is justified when pain symptoms are present. Another indication is when a young, subfertile woman presents with a normal transvaginal ultrasound and her partner's semen analysis is normal. If minimal or mild endometriosis is diagnosed and adequately treated and both tubes are patent, level one evidence suggests her chances of conceiving naturally will be increased by 60 per cent.¹⁰

What about endometriomata?

This leaves the controversy around the treatment of endometriomata. The arguments in favour of early surgical treatment have been listed as the risk of spontaneous rupture, the impact on normal ovarian function, the high probability of other, often deeply infiltrating disease, the risk of abscess formation when inadvertently punctured during IVF, and the potential risk of malignant transformation. The latter is of particular concern, but the risk of ovarian cancer should be put in perspective. There is one extra ovarian cancer for every 10,000 women with endometriosis and this woman is likely to be close to menopause, with a large endometrioma in excess of 9 cm diameter.¹⁶ Vercellini puts it like this: '...in the worst scenario, the lifetime probability of developing ovarian cancer increases from 1/100 to 2/100. In other words, a woman with untreated endometriosis has a 98 per cent probability, instead of 99 per cent, of not developing an ovarian malignancy'.¹⁷

Excision of the cyst wall has proven to be superior to ablation of the endometriosis on the cyst wall. RCTs in women with an endometrioma larger than 3 cm have shown that laparoscopic excision was more successful in reducing all types of endometriosisrelated pain.¹⁸ The recurrence rate was also lower (OR 0.41; 95% Cl 0.18–0.93) and, more importantly, the subsequent spontaneous pregnancy rate was five-fold higher (OR 5.21; 95% Cl 2.04– 13.29). What remains unclear though is whether excision is actually better than no intervention at all. Indeed, a meta-analysis of five non-randomised studies concluded that surgical management of endometriomas has no significant effect on ovarian response to stimulation and IVF pregnancy rates compared with no surgery.¹⁹

Ovarian surgery also has an inherent risk. Benaglia and colleagues followed 93 women undergoing IVF following excision of a unilateral endometrioma.²⁰ Complete absence of follicular growth was observed in 12 operated ovaries while this event never occurred in the contralateral gonad (P<0.001). The frequency of severe ovarian damage following surgery was thus 13 per cent.

Conclusion

It is great to see that new, high quality evidence is emerging. Some questions can now be answered, but hopefully this short review has also planted some fertile seeds of doubt. Don't get me wrong, I like my surgery, but it is vital to always re-examine why we are operating.

'A good surgeon knows how to operate. A better surgeon knows when to operate. The best surgeon knows when not to operate.'

References

- Chand AL, Murray AS, Jones RL, Hannan NJ, Salamonsen LA, Rombauts L. Laser capture microdissection and cDNA array analysis of endometrium identify CCL16 and CCL21 as epithelial-derived inflammatory mediators associated with endometriosis. *Reproductive Biology and Endocrinology* 2007; 5:18.
- Kao LC, Germeyer A, Tulac S, Lobo S, Yang JP, Taylor RN, Osteen K, Lessey BA, Giudice LC. Expression profiling of endometrium from women with endometriosis reveals candidate genes for disease-based implantation failure and infertility. *Endocrinology* 2003;144:2870-81.
- Stephens A, Hannan N, Rainczuk, A, Meehan K, Chen J, Nicholls P, Rombauts L, Stanton P, Robertson D. Post-translational modifications and protein-specific isoforms in endometriosis revealed by 2D DIGE. J Proteome Res. 2010; 9:2438-49.
- D'Hooghe TM, Debrock S, Hill JA, Meuleman C. Endometriosis and subfertility: is the relationship resolved? *Semin Reprod Med.* 2003; 21:243-54.
- 5. Barnhart K, Dunsmoor-Su R, Coutifaris C. Effect of endometriosis on in vitro fertilization. *Fertil Steril.* 2002; 77:1148–55.
- D'Hooghe TM, Bambra CS, Raeymaekers BM, Riday AM, Suleman MA, Koninckx PR. The cycle pregnancy rate is normal in baboons with stage I endometriosis but decreased in primates with stage II and stage III-IV disease. *Fertil Steril*. 1996; 66:809-13.
- Jacobson TZ, Duffy JM, Barlow D, Koninckx PR, Garry R. Laparoscopic surgery for pelvic pain associated with endometriosis. *Cochrane Database Syst Rev.* 2009 Oct 7;(4):CD001300.
- 8. Guo SW. Recurrence of endometriosis and its control. *Hum Reprod Update* 2009; 15:441-61.
- Vercellini P, Somigliana E, Viganò P, Abbiati A, Barbara G, Crosignani PG. Surgery for endometriosis-associated infertility: a pragmatic approach. *Hum Reprod.* 2009; 24:254-69.
- Jacobson TZ, Duffy JM, Barlow D, Farquhar C, Koninckx PR, Olive D. Laparoscopic surgery for subfertility associated with endometriosis. *Cochrane Database Syst Rev.* 2010 Jan 20;(1):CD001398.

References continued on page 42.

Lifestyle, periconception and fertility problems in men and women



Dr Anne Clark FRANZCOG CREI Medical Director Fertility First, Sydney

The incidence of infertility in Australia, one in six couples, has remained the same over the last three generations and affects first and subsequent pregnancies equally.

However, societal changes, particularly later marriage and increased divorce, have impacted significantly on couples so that they might not be in a position to have children until the time their fertility has already started to decline. This decline becomes most significant for both men and women from their mid 30s onwards.

Despite enormous advances in the management of fertility problems, such as in vitro fertilisation (IVF), lifestyle factors have been virtually ignored

as a preservation and/or treatment option to improve the chance of conception. Lifestyle factors are not only important to boost conception, but also to maximise a healthy periconceptional period and therefore a healthy ongoing pregnancy. Dose-dependent exposures of adverse lifestyle factors during this window can result in permanent, adverse, irreversible effects, which can continue into subsequent generations.

'Improvements in lifestyle and nutritional risk factors not only enhance the long-term health of prospective parents, but are important aspects of maximising fertility and pregnancy outcome.'

Much is now known about the negative impact of lifestyle issues on a couple's fertility, in particular increased weight, smoking, excessive caffeine and alcohol intake, but unfortunately, that information has not been well conveyed to couples. For example, although cigarette smoking now accounts for 13 per cent of all fertility problems (less than tubal disease, which only makes up ten per cent), when surveyed, only one in five women knew it impacted on fertility. Even less women realised that smoking brought menopause forward by one to four years, decreasing further the time in which a woman has to conceive, particularly if she is already in her 30s. Most men are unaware that their smoking around the time of conception increases by four times the risk of the child developing a cancer in childhood.

Men rarely get half the attention when it comes to fertility assessment, even though we know sperm contribute an equal amount of genetic material to a pregnancy and the placenta is largely dependent on expression of genes from the paternal chromosome. Fifty per cent of men with normal sperm counts and 70 per cent of men with abnormal sperm counts who present with fertility problems have been shown to have increased levels of sperm DNA damage. This damage reduces the chance of pregnancy, increases the miscarriage rate three to four times and can lead to genetic problems in the offspring (see Table 1). Much of this damage is due to an accumulation of lifestyle effects. Inadequate nutrition, increased weight, smoking, substance abuse and excessive coffee and alcohol intake are all lifestyle factors that increase oxidative stress, the principal cause of sperm DNA damage. Raised plasma homocysteine levels are also strongly associated with decreased fertility and poorer embryo quality. Both can be readily corrected in up to 70 per cent of affected men within two to three months with the appropriate lifestyle changes and antioxidant/ nutritional supplements. This should be the first line of treatment before any other fertility program is embarked upon, otherwise chance of success will be significantly compromised.

It appears that much of what was thought to be a reduction in a woman's fertility over time is actually a reflection of changes for both partners. The likelihood of conception for spontaneous pregnancies and IVF is halved for women 38 to 40 years of age if their partner is 40 years or older, the likelihood of miscarriage is doubled and there is an increased incidence of congenital anomalies and genetic disorders. Once both partners are aged 40, for example, half the risk of having a child with Down's syndrome is related to the male partner alone. These poor outcomes associated with increased paternal age are once again associated with increasing sperm DNA damage as a result of increased oxidative stress, as above, and should be treated the same way.

At Fertility First, it is now routine practice for both partners to be screened for nutritional deficiencies and all men have an assessment of sperm DNA fragmentation as part of their initial assessment. Fifty-nine percent of men (n = 3264) and 62 per cent of women (n = 3986) were found to have a deficiency of folate, iodine and/or vitamin D. Fifty-three percent of men with normal sperm counts and 70 per cent of men with abnormal sperm counts had abnormal levels of sperm DNA damage. Table 1 shows the impact of these issues on fertility, fertility outcomes and the child's long-term health.

However, apart from studies looking at cigarette smoking, alcohol and caffeine consumption and extremes of body mass index, there is very little data available on the impact of changes in lifestyle on fertility and fertility outcomes.

Fertility First's experience is that correcting these deficiencies and/ or making the required lifestyle changes, though it seems a very low key approach to a significant problem, for up to 30 per cent of couples it is the only treatment required for a spontaneous healthy ongoing pregnancy to occur. Indirect evidence of the positive effect of this approach on neonatal outcomes can be seen in outcome data for twins over the past five years. Table 2 shows the difference in birth weight and gestational age at birth for twins conceived at Fertility First, compared to the national data for all patients attending Australian and New Zealand fertility units. As periconceptional health measures have increased, there has been a corresponding significant improvement in both measures of neonatal wellbeing, compared to Fertility First's initial 2003 statistics and to the national figures, which have shown no change over the five-year period.

There are some additional points that are important for selected patients. Firstly, women with polycystic ovarian syndrome (PCOS), who are already predisposed to higher serum homocysteine levels, should take additional B-group vitamins as well as folic acid when started on metformin therapy. After three months of metformin, there is a 27 per cent rise in homocysteine levels, but these are only decreased by eight per cent if folic acid supplementation alone is used.

Table 1. Impact of nutritional deficiencies and sperm DNA damage on fertility and pregnancy outcomes.

Women				Men
	lodine deficiencyª	Vitamin D deficiency ^ь	Raised homocysteine levels ^c	Increased sperm DNA damage ^d
% of new Fertility First patients affected	57%	30%	19%	53%
Causes infertility	Yes	Yes	Yes	Yes
Causes long- term adverse health outcomes for children	Yes – irreversible reduction in IQ of up to 10 points, linked to autism.	Yes – increased risk of multiple sclerosis and schizophrenia as an adult, rickets.	Yes – increased risk of congenital malformations and asthma.	Yes – increased risk of congenital malformations, Down's syndrome, childhood cancers, autism, schizophrenia.
Increases miscarriage rate	Yes	Yes	Yes	Yes
Increases pregnancy complications	Yes	Yes	Yes	Not studied to date
Pregnancy- induced hypertension	Yes	Yes	Yes	Not studied to date
Placental abruption	-	-	Yes	Not studied to date
Intra-uterine growth retardation	_	Yes	Yes	Not studied to date
Prematurity	_	Yes	Yes	Not studied to date
Low birth weight	Yes	Yes	Yes	Not studied to date
Still birth	Yes	_	Yes	Not studied to date

a. (Allen, et al, 2006)

c. (Vollset, *et al*, 2000) d. (Simon, *et al*, 2010) Secondly, women using 'over-the-counter' pain relief should be warned to avoid the prostaglandin synthetase inhibitors, such as aspirin, Indocid and Nurophen, mid-cycle as they can inhibit the egg's release from the follicle at ovulation by 50 to 100 per cent, depending on which drug is taken.

Thirdly, couples trying to conceive should be warned not to abstain until the day of ovulation. The longer the sperm sit in the testicular ducts and epididymis, the longer the exposure to oxidative stress and as a result the greater the increase in sperm DNA damage. Intercourse several days before the expected day of ovulation and on the day or day before is ideal. Normal sperm maintain their potency in a woman's reproductive tract for up to three days, so daily intercourse is not necessary and reduces the likelihood of the couple's physical relationship becoming one of just 'making babies' as opposed to making love.

To conclude, improvements in lifestyle and nutritional risk factors not only enhance the long-term health of prospective parents, but are important aspects of maximising fertility and pregnancy outcome. They are practical, cost-effective, readily amenable curative and/or preventive measures and therefore should be the first line of treatment for any fertility problems.

Fertility and reduction in fertility with increasing age is a couple issue, not just a woman's issue, so good reproductive outcomes require an equal focus on both partners. 'It takes two to tango.'

Infertility is a World Health Organization classified disease, it is not a choice. It is the source of much pain, not just for the couples involved but also their families. They need our support and compassion throughout the treatment process, whatever it may be.

References

- Dun JT and Delange F. Damaged reproduction: The most important consequence of iodine deficiency. J Clin Endocrinol Metab. 2001; 86, 2360-3.
- Simon L, Brunborg G, Stevenson M, Lutton D, McManus J, Lewis SEM. Clinical significance of sperm DNA damage in assisted reproduction outcome. *Human Reproduction* May 2010; Vol 25 No.7 pp.1594-1608.
- Vollset SE, Refsum H, Irgens L, Emblem B, Tverdal A, Giessing H, Monsen A, Ueland PM. Plasma total homocysteine, pregnancy complications and adverse pregnancy outcomes: the Hordaland Homocysteine Study. *American Journal of Clinical Nutrition* April 2000; Vol 71, pp. 962-68.
- 4. WHO (2004) *lodine Status Worldwide*. WHO Press Geneva.

Table 2. Twin birth weight and gestational age comparisons: Fertility First and Australian/ New Zealand ART patients.

	ANZARD ART Patients*		Fertility First Patients	
	2003	2007	2003	2008
Average birth weight (grams)	2363	2370 ²	2447 ¹	28671,2
Average gestational age (weeks)	35.0	34.91	35.1 ³	37.4 ^{1,3}

*ANZARD Data Published 2005-2009 (www.preru.unsw.edu.au)

2. p < 0.02

3. p < 0.05

An overview of surrogacy in Australia



Surrogacy is a process whereby one woman (the surrogate) carries a pregnancy for another person or couple (the commissioning or intended parent/s). Surrogacy may allow those who are otherwise unable to conceive or carry a child to realise their desire to become parents.

Although surrogacy is well-known as one of the main issues of discussion in reproductive bioethics, there is nothing inherently 'advanced' about the concept itself. There are multiple references to its practice in the Bible's *Book of Genesis* and there is documented evidence it was widely used in ancient civilisations as a remedy for childlessness. Traditional cultures also embrace it for this purpose.

Different types of surrogacy are recognised.

Traditional surrogacy

Dr Bronwyn Devine

FRANZCOG

This involves the surrogate conceiving a pregnancy through insemination (either by sexual intercourse or assisted methods) with sperm from the commissioning male. Throughout history and across the world today, this is the most common form of surrogacy practised.

Gestational surrogacy

This involves the surrogate acting as a 'gestational carrier'. Embryos are created with in vitro fertilisation (IVF) techniques from the sperm and oocytes of the commissioning parents, then transferred to the uterus of the surrogate in the hope that pregnancy will be achieved. This, in its strictest form, is the only type of surrogacy practised in Australia at the present time. In other words, it has not been possible in Australia to date to facilitate a surrogacy arrangement where gametes from a third party donor or from the surrogate herself are utilised in the creation of embryos.

In the United States and India, where surrogacy is largely a commercial enterprise, the surrogate is usually compensated for her services. It is not unusual for companies to suggest to prospective commissioning clients that their costs will be in the order of US\$30,000 to \$100,000, including a sizable payment to the surrogate, who may or may not be known to the intended parent/s. Surrogacy clinics overseas are also allowed to procure surrogates for their clients, a practice that is illegal in the Territory of ACT. In all Australian jurisdictions it is illegal for a surrogate to receive compensation. Before any proposed arrangement receives preliminary approval, it must be clearly evident that the surrogate has a purely altruistic reason for agreeing to carry a child for someone else. The commissioning parents may cover 'reasonable costs' (for example, medications, obstetric care, investigations and travel), but there must be no outright payment for the 'service' itself.

The first Australian case of a successful surrogacy arrangement occurred in 1986 under the care of Professor John Leeton at

Monash IVF. Unfortunately, following this case, the Victorian Government quickly legislated to prohibit surrogacy in all its forms. This legislation was later modified. In keeping with the policy that only those suffering infertility could access fertility services in Victoria, however, it was stipulated that surrogacy could proceed only if the surrogate herself was infertile. Success rates must have been very poor indeed!

Around this time, other State governments also moved to make surrogacy a criminal offence, until New South Wales and the ACT alone were without legislation of any kind. In 1994, however, the ACT Government set forth plans not only to illegalise surrogacy, but also to make discussion with a patient of the processes involved, grounds for a professional misconduct charge against the doctor responsible. The medical director at Canberra Fertility Centre, Dr Martyn Stafford-Bell, and others campaigned vigorously against this proposed legislation. When the bill came eventually to be tabled in the Legislative Assembly, the opposition and minor parties were able to move an amendment prohibiting commercial surrogacy, but allowing altruistic surrogacy within the ACT. This was documented in the *Substitute Parents Agreements Act 1994*.

With non-commercial surrogacy now excluded from prohibition within the ACT, a decision was made by Canberra Fertility Centre to assess the feasibility of starting a surrogacy program at the unit. After much consideration, a set of selection guidelines was established and policies set in place for mandatory psychological testing, legal advice and counselling to be sought by all parties involved. In 1995, the surrogacy program at Canberra Fertility Centre was established and has since treated patients from all states of Australia. Approximately 12 new 'cases' are seen each year, though a greater number of requests are received annually by the unit. Many requests are unable to be accommodated due to strict inclusion criteria.

Absence of a functional uterus is the commonest reason for seeking to enter the surrogacy program. Mullerian agenesis (or occasionally dysgenesis) is the most frequent indication, but previous hysterectomy (most often for carcinoma of the cervix, with preservation and transposition of the ovaries, or peripartum following massive haemorrhage) is the second most common cause. Other indications include medical conditions in the commissioning female partner that contraindicate pregnancy (but not standard IVF stimulation regimens) and cases of recurrent implantation failure and recurrent miscarriage.

At Canberra Fertility Centre, it is essential that the commissioning parents be either married or in a de facto relationship. Together, they must be able to provide suitable gametes for the creation of embryos. The commissioning female partner must be aged 40 years or less and the intended parents should have a reasonable expectation of a normal lifespan, at least until any child born as a result of the surrogacy arrangement should reach legal majority. The surrogate must have proven fertility and at least one child, although it is not necessary that she have completed her family. She should give a history of uncomplicated pregnancies, labours and births. Ideally, the surrogate is a family member or close friend who approaches the couple in the first instance with a genuine offer of help. Rigorous psychometric testing by an independent practitioner is undertaken by all members of the group (the intended parents, the surrogate and her partner) prior to their first appointment at the unit. They must seek full legal advice regarding surrogacy and the surrogate must be assessed, by an obstetrician and gynaecologist, as being fit for pregnancy. Written documentation of all such assessments must accompany the commissioning couple's letter of referral. The four (or three if the surrogate is a single woman) then meet with the treating fertility specialist and clinical psychologist over two consecutive days at the Canberra Fertility Centre. If all criteria are satisfied, the unit will submit an application for independent ethics committee approval. This may take several months to be processed, but there is a mandatory three-month cooling off period for the group effective from the day of first meeting with the treating specialist.

As with all assisted reproductive technologies, results are predominantly influenced by age of the oocyte. In general, young women with congenital absence of the uterus and those with suspected implantation failure or recurrent miscarriage of unknown aetiology do well with surrogacy. Results for women with medical conditions precluding pregnancy are also reassuring provided oocyte quality is reasonable. Commissioning women with a history of radical hysterectomy and ovarian transposition do less well presumably because of subtle vascular damage to the ovaries.

'Ultimately, it will be for individual units and their ethics committees to assess risks and decide what services they are going to offer.'

Throughout the world and even within Australia, jurisdictions differ with respect to the status of children born as a result of IVF procedures where 'donated reproductive tissues' are used. This is an important consideration and those undergoing surrogacy must be fully informed of the legal implications of their treatment. In all Australian jurisdictions, it is provided that '...when a woman gives birth to a child...the birth mother is presumed to be the legal mother of that child...' (Artificial Conception Ordinance 1985). This means that the intended parents in a surrogacy arrangement must apply to adopt their own genetic offspring. As well, for a number of years in the ACT, commissioning parents were unable to have their names listed on their child's birth certificate. Despite numerous attempts by clinicians and patients to have the Ordinance modified, the ACT Government remained steadfast. Eventually, one Canberra couple took their claim to be recognised as their son's parents to the Supreme Court. With the legislation in place, the judge was unable to grant their request, but was scathing of a government that had engineered a bill to allow surrogacy and then refused to move forward to acknowledge children produced by such a process. There was a frenzy of local media coverage and within a short period of time, the Ordinance duly modified. This resulted in the Parentage Act (ACT) 2004. The Act continues to provide that the woman giving birth is the child's mother and her legal partner the child's other parent, regardless of the genetic status of that child. It allows, however, for couples to apply to the court between six weeks and 12 months after the birth of a child, to have their names listed

as the parents on that child's birth certificate. Other States differ slightly in their legal handling of these issues.

Until recent years, there has been marked variance between the States with respect to surrogacy law. Decriminalisation of noncommercial surrogacy in Western Australia (2008), South Australia (2009) and Queensland (2010) has meant that enabling legislation now exists in all of these States, as well as in Victoria, Tasmania and the ACT. In New South Wales, there is no specific legislation, but in 1998 the *New South Wales Law Reform Commission Report* recommended that: '...commercial surrogacy be prohibited by law and non-commercial surrogacy not be encouraged'. The report also suggested invalidation of 'surrogacy contracts' and sanctions against those involved in 'soliciting, servicing, payment or promotion of such contracts'.

Throughout Australia, the legislation is now relatively uniform. While altruistic surrogacy in general is allowed, the restrictions governing this practice vary across jurisdictions. Traditional surrogacy is permissible in some, for example. As well, the use of 'third party' sperm and/or oocyte donors is likely to become accepted practice within a surrogacy arrangement. This will allow both women and men in same sex relationships, commissioning females with ovarian failure or males with azospermia, and individuals with androgen insensitivity syndrome (AIS) to access surrogacy services within Australia. Those who oppose such moves express concern about increased rates of 'refusal to relinquish' when the surrogate is both the genetic mother and the gestational mother, and the complexity of 'too many parents' in the mix when third (and fourth) parties are involved.

Ultimately, it will be for individual units and their ethics committees to assess risks and decide what services they are going to offer. Commercial surrogacy, however, is prohibited.

The recent legislative changes which have made the practice of surrogacy accessible to patients throughout Australia, are most encouraging. There is now a committee of Federal and State Attorneys-General attempting to produce uniform laws across all Australian States and Territories. When this is achieved, all surrogacy patients should be able to be treated in their home State. Patients, who for the past 15 years have travelled across the country to have access to surrogacy within the ACT, assure us this will be a major coup for those facing a barrage of physical and emotional stressors in the hope of achieving a successful pregnancy through surrogacy.

References

- 1. Appleton T. Surrogacy. Curr Obstet Gynecol. 2001, II: 256-7.
- Phillips S. Someone Else's Child: A Surrogate's Story. 2010. University of Queensland Press.
- 3. Report 58 (1988). Artificial Conception/In Vitro Fertilization. Law Reform Commission of NSW: published 2002 on lawlink.nsw.gov.au .
- 4. Statutes Amendment (Surrogacy) Amendment Act (2010). South Australian Government, Adelaide 2010.
- 5. *Parentage Act 2004*. Australian Capital Territory Government, Canberra 2010 (Republication).
- 6. Surrogacy Act 2010. Queensland Government, Brisbane 2010.
- 7. Surrogacy Contracts Act 1993. Tasmanian Government, Hobart 1993.
- 8. *Artificial Conception Ordinance 1985*. Australian Captial Territory Government.
- 9. Baslington H. The social organization of surrogacy: relinquishing a baby and the role of payment in the psychological detachment process. *J Health Psychol.* 2002, 57-71.

structural anomalies

Congenital malformations of the female genital tract represent a group made up of a wide range of deviations from the normal anatomy.

Their true prevalence in the general population is still debated, with older studies suggesting a mean prevalence of four per cent, while newer studies including more accurate diagnostic methods indicate a mean prevalence of closer to seven per cent.

Uterine and related

These anomalies may present in many broad fashions with the features of obstruction to menstrual flow, inability to establish sexual intercourse or reproductive failure.

These malformations arise from abnormal embryological development of one or both of the Mullerian (paramesonephric) ducts. The most well-recognised condition is the failure of the ducts to form, as in Mayer-Rokitansky-Kuster-Hauser syndrome, but there are many variations even in this condition with partial formation of the structures.

Much debate exists surrounding the classification of these malformations and we do not have, as yet, a user-friendly system that allows us to classify these entities and allow most appropriate treatment and discussion of the prognosis for these patients, particularly in terms of future fertility and reproductive outcomes. Most clinicians agree that any such system should be simple and functional, must be based in anatomy, ideally be given in one page, and allow for complete classification with the frequency of the anomalies being taken into consideration.

Case study

The following case illustrates the difficulties that can arise for diagnosis, management and future outcomes for the young patient presenting with a congenital malformation.

A 15-year-old girl with menarche at 13 years of age and regular cycles presented with acute lower abdominal pain. Ultrasound revealed a large pelvic mass (6 cm), thought to be a left endometrioma. Emergency laparoscopy revealed an inflammatory mass on the left side of the pelvis with the left ovary adherent to it. Filmy adhesions and intraperitoneal blood were also present. No definitive management was possible at this procedure and she was referred on to a tertiary centre. Further studies (MRI) (see Figure 1) revealed a non-communicating left uterine horn distended with blood. There was also evidence of a left haematosalpinx and a normal left ovary adherent to both structures. It was known from birth that her left kidney was absent.

She was placed on a continuous oral contraceptive pill (OCP) for two months and then definitive surgery was planned as a combined multidisciplinary procedure. Left hemi-hysterectomy and left salpingectomy using a laparoscopic approach was performed, with careful dissection and preservation of the left ovary. The cervix was clearly absent on this side and a normal right unicornuate uterus and associated structures were identified at the time of surgery. Assessment of the renal tract and vagina was also undertaken at the time of surgery. This showed a normal right renal system, left renal agenesis and the vagina exhibited normal dimensions.

The patient has recovered well. She has been counselled regarding possible future reproductive outcomes and close obstetric surveillance has been advised.

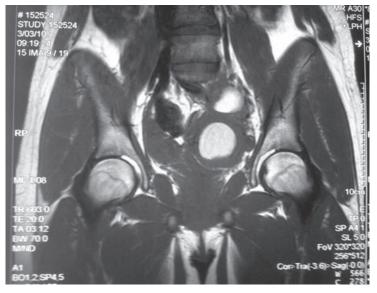
Classification of malformations

In 1988, the American Fertility Society (AFS) devised the most commonly used diagnostic classification (see Figure 2) based on the work of Buttram and Gibbons (1979). However, many anomalies are not included in the main categories, such as those disorders resulting from cervical or vaginal aplasia/dysplasia, making it incomplete and it is very difficult to categorise complex anomalies. Although other classifications have been proposed, including clinical and embryological classifications and the extensive VCUAM system (vagina, cervix, uterus, adnexae and associated malformations), these are not thought to be user-friendly and so the AFS system is still the most popular, as it is based in anatomy and seems to best correlate with pregnancy outcome.

Diagnosis and prevalence

The method used to investigate anomalies will impact on the frequency and accuracy with which the diagnosis is made. Saravelos and colleagues² assessed the prevalence of disorders in different population groups based on their assessment of the diagnostic procedure used. They classified the diagnostic method according to diagnostic accuracy as follows.

Figure 1. Case study MRI showing obstructed uterine horn and cervical agenesis.



Dr Kim Matthews

FRANZCOG CREI

Dr Peter Benny

FRANZCOG CREI

Medical Director

Next Generation

Fertility, NSW

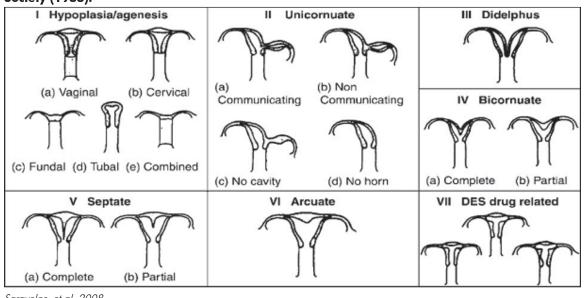


Figure 2. Classification of congenital uterine anomalies as described by the American Fertility Society (1988).

Saravelos, et al, 2008.

- **Class 1a.** Investigations capable of accurately identifying anomaly (greater than 90 per cent accuracy) and classifying into the appropriate subgroup.
 - Hysteroscopy with laparoscopy, sonohysterogram, 3D ultrasound.
- Class 1b. Investigations capable of identifying anomaly (greater than 90 per cent accuracy) but unable to classify into appropriate subtype.
 Hysteroscopy alone.
- **Class 2.** Investigations capable of identifying uterine anomalies with accuracy less than 90 per cent.
 - Hysterosalpingogram, 2D ultrasound.
- **Class 3.** Investigations in which accuracy has not been assessed MRI.

When they assessed studies of prevalence using this classification, they found a prevalence rate in the general fertile population of 6.7 per cent if more accurate investigations were utilised compared with 2.4 per cent with Class 2 accurate methods (see Table 1).

Table 1. Prevalence of uterine anomalies in the general fertile population.

Investigation	Studies	Cases n	Total n (%)
Class Ia	4	4521	305 (6.7)
Class Ib	1	323	20 (6.2)
Class 2	6	4846	116 (2.4)
Total	11	9690	441 (4.6)

It should be noted that these studies were done in later reproductive life, so most females presenting with menstrual obstruction in adolescence or inability to have coitus are not included. Most investigations of uterine anomalies are performed in women presenting with subfertility or recurrent miscarriage. It is the author's experience that MRI is an extremely useful diagnostic tool in the workup of the adolescent with an obstructive anomaly when planning definitive surgical management. The relative prevalence in these groups when compared with the general population (using Class 1a investigations) is shown in Table 2a and 2b. This data would suggest there is an increased prevalence of anomalies in recurrent miscarriage, but not the infertile population suggesting a cause and effect in miscarriage alone. This may not be the entire truth as there is variation in the distribution of subtypes in women within different population groups.

Table 2a and 2b would suggest that hypoplastic uteri and septate uteri are more likely to be associated with infertility when Class 1a investigations are used.

Treatment

Obviously, this will depend on the presentation and stage of reproductive life the young woman is at.

For obstruction, the aim is to relieve the obstruction. This can range from a very simple release of a low vaginal septum to extremely complex surgery. The most important part is ensuring the right procedure is planned and adequate diagnosis and workup is essential. The use of continuous OCP can facilitate this and allow appropriate referral if required. It is fair to say that no two procedures are ever the same in this setting and basic sound anatomical approaches are required. The use of a combined approach with laparoscopic and vaginal operators working together is often beneficial for the best outcome.

If vaginal stenosis at any level is an issue, appropriate counselling and use of dilators can be helpful. Surgery with the input of a multidisciplinary team may also be required, particularly if previous multiple surgeries as an infant has been required, such as in infants with cloacal abnormalities.

Where infertility and recurrent miscarriage are the presentation in later reproductive years, uterine anomalies are an important issue to consider, particularly in determining whether treatment is possible and likely to improve outcome. The diagnosis of a unicornuate uterus with non-communicating canulated rudimentary horn must be treated to prevent ectopic pregnancy in that horn, but other anomalies are less clear-cut. The correction and treatment of didelphic, bicornuate or unicornuate uteri is either impossible or complex and unlikely to improve the pregnancy outcome. However, the advent of operative hysteroscopy using scissors, resectoscope or more recently, bipolar diathermy, in such instruments as the versapoint have meant that uterine septa can be readily divided. It is still debated whether this will improve the outcome of the pregnancy if it occurs, or improve fertility rates in the subfertile population. Acien³ (see Table 3) in small numbers suggested term delivery was significantly less likely to occur when women conceive after a diagnosis of uterine anomaly and pregnancy outcome appeared to improve after resection of the septum, although it is a less significant effect if the anomaly is arcuate or subseptate.

Conclusion

Congenital anomalies of the female genital tract represent a small but significant challenge to our practice. They may present at many ages in many guises. Appropriate assessment, diagnosis and treatment are the mainstays. Support of the individual nature of the patient's condition needs to be acknowledged and managed. A multidisciplinary approach is appropriate for the more complex of these conditions. The true prevalence and implications for future fertility potential is yet to be determined.

References

- American Fertility Society. The AFS classification of adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, Mullerian anomalies and intrauterine adhesions. *Fertil Steril.* 1988; 49:944-55.
- Saravelos SH, Cocksedge KA, Li T-C. Prevalence and diagnosis of congenital uterine anomalies in women with reproductive failure: a critical appraisal. *Hum Reprod Update* 2008;14:415-29.
- Acien P. Reproductive performance of women with uterine malformations. *Hum Reprod.* 1993; 8:122-6.
- Grimbizis G, Campo R. Congenital malformations of the female genital tract: the need for a new classification system. *Fertil Steril.* 2010; 94:401-7.

'Endometriosis and fertility', references continued from page 35.

- Teague EM, Print CG, Hull ML. The role of microRNAs in endometriosis and associated reproductive conditions. *Hum Reprod Update* 2010;16:142-65.
- Al-Jefout M, Dezarnaulds G, Cooper M, Tokushige N, Luscombe GM, Markham R, Fraser IS. Diagnosis of endometriosis by detection of nerve fibres in an endometrial biopsy: a double blind study. *Hum Reprod.* 2009;24:3019-24.
- Somigliana E, Vercellini P, Vigano' P, Benaglia L, Crosignani PG, Fedele L. Non-invasive diagnosis of endometriosis: the goal or own goal? *Hum Reprod*. 2010 Jun 2. [Epub ahead of print].
- Sutton CJ, Pooley AS, Ewen SP, Haines P. Follow-up report on a randomized controlled trial of laser laparoscopy in the treatment of pelvic pain associated with minimal to moderate endometriosis. *Fertil* Steril. 1997; 68:1070-4.
- Abbott J, Hawe J, Hunter D, Holmes M, Finn P, Garry R. Laparoscopic excision of endometriosis: a randomized, placebocontrolled trial. *Fertil Steril.* 2004;82:878-84.
- Rombauts L. A word from the Editor. WES e-Journal 2009;11(5):2-3.
 Vercellini P. The endometriosis-ovarian cancer connection:
- challenging conventional wisdom. WES e-Journal 2010;12(2):3-7.
 Hart RJ, Hickey M, Maouris P, Buckett W. Excisional surgery versus ablative surgery for ovarian endometriomata. Cochrane Database
- Syst Rev. 2008 Apr 16;(2):CD004992.
 Tsoumpou I, Kyrgiou M, Gelbaya TA, Nardo LG. The effect of surgical treatment for endometrioma on in vitro fertilization outcomes: a systematic review and meta-analysis. *Fertil Steril.*
- 2009;92:75-87.
 Benaglia L, Somigliana E, Vighi V, Ragni G, Vercellini P, Fedele L. Rate of severe ovarian damage following surgery for endometriomas. *Hum Reprod.* 2010;25:678-82.

Table 2a. Prevalence of anomalies in population gr	oups
with Class la investigations.	

Population group	Studies	Cases	Total n (%)
General	4	4521	305 (6.7)
Infertile	10	7332	538 (7.3)
Recurrent miscarriage	4	1257	202 (16.1)

Adapted from Saravelos, et al, 2008.

Table 2b. Percentage of anomaly subtypes in different population groups.

P opulation group	Number	Hypoplastic %	Unicornuate %	Didelphys %	Bicornuate %	Septate %	Arcuate %
General/ fertile	250	_	0.4	0.4	4	27.2	68.0
Infertile	510	9.4	6.1	2.9	10.8	46.1	24.7
Recurrent miscarriage	132	_	2.3	0.8	5.3	26.5	65.2

Table 3. First pregnancy outcome in untreated women anomaly compared to women without anomaly.

	Anomaly	Normal
	First pregnancy	First pregnancy
Pregnancies	142	26
Preterm delivery % 22-28 weeks 29-37 weeks	34 (24) 6 28	2 (8) 1 1
Term delivery (%)	64 (45)**	21 (81)

Adapted Acien P. Hum Reprod. 1993 ** P<0.001.

Medical pamphlets

RANZCOG members who require medical pamphlets for patients can order them through: Mi-tec Medical Publishing PO Box 24 Camberwell Vic 3124 ph: +61 3 9888 6262 fax: +61 3 9888 6465 Or email your order to: orders@mitec.com.au

You can also download the order form from the RANZCOG website: www.ranzcog.edu.au .

Male fertility



A/Prof Stephen Robson FRANZCOG

The new millennium did not begin well for men. Suggestions that male fertility was declining across the developed world caused a near-frenzy in the lay press. Studies had suggested that sperm concentrations in routine semen analyses had steadily fallen across Western Europe since the Second World War.

At the same time, stories appeared about the inexorable decline of the Y-chromosome. Scientists had declared that in our evolutionary past, the Y-chromosome had hosted more than a thousand different genes. Nowadays, this little chromosome has fewer than one hundred and was being

described as a 'genetic wasteland' that would soon disappear, taking with it the whole process of human sexual reproduction. Just to top things off, Australian researchers reported a technique of using somatic cells, instead of sperm, to fertilise oocytes. The future of men seemed gloomy. A decade later, we're still here but some of us are probably hanging by a thread. This pullout article aims to put the evaluation and management of male fertility in a modern perspective.

'Management of fertility delay involves a couple and, in most circumstances, discussions should be undertaken with both partners.'

What is male fertility?

It is often quoted that male factors alone contribute to almost onethird of fertility problems for couples and that a combination of male and female factors together make up another third. With this in mind, it is worth seeking a working definition of 'male fertility'. Although semen analysis is the prime tool used to assess the male side of reproduction, it is only part of the story. Male fertility is best thought of in a more holistic sense. It is the ability of a man to consistently make and ejaculate sufficient numbers of normal sperm into the female reproductive tract at the fertile time. Any assessment of male fertility should thus address not just a single semen analysis, but the broad and typical trend over time, and how well the ejaculate is delivered.

Spermatogenesis and ejaculation

At the risk of stating the obvious, spermatozoa are manufactured in the testes. The testes contain the elongated seminiferous tubules, as well as interstitial cells, vessels and fibrous tissue. The covering of the testis is a thick, fibrous, inelastic layer called the tunica albuginia. Luteinising hormone (LH) secreted from the anterior pituitary stimulates the interstitial Leydig cells to convert cholesterol to androgens, the most common being testosterone. Testosterone in the serum provides negative feedback to pituitary gonadotrophs, regulating the level of LH. Testosterone is present in high concentration in the testicular tissues and is transported across the blood-testis barrier to the Sertoli cells that line the seminiferous tubules. At the same time, follicle stimulating hormone (FSH) is secreted and acts in concert with testosterone to stimulate sperm production.

The Sertoli cells are in intimate contact with spermatogic cells and facilitate the manufacture of spermatids. This process releases Inhibin B (InhB) which diffuses into the blood and provides a separate negative feedback loop, regulating FSH secretion. The seminiferous tubules fill with fluid secreted by the Sertoli cells and myoid cells in the tubular wall generate wave-like contractions that move this fluid to the rete testis and out to the epididymus. The spermatozoa mature as they move from the epididymus, along the vas deferens, to be stored in the seminal vesicles under the bladder.

Ejaculation occurs as part of a spinal reflex. The contractile seminal vesicles move the sperm into the posterior urethra, along with a large amount of prostatic fluid. Rhythmic contractions of the pelvic floor muscles increase the intra-urethral pressure and a sphincter mechanism closes the outlet of the bladder, so the semen (the mixture of sperm and fluid from the prostate and seminal vesicles) is ejected from the urethral meatus.

Initial assessment of the male

During a fertility consultation, it is important to have the male actually present and to take a history and, if necessary, perform an examination. It is not uncommon to have a woman present for such a consultation alone, something that is not appropriate even

How to... is a new 'pullout' feature article providing Trainees with basic information on, and step-by-step illustrated instructions outlining, some of the medical procedures that they may encounter as obstetricians and gynaecologists.

Suggestions or comments are welcome and should be forwarded by email to: ranzcog@ranzcog.edu.au or by mail to: 0&G Editors, 254-260 Albert Street East Melbourne, Victoria, Australia 3002 if the results of a semen analysis are available and are normal. Management of fertility delay involves a couple and, in most circumstances, discussions should be undertaken with both partners. That said, it is also important to give each partner the opportunity to provide sensitive information in private. In the same way that some women will be reluctant to disclose a history of previous infections or pregnancies, some men won't own up to previous pregnancies or infections in front of their partners.

Men should be asked about previous fertility, onset of puberty and any developmental delays. Also obtain previous relevant surgical history (such as testicular maldescent, hernia or varicocoele surgery) and past injuries or infections (such as mumps orchitis). General health (especially diabetes or cardiovascular medications), smoking, non-prescription drug use and family history may all yield relevant information. Men should also be asked about any erectile difficulties, ejaculation problems and frequency of intercourse. It is common to find that long periods of infertility deplete the allure of intercourse for even the most ardent male, so coital frequency is not just a meaningless bit of history. Men with a prostate history may have retrograde ejaculation.

Examination

If the man has a completely unremarkable history, a consistently normal semen analysis, and especially, if he has been responsible for pregnancies in the past, it may be permissible to omit the examination. However, even the slightest abnormality should prompt a thorough examination. This is best done with the patient standing, trousers and underwear around the knees and shirt lifted to just above nipple level. Note the height and weight, pattern of bodily hair and look for gynaecomastia. Check the inquinal regions carefully for incisions or herniae. Note the penis and whether there is evidence of hypospadias. The testes should both be in the scrotum and normal in size. Accurate estimation of testicular volume requires a Prader orchidometer to provide a comparison (Figure 1). Palpate the cord for swellings and to check for the presence of the vasa. Varicocoele is a relatively common finding, usually on the left side and it feels like a 'bag of worms'. The vasa are very firm, about the size and consistency of a piece of spaghetti cooked al dente.

Semen analysis

A man is only as good as his last semen specimen, so it is important to optimise the value of the test. A couple of days of ejaculatory abstinence is normally advised, but this only makes sense if decisions are being made about, for example, the use of IVF techniques. What is more important is that there are no delays in examination for motility and that the sample is kept warm. I think it makes sense to give the specimen under 'battle conditions'. If the man ejaculates twice a day, or only once a month, then so be it – the results will reflect the 'normal' state of the sperm during intercourse. If such a random sample is perfectly normal (and 'normal' is discussed below), then that is indeed reassuring. If the results are disappointing, then it is important to repeat the test at least once (with the appropriate instructions about abstinence for repeats next time).

Semen analysis results vary incredibly for the same man at different times, so never be pessimistic after one bad result. The World Health Organisation (WHO) have recently completed a study of more than 4500 healthy fertile men and have revised their range of normal values for semen analysis. Volumes between 1.4 and 1.7 ml, with a concentration of 12 to 16 million sperm per ml and total of between 33 and 46 million sperm in an ejaculate were found to be the 95 per cent confidence intervals. Normal values for normal sperm morphology (shape) were only three to four per cent, and forward motility of between 31 and 34. These new values are considerably lower across the board as compared to the older WHO guidelines.

Specific clinical issues

Normal semen analysis and normal female findings In this common circumstance, the options depend on the duration of infertility and age of the woman. When the delay has been perhaps a year and both partners are under 35 years of age, either timed intercourse (using a cycle track with hormone levels and follicular ultrasound) or intrauterine insemination (IUI) were found to be equally effective in a *Cochrane* review. Insemination involves washing and concentration of a semen specimen, and insertion through the cervix with a catheter. Strict timing of the insemination to occur at ovulation does not seem to increase the pregnancy rate, though performing two inseminations a few hours apart does. With long durations of infertility, or older women in particular, early recourse to IVF might be advisable.

Reduced motility

When the proportion of motile sperm is reduced, IUI may be of value though the evidence for this is weak. Another approach that has been suggested is daily ejaculation. The reasoning behind this is that more regular ejaculation might reduce exposure of sperm to oxidative stressors in seminal fluid (from leucocytes, for example, although sperm themselves seem to release reactive oxygen species [ROS]). When motility problems are severe, IVF techniques involving injection of individual sperm into oocytes (intracytoplasmic sperm injection [ICSI]) are required (Figure 2).

Severe sperm problems

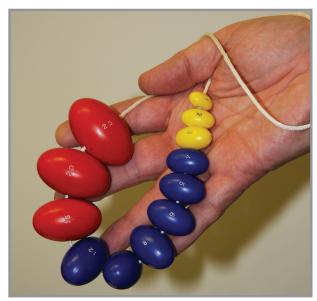
Problems with sperm numbers, movement and shape often go hand in hand. When severe, it is important to think about a number of important issues. The lower the sperm concentration, the higher likelihood of a chromosomal abnormality in the man. Men with azoospermia have a 15 per cent prevalence of chromosomal abnormalities such as Klinefelter's syndrome (47XXY karyotype). Also possible is an effect of cystic fibrosis (CF) mutations – congenital absence of the vas deferens. It is important to check for the common CF mutations such as DF508 in both the man and his partner. Small deletions of genetic material on the muchmaligned Y-chromosome also become more likely, such as DAZ (deleted in azoospermia) and RBM (RNA-binding motif) deletions. These may be inherited by male offspring if IVF treatment results in a pregnancy.

No sperm

A persistent complete absence of sperm is an alarming finding. It is important to remember that intercurrent illnesses, especially those where the man has a high fever for more than a day, can completely wipe out sperm and it will take up to two months for sperm to return to the ejaculate. If consecutive semen analyses yield no sperm, then the possibilities are two-fold: either sperm are being made and not reaching the outside world (obstructive azoospermia); or sperm are not being made, either at all, or in sufficient numbers to reach the ejaculate (non-obstructive azoospermia).

The commonest cause of obstructive azoospermia in our society is vasectomy. Congenital bilateral absence of the vas deferens (CBAVD) associated with CF is another. Typical findings are of normal testicular volume with epididymal distension. Hormone studies will usually reveal normal levels of FSH and LH. Sperm can often be obtained using surgical aspirations, typically with percutaneous epididymal sperm aspiration (PESA) (Figure 3) or, if unsuccessful, by needling the testicular substance to obtain

Continued on page 50.



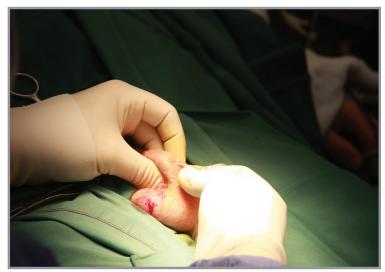
1. The author's trusty orchidometer.



2. The process of intracytoplasmic sperm injection (ICSI), where a single sperm is injected into the cytoplasm of a mature oocyte. Photo courtesy of Dr Chris Copeland.



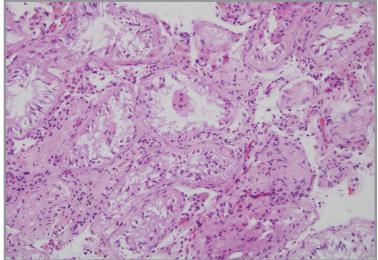
3. Percutaneous epididymal sperm aspiration (PESA), where a butterfly needle is passed into the epididymus.



4. Needle biopsy of the testis. Small fragments of seminiferous tubules are obtained, from which sperm cells can be microdissected.



5. Open testicular exploration and sperm extraction (TESE). An incision in the tunica allows seminiferous tubules to bulge out and be biopsied.



6. Sertoli cell-only syndrome. Testicular biopsy reveals no evidence of spermatogenic cells, only tubal Sertoli cells. Photo courtesy of Dr Jane Twin.

fragments of seminiferous tubules (Figure 4). Immature sperm obtained this way can be used in conjunction with ICSI to fertilise oocytes in IVF.

Non-obstructive azoospermia can be either pre-testicular or testicular. Pre-testicular causes are usually hormonal, typically with low levels of FSH and LH. They may be associated with other endocrine disturbances (such as a prolactinoma) or be part of a panhypopituarism. It is important to measure prolactin, thyroidstimulating hormone (TSH) and adrenocorticotropic hormone (ACTH) levels in this circumstance and imaging of the pituitary may be necessary. These cases may respond to endocrine therapies, such as FSH and LH (or hCG) injections, though this will take months to have an effect.

Testicular failure is often only diagnosed when a reasonable amount of tissue can be obtained from an open testicular biopsy (Figure 5). Typically the testes are small and soft, and levels of FSH and LH are high with a low testosterone level. Causes include Sertoli cell-only syndrome (Figure 6), Klinefelter karyotype, previous mumps orchitis, or chemotherapy. Occasionally, a testicular tumour is discovered, highlighting the importance of examination. Testicular maldescent used to be blamed, but it is likely that the two conditions are both manifestations of a common underlying abnormality in fetal development. In these circumstances, donor sperm is often the only solution.

'It is still important to advise men to regain normal fitness, have a healthy diet, cease smoking and any non-prescription drugs, and minimise alcohol intake.'

Lifestyle and male fertility

Women trying for a pregnancy are usually badgered with lifestyle advice and it seems only fair that men have the same advice meted out to them. It should be pointed out, though, that lifestyle changes to improve male fertility have much weaker evidence to support them. For example, a recent systematic review of the effect of obesity on male fertility did not demonstrate a strong effect. Similarly, although there is evidence that persistent heating of the testes (for example, as occurs in taxi drivers in hot weather) may have an effect on semen parameters, wearing loose underwear and keeping the testes cool may not necessarily increase pregnancy rates. It is still important to advise men to regain normal fitness, have a healthy diet, cease smoking and any non-prescription drugs, and minimise alcohol intake.

It is known that oxidative stress is associated with increased levels of DNA damage in sperm, which in turn has been associated with poor fertilisation, and even poor pregnancy outcomes such as miscarriage. The proportion of sperm with DNA damage can be estimated with techniques such as the SCSA (sperm chromatin structure assay) test. Unfortunately, trials of anti-oxidant therapy have yielded controversial results and the jury is still out. Recommendations have even been made about using testicular sperm from biopsies in men with very high levels of DNA damage in their sperm, yet evidence for this is still weak.

Summary

Male fertility is a difficult thing to define and involves more than the usual surrogate measure of a semen analysis. The basis of evaluation of male fertility is a careful history and examination, and repeated semen analyses. Additional tests can help define the underlying nature of some problems, but few effective therapies are available. Treatment usually involves making the best of the sperm available, often with the assistance of IVF techniques. Fortunately, subsequent analyses have cast doubt on reports of a decline in male sperm concentrations and the outlook for the Y-chromosome has improved with new discoveries. Sex is likely to be around for the foreseeable future.

References and further reading

- 1. American Society for Reproductive Medicine. Evaluation of the azoospermic male (technical bulletin). *Fertil Steril.* 2008; 90: S74.
- American Society for Reproductive Medicine. Sperm retrieval for obstructive azoospermia (technical bulletin). *Fertil Steril.* 2008; 90: S213.
- Cantineau AEP, Heineman MJ, Cohlen BJ. Single versus double intrauterine insemination (IUI) in stimulated cycles for subfertile couples. *Cochrane Database of Systematic Reviews* 2003, Issue 1. Art. No.: CD003854. DOI: 10.1002/14651858.CD003854.
- Cantineau AEP, Janssen MJ, Cohlen BJ. Synchronised approach for intrauterine insemination in subfertile couples. *Cochrane Database* of Systematic Reviews 2010, Issue 4. Art. No.: CD006942. DOI: 10.1002/14651858.CD006942.pub2.
- Cooper TG, NoonanE, von Eckardstein S, et al. World Health Organisation reference values for human semen characteristics. Hum Reprod Update 2010; 16: 231.
- Helmerhorst FM, Van Vliet HAAM, Gornas T, Finken MJ, Grimes DA. Intra-uterine insemination versus timed intercourse or expectant management for cervical hostility in subfertile couples. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD002809. DOI: 10.1002/14651858.CD002809.pub2.
- MacDonald AA, Herbison GP, Showell M, Farquhar CM. The impact of body mass index on semen parameters and reproductive hormones in human males: a systematic review with meta-analysis. *Hum Reprod Update* 2010; 16: 293.
- Ruwanpura S, McLachlan R, Meachem S. Hormonal regulation of germ cell development. J Endocrinol. 2010; 205: 117.
- 9. Sharpe RM. Lifestyle and environmental contribution to male infertility. *Br Med Bull*. 2000; 56: 642.
- te Velde E, Burdorf A, Nieschlag E, et al. Is human fecundity declining in Western countries? Hum Reprod. 2010; 25: 1348.
- 11. Tremellen K. Oxidative stress and male infertility a clinical perspective. *Human Reprod Update* 2008; 14: 243.
- 12. Visser L, Repping S. Unravelling the genetics of spermatogenic failure. *Reproduction* 2010; 139: 303.
- Weedin JW, Khera M, Lipshultz LI. Varicocoele repair in patients with non-obstructive azoospermia: a meta-analysis. J Urol. 2010; 183: 2309.

This section provides a demonstration of one technique for the operation and is not intended to be anything other than a guide and study aid for trainees. In every case, the surgeon should individualise the operation according to their own skills and techniques, the equipment available and the individual patient. RANZCOG does not endorse any one technique for this or any other procedure.

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.

Endometrial polyps as cancer precursors

The authors report their traditional teaching was that about 30 per cent of endometrial polyps in women aged over 65 years are associated with malignancy. They sought

to determine whether this was due to polyps being truly pre-malignant, with features distinctive from non-malignant endometrium, or whether the reported high rates of cancer in these women is due to the endometrial testing that they have by virtue of abnormal bleeding or other symtoms. The authors identified 1880 cases of endometrial polyps between 2000 and 2007 of which 1467 samples were suitable for further pathological analysis. 8.5 per cent of these cases had an associated endometrial cancer in the sections in the study. Interestingly, a third of these had cancer only in the endometrium adjacent to the polyp and not in the polyp itself. They compared the results for endometrial polyps with a sample of 1138 cases in which the primary diagnosis had been uterine fibroids. 11.7 per cent of the fibroid sample had an associated endometrial cancer, slightly higher than in the endometrial polyp group. The authors concluded that the apparent high rate of endometrial malignancy in women with endometrial polyps was a result of detection bias. Women with polyps often bleed resulting in further investigation, which then detected the cancer rather than the polyp itself predisposing to cancer. The authors make the elegant argument that the rate of endometrial cancer is similar in women who had surgery for fibroids in their study, and that as leiomyomata do not arise from endometrium, it is unlikely that they would be considered precursors of endometrial cancer.

Perri T, Rahimi K, Ramanakumar AV, *et al.* Are endometrial polyps true cancer precursors. *American Journal of Obstetrics and Gynecology* 2010; Vol. 203.

LUNA for chronic pelvic pain

Laparoscopic uterine nerve ablation (LUNA) involves the laparoscopic ablation of nerve trunks in the uterosacral ligament by laser or diathermy. It has been used as a treatment for chronic pelvic pain. This study prospectively randomised 487 women with chronic pelvic pain for longer than six months, with no or minimal endometriosis, adhesions or pelvic inflammatory disease, to receive either LUNA or laparoscopy without nerve ablation. Patients were blinded to their treatment. Follow-up continued for an average of 69 months. The results of the study showed no differences between the LUNA and non-LUNA groups in pain, including dysmenorrhea, dyspareunia and non-cyclical pain or quality of life. While a larger sample size would have allowed detection of a smaller difference between groups, the power calculations offered in the article provide convincing evidence that they had a reasonable chance of detecting a clinically significant difference.

Daniels J, Gray R, Hills RK. Laparoscopic uterosacral nerve ablation for alleviating chronic pelvic pain. *JAMA* 2009; 302: 955-961.

Home birth versus planned hospital birth

With a large randomised controlled trial of home versus hospital birth unlikely to ever be conducted, meta-analyses such as these may forever remain the highest level evidence available on this eternal question. The authors searched *MEDLINE* for all English language, developed country articles comparing planned hospital and home birth between 1950 and 2009. They found 12 studies (one from Australia) including a total of 342,000 home births and 207,000 planned hospital births. By far the largest study including over 500,000 births was performed in the Netherlands and published in *BJOG* in 2009. The meta-analysis reported significantly less medical intervention in home births, including less epidural, fetal heart monitoring, operative delivery, third degree tear, perineal laceration and retained placenta. Unfortunately, the odds ratio for neonatal death at home birth was 1.98 (1.19-3.28). This was higher (OR=2.87, 1.32-6.25) when deaths in non-anomalous (normal) babies were analysed separately. The authors attribute this to a higher rate of failed resuscitation and respiratory distress in home births compared to hospital births and suggest that improving the neonatal resuscitation skills of home birth providers would be a valuable intervention.

Wax JR, Lucas FL, Lamont M, *et al.* Maternal and newborn outcomes in planned home birth versus planned hospital births: a meta-analysis. *American Journal of Obstetrics and Gynecology* 2010; Vol. 203.

de Jong A, van der Goes BY, Ravelli ACJ, *et al.* Perinatal mortality and morbidity in a nationwide cohort of 529,688 low-risk planned home and hospital births. *British Journal of Obstetrics and Gynaecology* 2009; 116: 1177-84.

FELLOWS & DIPLOMATES PRACTICE PROFILE

Have you completed a Practice Profile in 2010?

Fellows and Diplomates can complete their Practice Profile for 2010 by logging in via our website:

FELLOWS:

www.ranzcog.edu.au/fellows/PracticeProfile.shtml

DIPLOMATES: www.ranzcog.edu.au/diplomates/PracticeProfile.shtml

The long barren years of Catherine de Medicis

A gynaecologist's view of history



Prof Caroline de Costa FRANZCOG

'O happy faith, after so long delay, That vouchsafes them the fruit for which they pray.'

Margaret of Navarre, writing to her sister-in-law, Catherine de Medicis, on the birth of Catherine's first child.

On June 30 1559, the French Court was at Paris for the marriage celebrations of Philip II of Spain to Elizabeth, daughter of Henry II of France and his Queen, Catherine de Medicis. The marriage had been arranged to cement the recent peace treaty of Cateau-Cambrésis that ended a series of wars with the Spanish for the control of Italy. Following the

wedding, a tournament was arranged for the entertainment of the guests; the participants included Henry himself, who was struck in the eye, inadvertently, by the lance of Captain Montgomery of the Scottish Guard. Henry died ten days later, leaving the throne to his 15 year-old son, Francis II. Francis lacked both maturity and experience so real power passed into the hands of his mother, Catherine, who was to reign, sometimes unofficially and sometimes as Regent, for the next thirty years.

History has not dealt kindly with Catherine, who is popularly considered both wicked and scheming. To determine her true character has become very difficult, novelists and film-makers having portrayed her as frequently as historians. Alexander Dumas for one shows her as inherently evil, plotting with her Florentine perfumer and poison maker, Réné, to murder her own son-inlaw, the future Henry IV. Balzac on the other hand described her as 'a great king'. Most serious historians of the period see her as moderate, concerned and rational, doing a difficult job at a difficult time, steering a path between Catholic and Protestant forces equally passionately involved in the Wars of Religion that engulfed France between 1560 and 1590.

Three of Catherine's sons were kings of France. The first was the inadequate Francis, who suffered chronic otitis media that progressed to a fatal cerebral abscess in 1560. The renowned French surgeon Ambroise Paré was called in and wanted to try burr holes to let out the pus. This was a new procedure – Paré had performed it only three times previously. Catherine hesitated and Francis died. Charles IX succeeded him, Catherine acting as Regent for the first three years of the reign. Charles was in poor physical health, mentally unstable, cruel and vain. It was he who took the decision to assassinate the Protestant leader Coligny, a botched attempt which led to the St Bartholomew's Day Massacre for which Catherine has traditionally been blamed. Charles died in 1574 and Catherine was again Regent while her third son Henry III returned from his previous post as King of Poland to take up the crown of France. Henry was weak and easily influenced by the Catholic party. He seemed more attentive to the trappings of power than to its substance and failed to end the religious wars despite Catherine's ongoing efforts in this direction. Stabbed by a fanatical Jacobin friar in 1589, on his deathbed he acknowledged as his heir the Protestant Henry of Navarre, who converted to Catholicism to become Henry IV, remarking, it is said, that 'Paris is worth a Mass'. Henry IV's tolerance of the Protestant Huguenots finally brought the wars to an end.

Catherine's marriage to Henry II was first suggested when she was only six years old and formally arranged when she was eleven. Catherine herself was never consulted – the marriage was political, made so that France could keep a foot in Italy. At the time, Henry was only the Second Son of France, so the alliance was not seen as particularly important until some years later when his brother died. Catherine's mother, who came from the French nobility, had died of puerperal sepsis within days of her birth, and soon afterwards her father, Lorenzo de Medicis, perished from a fever. The orphaned Catherine was brought up, in a Florence frequently subject to war, under the guidance of her uncle, who happened to be the Pope, Clement VII.

It was Francis I, father of Henry II and lover of all things Italian, who organised the match. The marriage was not popular in France. Catherine's dowry was considered too small and alliances between royalty and merchant families like the Medicis, however rich, were still unusual. Catherine would later be referred to contemptuously in France as 'the shopkeeper's daughter'.

Nevertheless, the wedding did take place, at Nice in 1533. So richly bejewelled was Catherine's wedding gown that it was impossible to tell its colour. It was considered that the couple were old enough (they were both 14) to consummate the marriage; presumably Catherine had already reached her menarche. Francis I 'put them to bed to watch them jousting and they jousted valiantly' and the Pope waited 34 days to see if his niece had conceived, but in vain. 'Never mind,' he consoled her, as he prepared to leave for Rome, 'a clever woman can always have children.' However, Catherine had none for ten years.

As a gynaecologist I find this intriguing, especially as the birth of Francis II, Catherine's first child, in 1544, was followed by the arrival of nine siblings. One son died in infancy and Catherine's final delivery, in 1556, was of twins (one a neonatal death, the other a stillborn breech extraction). Nearly five centuries later, knowing something of the personalities involved, I venture to suggest a possible cause for Catherine's initial infertility, and the likely means of its resolution.

Continued on page 56.

Henry II, as a child, was sent as a hostage to the Spanish court, as part of the ransom paid for his father, Francis I, taken prisoner in Italy. Henry did not return to France until he was eleven. On his return, his father found him a morose child and entrusted him to the care of a woman then at Court, Diane de Poitiers. Diane had been married very young to an aging aristocrat, who conveniently soon died.

Much has been written about the beauty of Diane and the few authentic portraits available do show her to have been very lovely. Already in her thirties by the time she took over Henry's care, Diane is said to have preserved her beauty with cold water, eschewed cosmetics and refused to dye her hair. Whilst initially her role was a maternal one, when Henry was 17 years old (and three years married to Catherine) they became lovers. Their relationship continued up until his death, when Diane was 60 and Henry 41. Diane exercised enormous influence over Henry's life, decisions and appointments. As Royal mistress, she was always placed near Henry at official engagements; he gave her land, castles and most of the crown jewels.

Henry, Catherine and Diane thus formed a ménage à trois throughout Henry's adult lifetime. Though cordial to Diane while Henry was alive, Catherine was very jealous. 'Never has a woman who loved her husband liked his whore,' she observed in a letter to one of her children many years after Henry's death. It appears that she loved him deeply, while he cared little for her, although he was devoted to their children when they finally made their appearance.

It has been well-documented that Catherine shared Henry's bed frequently, at Diane's bidding: 'Diane obliged Henry to sleep assiduously with his wife,' wrote one contemporary. So lack of opportunity was not the reason Catherine was failing to conceive. A more relevant detail perhaps is the fact that Henry had hypospadias. There are several reports of this including that of a 16th century physician, Nicolas Venette. As Henry eventually had at least 13 children, it is likely that the hypospadias was glanular or anterior penile, although history has not recorded this detail. In 1538, he supposedly proved his fertility by fathering a daughter with an Italian woman, Filippa Duci. The girl, named Diane de France, was brought up by Diane de Poitiers, who was rumoured to be her real mother.

As pregnancy eluded Catherine, she became increasingly desperate in her search for a solution. She surrounded herself with doctors, diviners and magicians. Given how little was known of female physiology, it is unlikely that any of their philtres and potions had much effect. As well as being a devout Catholic, Catherine was a firm believer in astrology and consulted the leading astrologists and fortune tellers of the day, including Nostradamus, who is said to have told her she would be the mother of three kings of France. She hung herself with medals and charms and would not ride on the back of a mule, since that animal is infertile.

One of the doctors she consulted was the prominent French physician Jean Fernel and some historians have attributed the cure of her infertility to him. Fernel translated works of the Roman physician Galen, believing that medical progress lay in resurrecting classical learning. He had, however, little knowledge even of such gynaecology as there was in the 16th century. He himself always denied having prescribed any treatment that might have brought about a solution, although he had no objection to people thinking so at the time – his reputation was greatly enhanced.

Other historians have speculated that Henry had an operation to correct the hypospadias. Surgery of all kinds was, however, in its infancy, anaesthesia and antisepsis unknown. Ambroise was at the stage of ligating bleeding vessels from war injuries, rather than pouring boiling oil over them. Summoned to the dying Henry II, he could do nothing to save him. It is inconceivable that any surgeon would have operated upon the Royal member to correct a congenital anomaly, or even imagined that by doing so he might solve what would have been thought of as Catherine's problem. Surgery for the correction of hypospadias was not developed until the late 19th century.

Undoubtedly, Catherine's failure to conceive was of concern to Diane. Her power at Court was enormous and she wanted to keep



Catherine de Medicis.



Diane de Poitiers.

that power. If Henry's marriage remained childless, if there were no male heir to the throne, divorce was inevitable. Indeed divorce was being encouraged by the powerful Guise family, who were close to the Court and who had a suitable bride ready. Catherine was docile and the arrangement suited Diane, but another wife might not be so amenable. Once Catherine achieved pregnancy, it must have suited Diane for her to be occupied with a confinement every year, leaving Henry free to devote more time to his mistress.

Diane would have known better than anyone the intricacies of the king's anatomy and function, and she probably had a good idea of Catherine's. Catherine is on the historical record as having holes bored in the roof of Diane's bedchamber, so that she could watch her husband and his mistress disport themselves; she is said to have found the spectacle very different from the disinterested performance she experienced in the marital bed. It is very possible that Catherine had a retroverted uterus. If this was the case, intercourse always in the missionary position with a perfunctory husband, and hypospadias present, then the problem may have been purely mechanical. Diane, a clever woman, may have given some advice to Catherine: turn on your stomach for ten minutes after lying with the king, ma chérie, or try different positions. Catherine, obeying such instructions and finding the counsel successful, would certainly have done the same thing again, achieving nine full-term pregnancies in 12 years.

Unfortunately, if such wisdom was offered, this was not recorded for posterity. We shall never really know the reasons for Catherine's

interesting obstetric history. After Henry's death, Catherine, now virtual ruler of France, turned against Diane. She and her friends were banished from Court, she was made to give up her beautiful château on the Loire and to return the crown jewels. Historians continue to debate Catherine's character and her role in the wars and politics of France, but there is no doubt she wielded enormous power in the last 30 years of her life. This power was entirely due to her role as the mother of sons who were kings of France; as a woman she could not have ruled in her own right. Had she never conceived, she would have been divorced and a non-entity. Catherine may well have owed her influence and her fame, which continues to this day, to Diane's prudent efforts to overcome her long years of barrenness.

References

- 1. Héritier J. *Cathérine de Medicis.* Trans. C. Haldane. London: Allen and Unwin, 1963.
- 2. Van Dyke P. Catherine de Medici. New York: Scribner, 1922.
- 3. Lavisse E. *Histoire de France*. Paris: Hachette, 1911.
- 4. Dumas A. La reine Margot. Paris: Boutan-Marguin, 1968.
- 5. Balzaz H. Sur Cathérine de Medicis, in La Comédie Humaine. Paris: Editions de Seuil, 1981.
- Herpin J. Jean Fernel, Médecin et Philosophe. Paris: Baillière, 1949.
 Mondor H. Ambroise Paré. In Dumesnil R, Bonnet-Roy F eds. Les médecins célèbres. Paris: Mazenrod, 1947.



The Royal Australian and New Zealand College of Obstetricians and Gynaecologists

WANTED: VOLUNTEER FACILITATORS FOR RANZCOG BASIC SURGICAL SKILLS WORKSHOPS

Fellows and Year 5 and 6 Trainees are needed to act as facilitators at the RANZCOG Basic Surgical Skills (BSS) workshops conducted annually in each State in Australia and in New Zealand. Attendance at a BSS workshop is compulsory for all Year 1 RANZCOG Trainees.

These practical, interactive two-day workshops are run on weekends and cover theatre etiquette, handling instruments, knot tying, incision/closure, episiotomy repair, haemostasis, electrocautery and stacks, hysteroscopy and laparoscopy.

Facilitators provide hands-on teaching and advice during the workshop and help with setting up on the day. Time commitment: ONE weekend per year.

Applications and enquiries: Shaun McCarthy, Training Services Manager tel +61 3 9412 2917, *fax* +61 3 9419 7817, *email: smccarthy@ranzcog.edu.au*

Syntocinon dosages at caesarean section



Dr Louise Ellard

Provisional Fellow in Anaesthesia

In the recent past there has been an endeavour, led by some anaesthetists, to reduce the dose of syntocinon administered during caesarean sections. This has resulted from interpretation of a mounting body of evidence suggesting that previous doses were unnecessarily high and may have been associated with significant adverse effects for the mother.

The transition to smaller doses has not been a smooth one and at times there has been spirited debate between anaesthetists and obstetricians regarding the appropriate dose for routine use. This sometimes results in the 'playing of games' regarding the dose requested and that given. The anaesthetist may enter the game with a low bid, then the obstetrician enters high. This mostly results in an amicable compromise, with

a dose somewhere in the middle, leaving both parties somewhat perturbed, convinced that the other doesn't guite understand the issues.

This review aims to explore syntocinon use during caesarean section from the viewpoint of the anaesthetist. What bolus should be given? Should this be followed by an infusion? Does this apply to all patients? Who should decide?

Anaesthetists play a dual role, simultaneously prescribing and then administering our chosen medications. In addition, at times we are asked to give a drug on behalf of the surgeon or proceduralist. Many drugs have a potential for adverse effects and require the anaesthetist to understand the action and interactions, despite the fact that they are prescribed by another physician. In the case of syntocinon, the prescriber does not seem as clearly defined and it remains unclear who is responsible for determining the dose and speed of injection. The dosing debate is spread over both anaesthetic and obstetric literature, however, the drive to reduce the 'standard' dose does seem to come primarily from the anaesthetic side of the drapes.

Pharmacological action

Syntocinon is synthetic oxytocin, identical in structure and function to the endogenous hormone secreted by the posterior pituitary. Syntocinon binds to the oxytocin receptor on uterine myometrial cells, promoting uterine contraction and thereby reducing blood loss from the placental site. The sensitivity of the uterus to oxytocin increases throughout pregnancy and reaches a peak at term.

Adverse effects

Syntocinon binds to vascular endothelial receptors causing vasodilation, a reduction in blood pressure and a reflex tachycardia. Blood pressure falls by an average of 30 mmHg after a five-unit bolus. Heart rate is also increased by a direct effect on the specific oxytocin receptors in the myocardium that affect atrio-ventricular conduction.

These haemodynamic changes peak within one minute of syntocinon administration and return to baseline within about five minutes. The rapidity of the changes is pertinent because the noninvasive blood pressure cycle is often set to two-minutely or more and such changes can be underestimated or missed altogether. Studies recording invasive blood pressure have been better able to define the scale of the haemodynamic changes.

Coronary artery disease is uncommon in women of childbearing age, however, myocardial ischemia can occur in its absence. Syntocinon-related hypotension and tachycardia can upset the balance between myocardial oxygen supply and demand sufficiently to induce ischemia. Syntocinon also has a vasoconstrictive effect in coronary vessels. In some studies, over 50 per cent of women demonstrated ST segment changes due to the combination of haemodynamic disturbance and coronary vasoconstriction. Nausea and vomiting can result from these sudden haemodynamic disturbances and flushing is due to cutaneous vasodilation. Syntocinon has a slight anti-diuretic effect and, when given in high doses or by continuous infusion, water intoxication can result. Since these adverse effects are dose-dependent, it seems prudent to use the minimum effective dose.

Why is haemodynamic disturbance a problem?

Haemodynamic fluctuations can be dangerous to vulnerable parturients and it is not always possible to determine vulnerability from the outset. A hypovolaemic patient or one with compromised cardiac function can respond lethally to a bolus of syntocinon. The confidential enquiry into maternal deaths in the United Kingdom from 1997 to 1999 highlighted this potential. In one case, the woman suffered multiple complications, including a high spinal and an undiagnosed placenta accreta. She was resuscitated from the high spinal and in response to blood loss from the adherent placenta, a request was made by the obstetrician for ten units of syntocinon. The anaesthetist voiced concern, as the systolic blood pressure at the time was 60 mmHg, however, ultimately this dose was given. Cardiac arrest ensued almost immediately and resuscitation was unsuccessful. Several issues were noted by the enquiry. Firstly, even in 1997, the recommended dose of syntocinon was five units, not ten. Secondly, the haemodynamic effects of syntocinon can be profound in the hypovolaemic patient. Thirdly, every medical practitioner administering any drug is responsible for ensuring that the dose is correct and appropriate. A request from another practitioner does not absolve the anaesthetist from this responsibility.

Are we giving too much?

The British National Formulary states that the bolus dose of syntocinon for caesarean section is five units given by slow intravenous injection, although 'slow' is undefined.

The 'ED90' is the dose of a drug that produces an effective response in 90 per cent of patients. A Canadian group studied 40 healthy women having elective caesarean sections at term, excluding women with risk factors for uterine atony. The bolus dose of syntocinon was chosen via an up-down method, based on the response of the previous patient. The obstetrician, blinded to the dose, determined uterine contraction to be either satisfactory or unsatisfactory. The ED90 for the initial bolus was estimated by logistic regression to be 0.35 units.

Another study published early this year aimed to determine the lowest effective bolus dose and randomised 75 patients to receive zero, 0.5, one, three or five units. There was no significant difference in the prevalence of adequate uterine tone between the groups at two minutes, when assessed by a blinded obstetrician. Based on the fact that patients who only received placebo developed adequate uterine tone, the ED90 was unable to be determined. However, when uterine contraction was scored on a verbal numerical scale, rather than simply adequate or inadequate, scores were significantly lower at two to three minutes in patients who received placebo.

'It seems that we should be giving less, giving it slowly and following with an infusion.'

A randomised double blind trial of 80 women undergoing elective caesarean section compared a bolus dose of either two units or five units, followed by an infusion of 10 units/hr. The group that received five units had greater fluctuations in heart rate and blood pressure, as well as a higher frequency of nausea and antiemetic use, with no difference in blood loss, uterine tone or request for additional uterotonics. In other words, the uterotonic efficacy of two units is similar to that of five units, whilst the haemodynamic effects are significantly less. It is also important to consider the speed of injection, as the adverse effects are greatly reduced when given slowly.

What if we don't give enough?

The importance of a well-contracted uterus cannot be ignored and we should also consider the risks of undertreatment. If an inadequate dose of syntocinon is chosen there is a risk of postpartum haemorrhage. In addition, alternative uterotonic agents may be given and these can be associated with an even greater incidence of adverse effects.

Intravenous syntocinon has a short half-life of five to ten minutes and the use of an infusion following the bolus dose has the advantage of maintaining uterine tone during the immediate postpartum period, when most primary postpartum haemorrhage occurs. In clinical practice, this is usually approximately 10 units/hr for four hours.

The anaesthetist's dilemma

The volume of local anaesthetic used in a spinal for caesarean section is approximately 2 ml and is carefully considered based on several factors. The difference of 0.1 ml can mean either an inadequate height of block or, conversely, a block that rises too high causing hypotension and vomiting. It can be frustrating to achieve an ideal dose, only to bolus the syntocinon and be left with a vomiting patient who will almost certainly believe that 'the anaesthetic' was to blame. Although our primary goal of patient safety should never be forgotten, if the same effect can be safely achieved with a smaller bolus and fewer side effects, then this should be our aim.

Where do we currently stand?

The current guidelines are clear: a five unit bolus of syntocinon given slowly is recommended. Clearly, ten units is excessive and potentially dangerous. The recent evidence is also strongly pointing to the fact that a much smaller bolus of around one unit is likely to be sufficient and safe.

It seems that we should be giving less, giving it slowly and following with an infusion.

There are clearly exceptions to the 'routine', including hypovolaemic patients and those with pre-existing cardiovascular disease in whom syntocinon should be used extremely carefully, if at all. Equally, there are women with risk factors for uterine atony who may require greater doses.

The lines of communication should be left open and dosing decisions should be made by both obstetricians and anaesthetists, ensuring that the major issues for a given patient are mutually understood.

References and further reading

- Wedisinghe L, Macleod M, Murphy D. Use of oxytocin to prevent hemorrhage at caesarean section – A survey of practice in the United Kingdom. *Eur J Obstet Gynecol Reprod Biol.* 2008; 137: 27-30.
- Carvalho J, Balki M, Kingdom J. Oxytocin requirements at elective caesarean delivery: A dose finding study. *Obstet Gynecol.* 2004; 104: 1005-1010.
- Svanstrom M, Biber B, Hanes M. Signs of myocardial ischaemia after injection of oxytocin: a randomized double-blind comparison of oxytocin and methylergometrine during caesarean section. *Br J Anaes.* 2008; 100: 683-689.
- Jonsson M, Hanson U, Lidell C. Norden-Lindeberg S. ST depression at caesarean section and the relation to oxytocin dose. A randomized controlled trial. *BJOG* 2010; 117: 76-83.
- Thomas J, Koh S, Cooper G. Haemodynamic effects of oxytocin given as IV bolus or infusion on women undergoing caesarean section. Br J Anaes. 2007; 98: 116-119.
- Sartain J, Barry J, Howat P, McCormack D. Intravenous oxytocin bolus of two units is superior to five units during elective caesarean section. *Br J Anaes.* 2008; 101: 822-826.
- Butwick A, Coleman L, Cohen S. Minimum effective bolus dose of oxytocin during elective caesarean delivery. Br J Anaes. 2010; 104: 338-343.

Want to locum in rural Australia?

Register as a SOLS Locum!

Do you want to: Help your rural colleagues? Keep up your obstetric skills? Experience rural Australia? For more information: www.ranzcog.edu.au/sols/index.shtml (03) 9412 2912 | sols@ranzcog.edu.au

The Specialist Obstetrician Locum Scheme is funded by the Australian Government

Epilepsy in pregnancy



Dr Sandra Lowe FRACP

The epilepsies comprise a group of disorders characterised by recurrent seizures and classified according to clinical or specific electroencephalographic (EEG) features.

Although epilepsy is the most commonly encountered neurological disease in pregnancy, it is still relatively rare, with a prevalence of 0.6 to 1.0 per cent. Medical therapy utilising antiepileptic drugs (AEDs) is the most common form of treatment, although surgery or no treatment may have a role in specific cases.

Preconception care

Ideally, all women with epilepsy should undergo counselling prior to pregnancy. The principles of drug review at this time are:

- 1. Withdraw any unnecessary medication where possible.
- 2. Use monotherapy where possible.
- 3. Use the smallest effective dose of medication.
- 4 Withdraw drugs with potential adverse fetal effects and replace with safer drugs if possible.

In the case of epilepsy, tampering with stable and effective medication does carry hazards for the patient. AED therapy is usually chosen with great care by the patient's neurologist and often after the failure of other drugs. For these reasons, it is advisable to consult with the neurologist before making any substantive change.

Preconception counselling may identify women who have been seizure-free for a number of years on minimal medication, particularly those with a normal EEG and normal cerebral imaging. In these cases, careful weaning of therapy over six months prior to pregnancy may be entirely appropriate, accepting a small risk of recurrence of seizures.

All women with epilepsy taking AEDs should receive high dose folate supplementation (5 mg), although the evidence for this being beneficial is limited. During pregnancy, antenatal screening for neural tube and cardiac defects with spine and nuchal translucency ultrasound should be performed at 12 to 13 weeks of amenorrhoea. Maternal alpha-fetoprotein testing at 16 weeks is less helpful. A careful 18 to 20 week morphology scan should be performed in a recognised centre. It is important to ensure the sonographer is aware of the patient's additional risks for each of these scans. Most clinicians agree that, for both the mother and her fetus, the benefits of controlling seizures outweigh the potential risks associated with the AEDs. Monotherapy is associated with significantly fewer adverse fetal effects than polytherapy. The genetics of epilepsy are complex and advice regarding heritability should be guarded.

Pregnancy

A minority of women with epilepsy experience an increase in seizure frequency during pregnancy, particularly those with poorly controlled epilepsy prior to pregnancy. A prolonged seizure-free period prior to pregnancy (nine to 12 months) is associated with a high likelihood of remaining seizure-free during pregnancy. A small minority of women will deteriorate during pregnancy and this may be explained

by changes in AED pharmacokinetics, as well as vagaries of patient compliance. In practice, tiredness, nausea, vomiting, sleep disturbance and emotional stress may be important factors affecting seizure frequency during pregnancy. These factors may be magnified around the time of delivery and immediate puerperium, especially with sleep deprivation that is almost inevitable at this time.

Whether seizure disorders themselves may cause an increase in congenital malformations or adverse pregnancy outcomes remains controversial. Seizures have been reported to cause significant fetal heart rate decelerations, presumably secondary to maternal hypoxaemia and acidosis. Single seizures are unlikely to be a significant problem whilst modern treatment of status epilepticus has reduced fetal mortality substantially. Trauma during seizures can result in placental abruption or uterine injury, as well as the usual maternal hazards of self-injury and aspiration pneumonitis. Recent analysis of the association between epilepsy and adverse pregnancy outcomes such as preeclampsia, lower birth weight, caesarean delivery, late pregnancy bleeding, premature labour and stillbirth failed to demonstrate any increased risk.¹

Antiepileptic drugs

During pregnancy, a number of factors influence drug levels, including altered absorption, protein binding, metabolism, renal clearance and non-compliance. Overall, there is a tendency to require an increase in AED dose during pregnancy. AED levels should be monitored by observation of the clinical response and regular (three-monthly) plasma unbound drug levels, where these are available. As the adverse effects of AEDs are believed to relate to peak levels, a change to smaller doses at more frequent intervals or sustained release preparations should be considered. Treatment should be maintained around the time of delivery and dosage reassessed postnatally, as toxicity may occur if the gestational higher dose is continued in the puerperium.

For most AEDs, transplacental drug transfer results in significant fetal exposure. This is true for both the older AEDs and newer agents. The use of AEDs during pregnancy has been associated with an increased incidence of congenital malformations, both major and minor, and neurocognitive impairment. Estimates of risk vary, but a recent study indicates 4.5 per cent (OR 2.6) frequency for AED monotherapy in utero exposure and 8.6 per cent (OR 5.1) for AED polytherapy.² This compares with a background rate of 1.6 to 2.1 per cent. Determining the magnitude of these risks is extremely difficult as epidemiological data are highly variable and large, randomised prospective studies are neither available nor feasible. Observational data from a number of national prospective drug registers is gradually becoming available and is starting to contribute significantly to our knowledge in this area (see Table 1).

Strong epidemiological data exist implicating valproate (one to two per cent)³ and carbamazepine (0.2 to one per cent)⁴ as particular risk factors for neural tube defect, specifically spina bifida. The predominant malformations seen in women with epilepsy are cleft lip or combined cleft lip and palate (valproate 1.5 per cent, phenytoin 1.2 per cent, carbamazepine 0.4 per cent, lamotrigine 0.2 per cent) and cardiovascular malformations (phenytoin 1.2 per cent, valproate 0.7 per cent, carbamazepine 0.7 per cent).

Hypospadias and gastrointestinal defects are also overrepresented. The relative risk of facial clefting has been estimated at 2.7 for untreated epileptics and 4.7 for woman taking anticonvulsants. Although the relative risk of congenital malformation with valproate is higher than with alternative agents, overall, the risk of monotherapy is low. This should be taken into account when changes in therapy are contemplated, especially if other therapies have previously been unsuccessful.

Very limited information is available about the newer AEDs such as levetiracetam, topiramate, gabapentin, vigabatrin and oxycarbazepine. Any patients exposed to these agents should be enrolled in prospective registries to allow appropriate data collection.

Almost all of the older AEDs (benzodiazepines, carbamazepine, phenobarbitone or primidone, phenytoin, trimethadione, valproate) have been associated with the fetal AED syndrome consisting of minor malformations and dysmorphism, for example, hypertelorism; low-set abnormal ears; short neck with low posterior hairline; bilateral single transverse palmar creases; and distal digital hypoplasia. The incidence of this syndrome has varied with the population studied, but in general, the risk appears to be about ten per cent in exposed fetuses. Aspects of this syndrome also appear to occur more commonly in children of women with epilepsy, even when untreated. Many of these features improve with age.

The use of AEDs, particularly valproate, but also phenytoin (not carbamazepine), has been associated with neurocognitive abnormalities in the offspring of women with epilepsy. The neurocognitive risk associated with valproate monotherapy (and, similarly, the rates of major malformation) appear to be doserelated, with adverse outcomes only increasing when the total daily dose is above 1100 mg. Animal studies suggest these cognitive effects are mediated by accelerated neuronal apoptosis. Newer data have failed to show any increase in the risk of haemorrhagic disease of the newborn where standard neonatal vitamin K therapy (1 mg) is administered.

Delivery and postpartum

Stress, sleep deprivation, pain, hyperventilation and erratic absorption of AEDs contribute to an increased risk of seizures during the emotional turmoil of labour and the immediate postpartum period. The route of delivery should be selected on obstetric grounds, although precautions should be taken whatever the mode of delivery. All women with epilepsy should have a canula inserted on admission to the delivery suite. AEDs should be continued at pregnancy doses during and immediately after delivery, but reduced

Table 1.

Malformation rates for monotherapy: absolute numbers (%) based on prospectively enrolled women.⁵

Registry	Valproate	Carbamazepine	Lamotrigine	Phenytoin
Australian	22/166 (13.3)	7/234 (3)	21/146 (1.4)	1/31 (3.2)
UK	44/715 (6.2)	20/900 (2.2)	21/647 (3.2)	3/82 (3.7)
North American	16/149 (10.7)	22/873 (2.5)	15/564 (2.7)	3/82 (3.7)
Finnish	28/263 (10.6)	22/805 (2.7)		
Swedish	26/268 (9.7)	28/703 (4.0)	4/90 (4.4)	7/103 (6.8)
Glaxo			22/802 (2.7)	

stepwise to prepregnancy doses over the first two or three postnatal days, as the increased requirements of pregnancy abate quickly. Where oral therapy is not possible, intravenous preparations of phenytoin, initially 10 to 15 mg/kg over approximately 20 minutes, then 100 mg IV every six to eight hours, may be given. Intravenous valproate at a dose of 400 to 800 mg (up to 10 mg/kg) by slow IVI, then 1 to 2 mg/kg/hr (max 2500 mg/day) is an alternative, particularly postpartum.

'Preconception counselling is important for any chronic medical disorder, including epilepsy. It is useful to encourage the woman to return for this purpose when she is considering another pregnancy, to review the state of her general health, her epilepsy and its treatment.'

If seizures do occur, appropriate supportive treatment with protection of the airway, oxygen and monitoring of the fetal heart rate should be commenced. Most seizures are self-limiting, however, if seizures are prolonged, treatment with intravenous clonazepam (1 to 2 mg over two to five minutes), lorazepam or diazepam (2 mg/min to max 10 mg) will usually terminate the seizure. Treatment with these drugs may cause maternal respiratory depression and fetal and neonatal sedation. Careful clinical assessment is required to exclude other causes of seizure in labour such as eclampsia.

The days following delivery are a time of particular risk for recurrent seizures. Adequate pain relief, assistance with mothercrafting, and measures to allow the new mother as much rest as possible will reduce the risk of postpartum seizures. Most AEDs are considered compatible with breastfeeding although the newborn should be observed for sedation. Levetiracetam, lamotrigine, topiramate and gabapentin are transferred into breastmilk at greater levels than other AEDs, but appear to be rapidly excreted by the newborn. Preconception counselling is important for any chronic medical disorder, including epilepsy. It is useful to encourage the woman to return for this purpose when she is considering another pregnancy, to review the state of her general health, her epilepsy and its treatment.

References

- Harden CL, et al. Practice parameter update: management issues for women with epilepsy – focus on pregnancy (an evidence-based review): obstetrical complications and change in seizure frequency: report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society. *Neurology* 2009 Jul 14; 73(2):126-32.
- Holmes LB, Harvey EA, Coull BA, et al. The teratogenicity of anticonvulsant drugs. N Engl J Med. 2001; 344: 1132-1138.
- Lindhout D, Schmidt D. In utero exposure to valproate and neural tube defects. *Lancet* 1986; 1(8494):1392-3.
- 4. Kallen AJ. Maternal carbamazepine and infant spina bifida. *Reprod Toxicol.* 1994; 8; 203-5.
- 5. Meador KJ, *et al.* Pregnancy registries in epilepsy: a consensus statement on health outcomes. *Neurology* 2008; 71(14):1109-17.

Primary amenorrhoea



Dr Sonia Grover FRANZCOG

When one is referred a teenager with primary amenorrhoea, there is often no clear distinction made between those teenagers who have pubertal delay and those who have menarchal delay.

The age at which one begins to be concerned by the lack of pubertal development is usually 14 years and for primary amenorrhoea is 16 years. The caveat for the menstrual delay is that menarche should occur within four years of breast development beginning. We are all aware there are familial patterns to these events, so that some families are simply late starters.

The causes of primary amenorrhoea include a long list of conditions, many of which general gynaecologists will rarely see in their working life. Like most lists, it is helpful to have some tricks to help one recall the possibilities.

There are various systems for helping one sort the possible differential diagnoses of primary amenorrhoea and hence to help you recall the possible causes for these young women. One system is a flow chart for causes of primary amenorrhoea dividing the diagnostic possibilities on the basis of height (less or greater than 150 cm). This has some clinical value in theory, particularly as you are on the lookout for clues from the moment you call the teenager into your consulting room. However, apart from Turner's syndrome (TS), I am not sure that I have seen any other conditions where height has helped to guide my diagnostic thinking and decisions. Besides, those girls who reach gynaecologists with primary amenorrhoea who turn out to have TS are usually not particularly short, as they have mosaic TS or one of the other variations. Those who do have a short stature have almost invariably been diagnosed in childhood, have been under the care of paediatric endocrinologists and all the relevant information is in the referral letter. Yes, there are other diagnoses where short stature may help guide your clinical processes. However, these are mostly relevant if you are working in those parts of the world where there are limited resources and medical services resulting in seeing a teenager with chronic malnutrition; untreated congenital adrenal hyperplasia (in whom there will be some evidence of virilisation); panhypopituitarism with growth hormone deficiency (where most likely they will also be thyroid hormone deficient and hence will have intellectual delay, as well as primary amenorrhoea); or Cushing's syndrome (excess cortisol).

In Australasia, these young people would have presented and been under medical care well before the issue of amenorrhoea arises. In reality, the teenager with other causes of short stature would have the details regarding their past history of head irradiation for cancer treatment, chronic renal disease requiring high dose steroids, or previous growth hormone and thyroxine treatment (for panhypopituitarism), all in their accompanying referral letter, which removes the diagnostic challenge for amenorrhoea and short stature.

Most often, these teenagers reach us with the referral letter saying, 'Thank you for seeing this teenager with primary amenorrhoea,' combined with some helpful investigation results. Usually, this includes the follicle-stimulating hormone (FSH), luteinising hormone (LH) and thyroid-stimulating hormone (TSH). Often, there will be a pelvic ultrasound as well. When the ultrasound report says 'no uterus seen' or 'rudimentary uterus only', it is essential to interpret this information in the context of whether estrogen exposure has occurred. For the teenager who has had no pubertal estrogens and no breast development at all, the uterus may be tiny and thus a challenge for both ultrasound and MRI to visualise. In the same way, as we do not expect either of these modalities to see a normal fallopian tube, neither should we expect a prepubertal uterus to be visualised. As gynaecologists primarily involved in the care of adult women, it is rare to have the opportunity to see just how small the non-estrogenised uterus in prepubertal girls actually is, but laparoscopies have resulted in reports of 'no uterine structure seen'. Yet, these young women, with estrogens, will subsequently menstruate and may carry a pregnancy.

Returning to the investigations that come with the teenager, the FSH and LH give us clear clues. This immediately allows us to separate the teenagers who have low gonadotropin levels and have 'not switched on', from the teenagers with high levels with ovarian or gonadal failure, and the third group where the results are within normal range for the reproductive years.

Even here things are not always easy. Despite your effort to collect visual clues to help guide you in the assessment of the teenager with low gonadotropins, the anorexic girl is often wearing loose clothing to hide her skeletal body shape and lack of breast development. For the anorexic, your careful history and examination revealing the low pulse rate, postural hypotension, lanugo and low BMI will confirm the diagnosis. With the low pulse rate and postural hypotension, you will be organising an urgent referral to an adolescent physician. Alternatively, your systematic questions regarding pubertal development may not reveal the fact that your patient with hypogonadatrophic hypogonadism is a high-level athlete, unless you specifically ask questions regarding 'activities' as part of your 'HEADSS' assessment (see Table 1). This information was probably not mentioned in the referral letter. For the high-level athlete, your careful history combined with the FSH and LH will make the diagnosis, but checking thyroid and prolactin levels (the latter of which is often not done prior to referral) ensures that you do not miss any significant and correctable causes.

Table 1. HEADSS assessment

This is a useful framework for history-taking in adolescents, commencing with the least threatening topics. Framing the questions in a broad manner and avoiding questions that require a 'yes' or 'no' answer is important.

HEADSS assessment

Home or housing Education and employment Activities Drugs Sexual activity and sexuality Suicide and depression screen Although low gonadotropins make up about one-third of delayed puberty, the physiological delay, weight loss and exercise are the commonest causes. A challenging group are the 'eating disorders not otherwise specified' group - the teenagers who do not have the body image distortion, exercise guite a lot and 'eat healthy'. Their gonadotropins are usually low, but not in the prepubertal range. It is only on very close questioning that you realise that their food intake (of lettuce leaves and no carbohydrates) does not match their exercise levels. A dietitian and the adolescent physician are invaluable in assisting with these young women, who are hard to convince that there is a problem, except that their bodies are clearly saying that all is not well as they are amenorrhoeic without any other explanation.

Where there is an inability to produce estrogens, the FSH will be elevated (hypergonadotropic hypogonadism). This may be a consequence of premature ovarian failure related to TS, or alternatively may be due to what is now more often termed premature ovarian insufficiency (POI), where the karyotype is normal (Fragile X syndrome needs to be excluded and you need to ask specifically for this). Another possibility is a disorder of sex development (DSD). This expression has replaced the term 'intersex' and applies to those conditions where there is atypical chromosomal, gonadal or anatomical sex development. Where the karyotype is 46XY and where there is no virilisation and no pubertal change, the condition will most likely be 46XY gonadal dysgenesis. In the presence of any Y material, either in the context of a mosaic TS or in a young woman with 46XYGD, it is important to remember that a gonadectomy is necessary to avoid the risk of malignant change that occurs in at least 30 per cent of these individuals.

'A multidisciplinary team for the care of the patient with many of these conditions is essential...'

In those young women who present with primary amenorrhoea but have some breast development (therefore do not appear to have pubertal delay), the range of diagnoses includes some of the above. The teenager with anorexia, or who is a high-level athlete, or who has POI or TS, may have commenced pubertal development, but then pubertal changes stopped and they may present with primary amenorrhoea. Another 46XY DSD that is usually associated with elevated gonadotropins but breast development is androgen insensitivity syndrome. In these young women, despite good breast development, there is scant pubic and axillary hair.

Then there are those teenagers who appear to have had a completely normal puberty, with normal secondary sex development but have not menstruated. Those with obstructive anomalies (imperforate hymen, transverse septum, cervical agenesis) will have presented with pain rather than primary amenorrhoea. Thus, you are left with those who have an absent uterus and the feature that will help you clarify the diagnoses is the presence or absence of hirsuitism or other virilisation. In the absence of virilisation, these will include the teenagers with mullerian agenesis who have normal ovaries (well seen on ultasound with normal follicles). For those with hirsuitism and acne, the most likely diagnosis is polycystic ovarian syndrome (PCOS). More marked androgenisation will lead to the consideration of diagnoses such as congenital adrenal hyperplasia (CAH) and other DSDs, including 17-ketosteroid reductase deficiency (17-KSRD) or 5-alpha reductase deficiency (5-ARD), where some clitoromegaly is likely to be present and inguinal gonads potentially palpable.

A multidisciplinary team for the care of the patient with many of these conditions is essential, whether it is the physiotherapist or nurse practitioner who assists with the care of the young woman who is making her vaging with dilators; the counsellor who assists with the discussions of being infertile for the young woman with TS, 46XYGD or vaginal agenesis; the endocrinologist who helps untangle 5-ARD from 17-KSRD; or our colleagues who will assist in reproductive technologies with IVF, using donor eggs for the young woman without functioning ovaries or who requires a surrogate.

We do need to keep abreast of the changing issues with these diagnoses. The level of current discussion and concern regarding offering donor eggs to women with TS, in light of their risk for aortic dissection despite optimal cardiac monitoring, poses new dilemmas and this was not a topic I discussed with my patients a few years ago.³ Neither would I have contemplated seeking advice and support from a clinical ethics team prior to performing a gonadectomy in the teenager with a DSD and testes a few years ago, but I would do so now.

So primary amenorrhoea now poses not only a challenging list of diagnoses to remember, but challenging new problems. As many of the diagnoses are uncommon and/or complex, it is worth remembering that colleagues are there to help or share these challenges with you.

References

- 1 Speroff L, Fritz MA. Chapter 11. Clinical Gynecologic Endocrinology and Infertility Seventh Ed. Lippincott Williams & Wilkins, 2005, Philadelphia.
- 2. Goldenring J, Cohen E. Getting into adolescents heads. Community Pediatrics July 1988: 75-80.
- 3. Carlson M, Silberbach M. Dissection of the aorta in Turner's syndrome: two new cases and review of 85 cases in the literature. J Med Genet. 2007; 44:745-749.

Need a break?

Apply for a SOLS locum now!

If you are a Specialist or GP Obstetrician in rural and remote Australia (ASGC-RA 2 to 5) you may be entitled to receive the following funding for locum relief (per financial year):

- 14 days of locum support
- locum travel costs
- locum travel time

Providing funding to support rural Specialist and GP **Obstetricians**

More information and application forms are available from: www.ranzcog.edu.au/sols/index.shtml (03) 9412 2912 | sols@ranzcog.edu.au

The Specialist Obstetrician Locum Scheme is funded by the Australian Government



Case study: how many embryos?



Andrew Took National Manager Medico-legal Advisory Service Avant

The courts examine the nature of a treating team's duty of care to a patient undergoing embryo transfer and the degree of responsibility borne by the consultant O and G.

In the recent case of G and M *v* Armellin¹, the ACT Supreme Court of Appeal considered a consultant's duty of care to a patient in the context of in vitro fertilisation (IVF) treatment performed in a private fertility facility. The decision is interesting in regards to how the courts - both at the primary hearing and the appeal – evaluated the relevant professional responsibility owed by a consultant as compared to that of the rest of the treating clinical team.

Background

Ms G and Ms M first consulted Dr Robert Armellin on 17 December 2002 seeking help for Ms G to become pregnant. Initially, they sought to have her impregnated by artificial insemination using donor sperm. After three unsuccessful attempts using artificial insemination, they were enrolled in an IVF program. That program involved the assistance of the Canberra Fertility Centre ('the Centre').

In July 2004, Ms G gave birth to non-identical twin girls following successful IVF by Dr Armellin on 12 November 2003. Ms G and her partner Ms M claimed they only wished to have one child, that they told Dr Armellin this, and alleged the doctor was negligent in inserting two embryos instead of one during the IVF procedure. Ms G and Ms M sued Dr Armellin for damages including the cost of raising the second child. However, they did not sue the fertility clinic where the procedure took place and Dr Armellin did not join the clinic as a third party to the proceedings.

At the trial², Bennett J of the ACT Supreme Court found that Dr Armellin had not been negligent in the context of the Centre's existent practice of determining the number of embryos to be implanted. Ms G and Ms M appealed against this decision. The ACT Court of Appeal found that Dr Armellin was ultimately responsible for the embryo transfer procedure and had breached his duty of care by failing to confirm the number of embryos for transfer with the Centre staff.

Dr Armellin sought leave to appeal to the High Court of Australia. High Court judge Heydon J noted that the Court of Appeal differed from the trial judge on one point – whether Dr Armellin was negligent in permitting more than one embryo to be transferred contrary to the wishes of Ms G. In dismissing³ Dr Armellin's application for appeal, Heydon J found that the contest was a factual one, that no question of law meriting an appeal had been identified, and that the reasoning of the Court of Appeal had not been successfully attacked.

Recounting the facts

The following is a summary of the factual findings the Court of Appeal relied upon in reaching its decision.

At Ms G's and Ms M's consultation with Dr Armellin on 11 August 2003 the following occurred:

- Ms G told Dr Armellin that she did not want a multiple pregnancy.
- Dr Armellin told the couple there was a risk of multiple pregnancy and advised them of the rate of that risk in the event of the transfer of two embryos.
- Dr Armellin told the couple that the chances of successfully becoming pregnant diminished unless more than one embryo was transferred.
- Ms G and Dr Armellin discussed the possibility that one embryo could produce more than one child. Ms G accepted that risk but understood it to be a low risk.
- Ms G and Dr Armellin discussed the number of embryos to be transferred. Ms G told Dr Armellin that she would let him and the Centre know before the embryo transfer whether she wanted one or two embryos transferred. No decision was made at this consultation about that matter.

On 12 August 2003, Dr Armellin wrote to the couple's referring practitioner about the consultation which occurred on the previous day. The letter said '...one or two embryos will be transferred...' and then continued, 'At this stage [G] is not sure as to how many embryos she wishes to be transferred but she will let us know before an embryo transfer...'.

Ms G and Ms M attended the Centre on 11 September 2003. Ms G completed a form that day, concerning the IVF program at the Centre. Ms G filled in the form and signed a request for IVF or gamete intrafallopian transfer. A nurse at the Centre told Ms G and Ms M to indicate on the form that 'up to two' embryos were to be transferred and to let the Centre know any time up to the procedure as to how many they wanted transferred. The signed form referred to 'embryo transfer of one to two embryos'.

On 10 November 2003, Ms G underwent a procedure to harvest eggs produced after the administration of hormone medication designed to stimulate the production of eggs. Six eggs were harvested. Five eggs were successfully fertilised with donor sperm. Before implantation there were only four healthy embryos available for implantation.

On 11 November 2003, a discussion occurred between Ms G and someone from the Centre about the number of available embryos. Ms G did not tell that person how many embryos she wanted transferred at that time.

Ms G was admitted to the John James Memorial Hospital, where the Centre was located, on 12 November 2003. Ms G and

Ms M did not tell the Centre, nor were they asked by the Centre, how many embryos they wanted transferred. Ms G decided to have one embryo transferred after she arrived in the theatre at the hospital.

Immediately before the procedure and before Ms G was sedated, she told Dr Armellin that she only wanted one embryo transferred. Ms G was then placed under sedation. Prior to the procedure, Dr Armellin completed an operation record which said: '...embryo transfer one embryo under sedation'. At that time, Dr Armellin believed that one embryo was to be delivered by the embryologist for transfer, but accepts that two were actually transferred.

Neither the embryologist, nor the Centre, had received notice from Dr Armellin of Ms G's decision for only one embryo to be inserted. Dr Armellin believed that the number to be transferred had been organised between the couple and the Centre. While the embryologist inserted the embryos, Dr Armellin was responsible for the transfer procedure. The Centre assumed that two embryos would be required in circumstances where:

- The Centre had not been in contact with the couple concerning the required number.
- There was no communication between Dr Armellin and the Centre or the embryologist on the required number of embryos to be inserted.

The first decision – findings of the primary judge on Dr Armellin's alleged negligence

Bennett J⁴ found that these IVF procedures occurred within a system of divided responsibility which involved the participation of a number of separately qualified people. After an analysis of the system in place, Bennet J found that the Centre should have ensured that the embryologist provided the requested number of embryos as nominated by the patient. Bennet J concluded⁵ that Dr Armellin was entitled to rely upon Centre staff to do what they were responsible for, namely to provide the number of embryos as nominated by the patient.

Bennet J^4 found that it was reasonable for Dr Armellin to have:

- Relied upon the Centre to act in accordance with their procedure;
- Confirmed the number of embryos to be implanted with Ms G; and
- To notify the embryologist accordingly.⁶

Accordingly, Bennet J found Dr Armellin was not negligent in failing to personally tell the embryologist just prior to the procedure of the number of embryos to be inserted.

Decision overturned – the reasoning of the ACT Supreme Court of Appeal

In a unanimous judgment the Court of Appeal overturned the decision of the trial judge. The Court of Appeal, while noting the involvement and responsibilities of the Centre and its staff, found that Dr Armellin was ultimately responsible for the implantation procedure, commenting: 'If there was a firm system in place requiring Ms G to have informed the staff of the Centre the day before the procedure about the number of embryos to be transferred, Ms G should have been told in clear terms about its existence. She was not told that at all. She was told that she could let Dr Armellin know before the transfer about the number of embryos to be transferred, as confirmed in Dr Armellin's letter of 12 August 2003. If that was not the case, Dr Armellin should not have said so in that letter. If a system was in place, Dr Armellin varied it.'⁷

The Court of Appeal found that this was not a situation where Dr Armellin could rely upon the Centre and its systems to determine the number of embryos to be implanted. The Court concluded that: 'It was negligent, in the circumstances, for Dr Armellin simply to assume that the embryologist was complying with the wishes of the appellants. That is especially so, given the arrangement about notifying Ms G's decision as confirmed in the 12 August 2003 letter and the absence of evidence of the appellants ever making a firm choice before the procedure about whether one or two embryos should be transferred.'⁸

Conclusion

The decision of the Court of Appeal provides further⁹ useful guidance on understanding the factors a court will find relevant in determining various responsibilities and respective liabilities of a treatment team when assessing a medical negligence claim. The timing of when the final decision by the patient could be communicated to the Centre and the consultant was critical to ensuring the patient's wishes and expectations could be met. The ultimate responsibility of the consultant was highlighted by the Court of Appeal in this case. However, in the author's respectful view, the decision does not necessarily mean that a consultant will be automatically liable for the failings of another member of the treating team solely by virtue of being the senior clinician.

The information in this article is general information relating to legal and/or clinical issues within Australia (unless otherwise stated). It is not intended to be legal advice and should not be considered as a substitute for obtaining personal legal or other professional advice or proper clinical decision-making having regard to the particular circumstances of the situation.

Footnotes

- 1. [2009] ACTCA 6 (1 May 2009).
- 2. G and M v Armellin (2008) 219 FLR 359.
- 3. Sydney Robert Armellin v CLG & Anor [2009] HCASL 275 (9 December 2009).
- 4. Above note 2 at [62].
- 5. Above note 2 at [91].
- Above note 2 at [91].
- 7. Above note 1 at [34].
- 8. Above note 1 at [36].
- 9. The decision of the NSWCA in *Elliot v Bickerstaff* [1999] NSWCA 453 involved a claim arising from a retained surgical swab and provided authority for the proposition that a consultant may reasonably rely upon other members of the treating team to perform the functions to which they have responsibility.

CPD Points for Past Meetings

Have you attended a conference and don't know how many CPD points to claim?

Download the 'point for past meetings' list from the website and check if your meeting is listed.

www.ranzcog.edu.au/meetingsconferences/ pastmeetings.shtml

Points for attendance at all RANZCOG accredited meetings are detailed on this list as well as some of the larger overseas meetings.

If you are attending an overseas meeting that is not included on this list please send a copy of the scientific program to:

Val Spark

CPD Senior Coordinator (t) +61 3 9412 2921 (f) +61 3 9419 7817 email: vspark@ranzcog.edu.au



 $O \sigma a$ 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.



How would you manage the delivery of a healthy 39-year-old woman with a singleton pregnancy following seven years of infertility and IVF treatment?

Dr David Molloy

FRANZCOG Clinical Director **Queensland Fertility Group**

The concept of unequal value for fetal outcome seems a incongruous. We have long been taught and indeed preached, that all babies are equally precious and each deserves the same chance at optimum outcome. This is true in principle but not always practised. Parents, in particular, have different views as to how 'precious' their baby may be. Some smoke, drink, engage in other high-risk activity or expose their baby to higher risks of birth trauma or harm by delivery choice or mode, for example, homebirthing. Invariably, obstetricians categorise risk. Unequal amounts of work may be put into the safe delivery of a low versus high-risk pregnancy. How then do you categorise a patient who may be having her only chance at a child? Is the fact that this pregnancy is likely to be a 'one-off' an additional factor which should alter your management beyond the usual risk parameters of age?

This particular case represents a hard won pregnancy with a low chance of replacing the baby if a disaster occurs. The Australian Institute of Health and Welfare (AIHW) data¹ suggests a live birth rate for a repeat IVF cycle at 39 to 40 years of age of nine per cent for each repeat future cycle of treatment. Seven years of infertility is hardcore infertility with a low chance of natural conception and a reliance on reproductive technology to conceive.

It therefore makes sense to give this patient the best possible chance to take home a live healthy baby, the trade-off being more interventions hoping to shade the odds wherever possible towards least risk. In my delivery days, I would class these pregnancies as high premium as well as high-risk. Many of these mothers have no objections to additional intervention - their only goal is to take a healthy baby home in their arms. Interventions in the last 12 weeks

Dr Sue Jacobs FRANZCOG



Optimal management of this woman's delivery begins at the first antenatal visit, at which time a thorough history needs to be taken in order to assess her level of risk in addition to her age of 39, infertility and IVF, each of which is associated with complications of pregnancy and delivery. Establishing a good rapport at the outset is essential as it will be

important that she feels confident with the advice given during pregnancy and delivery. She will receive much information about her risks and will need reassurance that with careful antenatal care and appropriate management the risks can be minimised.

of the pregnancy would include a double dose of betamethasone at 28 to 30 weeks and an ultrasound scan at 32 and 36 weeks for fetal assessment and intrauterine growth restriction. I would offer weekly visits from 32 or 34 weeks. These interventions lack an evidence base, like so much of obstetrics.

The key to risk reduction is to have a planned delivery by 39 weeks. Stillbirth risk increases exponentially from 37 to 41 weeks by a factor of 3 (1.3 to 4.6 /1000).² There is no gain in exposing this baby to that risk after 38 weeks. If the patient was very eager, an induction and labour could be carried out under closely monitored circumstances if the cervix was very favourable, with quick resort to caesarean section as soon as any risk factor or aberration in the course of the labour arises, for example, any meconium, suboptimal CTG trace, failure to progress, etc.

Elective caesarean section with regional anaesthesia is an ideal mode of delivery for this patient. A 39-year-old primigravida is unlikely to have a favourable cervix at 38 to 39 weeks and this group often labours poorly. A caesarean section at 39 weeks offers a defined endpoint and lowest risk outcome for the baby, with a comparable surgical risk for the mother to that of a vaginal delivery in a primiparous patient. In my recent obstetric days, my caesarean section rate was over 90 per cent for IVF pregnancies aged 38 years or older and all were delivered by 39 weeks. No disasters, thank goodness. Caesar rules!

References

Wang, et al. Assisted reproductive technology in Australian and New Zealand 2007. Series No 13 Cat. No. PER47 page 11. Hankins GD, Clark SM, Munn MB. Caesarean section on request at 39 weeks: impact on shoulder dystocia, fetal trauma, neonatal encephalopathy and intrauterine fetal demise. Semin Perinatol. 2006 Oct; 30(5):276-87.

Singleton IVF pregnancies are at higher risk of preterm birth and low birth weight babies compared to spontaneously conceived singleton pregnancies.¹ Subfertility/infertility per se appears to have an adverse impact on pregnancy outcomes, independent of ART/ IVF.² Maternal age over 35 is associated with lower birth weight (OR 1.8) and higher rates of preterm delivery (OR 1.7), when controlling for smoking, parity, multiple gestation and maternal medical disease.³ Stillbirth rates increase progressively with maternal age over 35 and the risk is magnified after 38 weeks gestation, sharply increasing after 40 weeks gestation.⁴ However, it must be remembered that the absolute risk of stillbirth in developed countries is low. Compared with women under 35, a woman aged 39 is more likely to be affected by hypertension (preexisting and/or pregnancyrelated), diabetes (pregestational or gestational) and higher BMI. Dysfunctional labour increases in a linear fashion with advancing maternal age.⁵

This woman's pregnancy should be managed with extra vigilance due to her high risk factors. As described she has no underlying health problems and normal pre-pregnancy BMI. Antenatal screening tests, including 75 g glucose tolerance tests at 16 to 18 weeks and 28 to 30 weeks, were normal. She has no other obstetric complications.

Fetal growth should be monitored carefully, both clinically at each visit, and sonograghically at 32 to 34 weeks gestation, with subsequent serial scans if indicated. I would advocate vaginal birth if presentation is cephalic and fetal growth is satisfactory. The advantages and disadvantages of vaginal birth versus elective caesarean section in her particular case should be discussed in detail at 36 weeks. Induction of labour (IOL) at 38 weeks should be advised if there is evidence of intrauterine growth restriction, oligohydramnios or any antepartum haemorrhage, even if small. If the woman does not have spontaneous onset of labour (SOL) by 39 to 40 weeks gestation, we would have further discussion about IOL. I would have a low threshold for IOL around 40 weeks, if no earlier indication. Continuous CTG monitoring in active labour is advisable due to high risk factors, preferably with telemetry to promote mobilisation. I would have a low threshold for caesarean section in labour. If it was decided to wait until 41 weeks gestation hoping for SOL, a formal ultrasound at 40 weeks should be considered and the importance of adequate fetal movements each day emphasised.

Management decisions regarding delivery should always be made together with the woman and her partner, with clear explanation of reasons for advice, listening carefully to each woman's hopes and concerns.

References

- Schieve LA, Meikle SF, Ferre C, et al. Low and very low birth weight in infants conceived with use of assisted reproductive technology. N Engl J Med. 2002; 346:731.
- Romundstad LB, Romundstad PR, Sunde A, et al. Effects of technology or maternal factors on perinatal outcome after assisted fertilisation: a population-based cohort study. *Lancet* 2008; 372: 737.
- Tough SC, Newburn-Cook C, Johnston DW, et al. Delayed childbearing and its impact on population rate changes in lower birth weight, multiple birth, and preterm delivery. *Paediatrics* 2002; 109:399.
- . Reddy UM, Ko CW, Willinger M, Maternal age and the risk of stillbirth throughout pregnancy in the United States. *Am J Obstet Gynecol.* 2006; 195:764.
- 5. Greenberg MB, Cheng YW, Sullivan M, et al. Does length of labor vary by maternal age? Am J Obstet Gynecol. 2007; 197:428.

RANZCOG members are invited to submit questions, tips or interesting cases to Qජය. Please send entries to Qජය @ OජG Magazine via: (email) ranzcog@ranzcog.edu.au (fax) +61 3 9419 0672 (mail) 254-260 Albert Street, East Melbourne, VIC, Australia 3002

Are you planning to survey members of RANZCOG?

Did you know that your survey must be submitted to the RANZCOG CPD Committee for approval?

This process was introduced in June 2000 to regulate the content and number of surveys being sent to the RANZCOG membership.

Documentation required by RANZCOG:

- RANZCOG criteria document detailing your survey
- Final survey
- Letter to be sent to participants with the survey
- Letter to CPD Chair from survey author detailing the purpose of the survey and identifying the class (eg Fellows/ Trainees/Diplomates) of College members that you wish to survey and the location (eg Australia, New Zealand or State).

RANZCOG requires that a disclaimer (as detailed in the approval letter) be appended to all approved surveys and that the applicant provide feedback of results and copies of any subsequent publications to the CPD Committee.

For further information and the survey criteria document please contact: Val Spark CPD Senior Coordinator (t) +61 3 9412 2921 (f) +61 3 9419 7817 (e) vspark@ranzcog.edu.au

MRANZCOG Research Assessors and Mentors Required

Do you have a strong research background? Would you like to support the development of research skills amongst our ITP trainees?

College House is looking for research assessors and mentors to provide appropriate feedback and guidance to trainees undertaking their research proposals and projects. The research project is a compulsory requirement within the ITP/Elective training program.

What is required?

You would be required to read the trainee's research proposals and provide feedback relating to the stated aims, hypothesis, project background, literature review, method, study design, statistics collection and analysis. This feedback is completed on a prepared template. As the College will also be conducting random audits on completed projects, you may be asked to assess a completed project as well.

RANZCOG is also preparing a mentor list so that trainees can be referred to a suitable research mentor if required. This position does NOT mean you would be mentoring a trainee for the duration of their research. Rather, you would be asked to provide timely advice and/or support on a needs only basis. Effective mentoring is not location specific and can utilise a range of technologies such as online, email and telephone communication.

If you are interested in being an assessor or mentor please send an email detailing your research interests and expertise to: Frances Gilleard (e) fgilleard@ranzcog.edu.au

If you have any questions please contact: Bronwyn Robinson (t) +61 3 9412 2979 (e) brobinson@ranzcog.edu.au

OSSIE Guide to Clinical Handover Improvement

Clinical handover is a high-risk area for patient safety and was identified by the Australian Commission on Safety and Quality in HealthCare (ACSQHC) as a priority project.

The Australian Medical Association (AMA) defined clinical handover as the transfer of professional responsibility and accountability for some or all aspects of care for a patient, or group of patients, to another person or professional group on a temporary or permanent basis (AMA Safe Clinical Handover Guide, *Safe Handover: Safe Patients*, 2006).

The ACSQHC funded a National Clinical Handover Initiative which included funding 14 pilot projects on clinical handover, one of which focused specifically on maternity care. The pilot study is called SHAREing Maternity Care: Clinical Handover between Visiting Medical Officers and Midwives, administered by Mater Health Services Brisbane (refer to article on opposite page).

In April 2010, the OSSIE Guide to Clinical Handover Improvement was endorsed by the Australian Health Ministers as a national guide to improving clinical handover practices.

A copy of the OSSIE Guide to Clinical Handover Improvement can be downloaded from the ACSQHC website at: www.safetyandquality.gov.au/.

FELLOWS & DIPLOMATES PRACTICE PROFILE

Have you completed a Practice Profile in 2010?

Fellows and Diplomates can complete their Practice Profile for 2010 by logging in via our website:

FELLOWS:

www.ranzcog.edu.au/fellows/PracticeProfile.shtml

DIPLOMATES:

www.ranzcog.edu.au/diplomates/PracticeProfile.shtml

Clinical handover *From project to policy*

Sara Hatten-Masterson

Coordinator Women's Health and Newborn Services Mater South, Brisbane

Breakdown in communication has been identified as a significant contributing factor in clinical incidents, sentinel events and patient complaints. Midwives and medical officers in both public and private practice have a unique relationship within the hospital setting.

The effective exchange of accurate information between midwives and medical officers is a fundamental element of patient safety and is vital to the success of the clinical communication process.¹⁻⁶ This exchange of information may occur face-to-face, but commonly for this group, it occurs via the telephone, or information is passed through multiple people. The accuracy, timeliness and relevance of this information and the style of communication used is vital to the success of clinical handover.

As many are aware, the last three years has seen a significant focus on clinical handover, both nationally and internationally. At Mater Health Services in Brisbane, we were fortunate to receive funding from the Australian Commission on Safety and Quality in HealthCare (ACSQHC) to develop, test and implement a clinical handover initiative aimed at enhancing the safety and quality of maternity care, focusing primarily on visiting medical officer (VMO) to midwife communication and handover post-caesarean section.

Previous work undertaken by our clinical safety and quality unit had already highlighted the well-known principles associated with good clinical handover, face-to-face communication and documentation. Along with a minimum dataset described within the mnemonic 'SHARE', improvement to a process that was frequent and important seemed possible. Some minor adjustment to support our other safety initiatives resulted in the final and now widely used mnemonic 'SHARED', standing for Situation, History, Assessment, Risk, Expectation/Escalation and Documentation (see figure below). It was anticipated that, once a pilot had been completed, the framework would provide a basis to build handover solutions specific to different clinical scenarios and specialties across Mater Health Services, for both the public and private facilities.

The handover trigger 'SHARED' is intended as a method for enhancing the quality and accuracy of information transferred between healthcare professionals from both inside and outside the organisation. Each letter of 'SHARED' represents an essential component of clinical handover and highlights the transfer of responsibility and accountability, not simply the transfer of information as necessitated by the Australian Medical Association in their *Safe Patients* guideline (AMA, 2006) and the United Kingdom National Patient Safety Agency (2004).

A number of support tools have been developed, continue to be developed and have had revisions made as part of the initial project, as well as through routine review processes within the organisation. These support tools include but are not limited to:

- Posters a simple prompt and marketing tool placed in tea rooms and handover rooms for the framework or specific target areas for clinical handover improvement.
- Lanyard cards an easy-to-carry, easy-to-read, double-sided prompt of SHARED and its components useful to all clinicians.
- Phone handover guide a prompt found near telephones and in the front of patients' charts to remind staff to be fully prepared before communicating around a critical situation or change in patient condition and to have important information available.
- 'I SHARED' sticker placed in patients' charts along with documentation of the phone conversation, including background, expectations and plan of care.
- Clinical pathway insert with a focus on interdepartmental transfer, to support the verbal handover process from the recovery room to the inpatient unit, for mother and baby as well as gynaecological patients, ICU and CCU.
- Induction of labour booking form.
- Birth suite journey board (medical and midwifery).
- Neonatology 24-hour observation sheet incorporating an endof-shift nurse handover prompt.

Although theses tools do not make good clinical handover by themselves, they serve as prompts, documentation in some instances and a marketing strategy, serving as a constant reminder of the importance of clinical handover. Since the projects inception, the anticipated uptake has occurred, with 'SHARED' being rolled out



across Mater Health Services, including both public and private facilities for adults, women and children, as well as being aligned strategically with work on the deteriorating patient, aligning with the ACSQHC National Consensus Statement: Essential Elements for Recognising and Responding to Clinical Deterioration.

'SHARED' as a mnemonic has also been successfully implemented by a number of other facilities, both maternity and non-maternity, as the method and trigger for their personalised clinical handover improvement activities.

'The effective exchange of accurate information between midwives and medical officers is a fundamental element of patient safety and is vital to the success of the clinical communication process.'

Making it work for the long-term

Within Mater Mothers Hospital, we have seen the uptake of our clinical handover work by key clinical leads allowing for an increased rate of handover improvement activities and a greater understanding of clinical communication. Further improvements have been seen with the incorporation of the 'SHARED' mnemonic and branding into: an induction of labour booking form for public and private women, providing consistent and improved baseline admission information; a referral for case discussion request for women in the antenatal setting; the introduction of multidisciplinary handover for public and private birth suites; and a focus on midwife to midwife end-of-shift handover, including a review of current practice and commencement on the development of a consistent and appropriate tool to support end-of-shift handover across the service, as well as the work process around end-of-shift handover.

The initial project included a pre- and post-study design using clinician surveys (VMOs and midwifery/nursing staff), chart audits, patient satisfaction surveys and a review of clinical incident data. Finding relevant and useful measures has proven to be a challenge for many people involved in clinical handover improvement and it is acknowledged that a combination of measures is most useful. Other measures to be considered include patient complaint data, sentinel event data and process measures, including compliance with tool usage and completion, as well as with other documentation, staff understanding of new process and time taken for handover.

Achieving long-term sustainable change for any initiative or improvement activity is challenging and requires patience and commitment. Using the ACSQHC publication *OSSIE Guide to Clinical Handover Improvement*⁶, creating a steering committee specifically for clinical handover improvement and work relating to the deteriorating patient, Mater Health Services has successfully commenced upon its journey to take clinical handover improvement from a project to 'how we do business here'.

References

Australian Council for Safety and Quality in Health Care. *Clinical Handover and Patient Safety: Literature Review Report.* Canberra, ACT: Australian Government, Department of Health and Ageing; 2005 March. Access at: www.health.gov.au/internet/safety/publishing.nsf/Content/AA1369AD4AC5FC2ACA2571BF0081CD95/\$File/clinhovrlitrev.pdf.

- WHO Collaborating Centre for Patient Safety Solutions. *Communication During Patient Hand-overs*. Geneva, Switzerland: World Health Organisation 2007 p.1-4. Access at: www. ccforpatientsafety.org/common/pdfs/fpdf/presskit/PS-Solution3.pdf.
- Association of Perioperative Registered Nurses. 'Hand-off' toolkit to improve transitions in care within the perioperative environment. AORN 2008 [updated 2008; cited 2008 February 20]; Access at: www.aorn.org/docs_assets/55B250E0-9779-5C0D-1DDC8177C9B4C8EB/44F40E88-17A4-49A8-86B64CAA80F91765/HandOff_Executive.pdf .[41]
- Pothier D, Monteiro P, Mooktiar M, Shaw A. Pilot study to show the loss of important data in nursing handover. Br J Nurs. 2005;14:1090-1093.
- 5. Sabir N, Yentis S, Holdcroft A. A national survey of obstetric anaesthetic handovers. *Anaesthesia*. 2006; 61:376-380.
- Australian Commission on Safety and Quality in Health Care (2010). OSSIE Guide to Clinical Handover Improvement. Sydney, ACSQHC. Access at: www.health.gov.au/internet/safety/publishing.nsf/content/ D0CEDF80C4623FF2CA25757D007F7828/\$File/OSSIE.pdf.



FETAL SURVEILLANCE EDUCATION PROGRAM

The RANZCOG Fetal Surveillance Education Program (FSEP) continues to deliver highly regarded fetal surveillance education to healthcare professionals in over 140 centres throughout Australia and New Zealand. As a RANZCOG program, the FSEP is not-for-profit and remains the leading cost-effective CTG education provider in Australasia.

- Our clinical content is of the highest quality, comprehensively addressing fetal surveillance and CTG use. Our popular face-to-face programs facilitate adult learning whilst being time and resource efficient.
- We are continuing to develop our assessment tool and have released our online program (OFSEP) to support our face-to-face programs.
- We have published a fetal surveillance handbook, *Fetal Surveillance: A Practical Guide*, to act as an additional resource, as well as meeting individual learning needs. The handbook can be purchased through the FSEP administrator.
- Our workshops are accredited with the appropriate medical representative bodies: ACMI, NZCOM, RACGP and ACCRM and it also attracts RANZCOG PR&CRM points. Additional PR&CRM points can also be earned by using our straightforward audit tool.

We are currently taking bookings for 2010 and 2011. Please contact the FSEP administrator if you are interested in booking or attending a FSEP session.

For further information, please contact:

FSEP Administrator (t) + 61 3 9412 2958 (e) fsep@ranzcog.edu.au (w) www.ranzcog.edu.au/fsep/index.shtml

Safe Motherhood for All: Part of the Global White Ribbon Alliance

Advocacy. Sharing resources. Good practice.

An exciting new maternal healthcare campaign is underway in Australia to promote safe motherhood practices worldwide. Safe Motherhood for All: Part of the Global White Ribbon Alliance will disseminate the latest research, create educational opportunities, encourage policy change and enable discussion Australia-wide.

The White Ribbon Alliance for Safe Motherhood (www. whiteribbonalliance.org) is an international coalition bound together by a common goal: to ensure that pregnancy and childbirth are safe for all women and newborns in every country around the world. The Australian coalition – Safe Motherhood for All: Part of the Global White Ribbon Alliance – will promote not just safe motherhood here in Australia, but the truly global dimensions of the issue, especially in developing countries.

Safe Motherhood for All is focused on achieving Millennium Development Goal 5 (MDG5: Improve Maternal Health) by 2015.

Recent forums have highlighted that there has only been a nine per cent reduction in the maternal mortality rate globally over the past ten years. The countries with considerable work to do on MDG5 are Papua New Guinea, Timor-Leste, India, Pakistan, Nepal and Bangladesh. Only 35 per cent of women in the Asia Pacific region give birth with a skilled birth attendant.

We know that every minute at least one woman dies from complications related to pregnancy and childbirth – 529,000 women each year – and that 10,000 babies per day are stillborn and the same number die within the first month of life. The freedom to bring life into the world is clearly not available to all. Dimity Fifer, Chief Executive Officer of Australian Volunteers International (AVI), Australia's largest and most experienced international volunteer cooperation organisation, is President of Safe Motherhood for All: Part of the Global White Ribbon Alliance. 'The statistics on maternal mortality globally are sobering. This is surely an issue of solidarity for women – and men. AVI, as always, looks forward to using relationships and the sharing of expertise and experience to achieve real and lasting change.'

'We look forward to the potential for collaboration in the area of maternal health. AVI will certainly include more volunteer assignments and linkage programs focused on midwifery education, health system strengthening and support for community-based responses. We are currently liaising with RANZCOG about this potential.'

Watch this space for announcements about the new website for Safe Motherhood for All: Part of the Global White Ribbon Alliance. Further information on the Australian coalition will be published in OCGMagazine as the initiative develops.

To contact your local network for further information email: wraaustralia@gmail.com.

ATTENTION DRANZCOG AND DRANZCOG ADVANCED HOLDERS

Do you have your Women's Health Points for the current triennium?

For those holders of the DRANZCOG and DRANZCOG Advanced due to recertify this triennium, time is running out. If your Diploma certificate has an end date of 31 December 2010, you have a recertification requirement in the current triennium and must obtain a total of 40 Category 1 points in Women's Reproductive Health activities before 31 December 2010.

Where to find activities

The list of Women's Reproductive Health activities can be found on the Meetings Calendar in the latest issue of *O*&*G* Magazine or on the RANZCOG website: www.ranzcog.edu.au/meetingsconferences/index.shtml

The College

College Statements Update



Michael Permezel FRANZCOG Chair, Women's Health Committee

The Women's Health Committee (WHC) approved six new statements in July 2010, which were subsequently endorsed by Council. New and revised College statements can be viewed on the College website at: www.ranzcog.edu.au/womenshealth/statementsupdate.shtml.

New College Statements

C-Obs 34: Maternity Services to Remote and Rural Communities in Australia

The Provincial Fellows Committee developed this statement which clearly outlines specific needs and issues relevant to remote and rural Australia.

C-Obs 36: Term Prelabour Rupture of Membranes (Term PROM)

With increasing evidence that clinical chorioamnionitis is linked to the pathogenesis of many cases of cerebral palsy, the Women's Health Committee has developed this statement which assesses the evidence with respect to early versus delayed induction of labour.

C-Obs 37: Delivery of the Fetus at Caesarean Section

The development of this statement was prompted by two coroner's reports in which bad outcomes followed difficulty with delivery of the fetus at caesarean section. The obstetrician is placed in an unenviable position when presented with an undiagnosed breech deep in the pelvis in advanced labour and no antenatal work up with respect to size, attitude and fetal morphology.

C-Obs 38: Planned Vaginal Birth after Caesarean Section

Few issues provoke passionate discussion more than a 'Trial of Scar'. The College has summarised relevant issues in this statement and include some infrequently stated observations. These include:

- The greatest fetal risk of attempting vaginal birth is that of a post 39-week pregnancy event (for example, unexplained stillbirth), unrelated to the presence of the scar. Fetal consequences of uterine rupture are likely to be numerically less frequent.
- When all fetal risks are considered together, the fetal consequences of attempting vaginal birth after caesarean section are at a risk level at which many women indicate that they would opt for elective caesarean section rather than attempting vaginal birth.
- 3. The likely future family size and the attendant risks of placenta accreta are very important factors in the decision equation.

C-Obs 39: Caesarean Delivery on Maternal Request

This statement overlaps to some degree with the statement above, in that many of the same considerations apply, including the risk of placenta accreta with repeated caesarean sections and a fetal benefit related to late pregnancy events occurring beyond 39 weeks gestation. The College position is akin to that of a New South Wales Health directive. That is, the obstetrician has an obligation to ensure that the mother's consent to caesarean section is fully informed.

C-Obs 40: Maternal and Perinatal Data Collection

Experience in specific jurisdictions attests to the importance of accurate and transparent data collection systems that identify the intended model of care and the place of birth, both at booking and at the onset of labour. Such data is not collected nationally at present. It is only through rigorous data collection, regular audit and transparent reporting, that new models of care can be appropriately evaluated.

Revised College Statements

The following statements were re-endorsed at July Council with minor or no amendments:

- C-Obs 1: Obstetricians and Childbirth: Responsibilities
- C-Gyn 1: Female Genital Mutilation (FGM)
- C-Gyn 5: Screening for the Prevention of Cervical Cancer
- C-Trg 4: Use of Lasers in Obstetrics and Gynaecology by Fellows and Trainees of RANZCOG
- C-Gen11: Perinatal Depression
- C-Gen 6: Guidelines for Visiting Surgeons Conducting Demonstration Sessions
- C-Gyn 3: Intrauterine Contraceptive Devices and Infection
- C-Obs 17: Intrapartum Fetal Surveillance Guidelines

Statements of Other Bodies Endorsed by Council

Antenatal Magnesium Sulphate Prior to Preterm Birth for Neuroprotection of the Fetus, Infant and Child – National Clinical Practice Guidelines

This guideline was developed by an expert group on which the College had representation. The College had endorsed the guideline and interested readers are directed to Professor Sue Walker's article on the subject in the Autumn 2010 edition of *O&G Magazine*, page 38.

New Statements Under Development

- Clinical handover
- Decreased fetal movements

Prescriber Status for Mifepristone

RANZCOG has developed an aide package to assist Fellows with their application to the Therapeutic Goods Administration (TGA) to become an authorised prescriber for Mifepristone. If you would like a copy of the aide to be emailed to you, please contact RANZCOG on +61 3 8415 0408.

C-Obs 34: Maternity Services in Remote and Rural Communities in Australia

Date of this document: July 2010 First endorsed by Council: July 2010 Next review due: July 2013

1. Provision of maternity services to remote and rural communities

The maternity care needs of rural populations must be met within a context of competing social, political and financial priorities and significant limitations in workforce availability. Each community should be assessed according to determined guidelines, taking into consideration local resources, rather than as a reactive response to a local crisis or in the course of political expediency.

In planning the locations of maternity services in rural and remote communities, there needs to be a clear understanding of what constitutes 'rural and remoteness'. Canadian data¹ suggest that by using a Rural Birth Index (RBI), which takes into consideration birth numbers with a defined geographic zone, isolation from the next available well-resourced maternity unit and population vulnerability, it is possible to quantify need and appropriately guide the development and maintenance of maternity services in rural British Columbia. Whilst the Australian healthcare system is significantly different to that of Canada, it may be possible to develop a similar planning tool relevant to the Australian healthcare context. Planning must also take into account the increasing cultural diversity and needs of rural Australia.

2. Models of care

Care for pregnant women in rural and remote Australia should consist of a collaboration between specialists, GPs, midwives, Aboriginal health providers and other approved providers of healthcare working together to support rural maternity services.

Maternity care providers cannot act in isolation if optimal pregnancy outcomes are to be achieved. Shared care arrangements between various members of the collaborative care team should be encouraged and well-defined according to locally agreed protocols.

Each maternity care service in rural/remote areas should establish risk assessment and referral criteria for pregnant women and newborn babies. Each mother should be assessed individually and on an ongoing basis throughout her pregnancy. All members of her healthcare team, led by a designated specialist or GP obstetrician, should be involved in the process of assessment.

Communities should be well-informed with regard to the level of maternity care services available locally and how these services are supported at regional and tertiary levels. Women and their health carers need to be cognisant of the possible limitations of local services if unexpected complications arise.

There should be regular opportunities for all the carers to be involved in interdisciplinary meetings to optimise the care for mothers-to-be and to review the outcomes of the services. This is a risk management priority.

- a. Rural/remote GPs in the maternity care workforce
- Women in rural communities should have early access to skilled GP assessment and counselling. Individual risk assessment and counselling, particularly with respect to early pregnancy screening tests, are important in helping women to make well-informed decisions concerning their ongoing care. This is a risk management priority.
- 2. Rural GP obstetricians should be involved in the development of maternity service policies/protocols/guidelines to guide the appropriate level of care for pregnant women.
- Rural GPs practising obstetric and other procedural activities should be provided with the appropriate recompense to fulfil ongoing education and skills maintenance requirements for College recertification and for reaccreditation of hospital procedural clinical privileges.
- 4. Rural GP obstetricians need to be assured that there will be adequate relief for study and recreational purposes. The Specialist Obstetrician Locum Scheme (SOLS) program has demonstrated the effectiveness of this. This is a workforce priority.
- 5. In many rural/remote areas, the GP obstetricians are key figures in the maintenance of maternity care services. They may also fulfil other essential community roles such as providing anaesthetic and/or paediatric services. The loss of a GP obstetrician from a community may also see the loss of an anaesthetist and/or a paediatrician.
- b. Provincial O and G specialists
- 1. Specialist obstetricians have key roles in provision of regional maternity services.
- Specialists in the rural/remote areas work with other healthcare providers including GPs, midwives, Aboriginal health providers and others approved by local health services. In addition to their clinical expertise, specialist obstetricians contribute to maternity services with roles in clinical leadership, education, training and clinical governance activities.
- 3. To help sustain a rural specialist obstetrician workforce, conditions of employment should be balanced to reduce the disparity of work conditions between urban and rural/ remote practitioners. Well-considered on-call arrangements for specialist obstetricians are essential to maintain safe working conditions and a sustainable work/life balance for specialists.
- 4. Appropriate remuneration for and access to Continuing Medical Education/Practice Improvement activities is important in maintaining a well-skilled rural specialist workforce.
- 5. Reliable and affordable expert locum support for specialist obstetricians is needed to provide continuity of high quality regional specialist services.
- c. General workforce issues
- All maternity healthcare providers should have the appropriate accreditation from the health service provider that is responsible for the care of pregnant women and their newborns.

- All maternity healthcare providers should be involved in Continuing Education and Continuing Practice Development activities.
- Designated funding to monitor quality of maternity care service provision is important to maintenance of high care standards. Monitoring should include quality and equity of access for rural women to services provided by obstetricians, midwives, maternal and child health nurses, physiotherapists, audiologists, radiology and laboratory service providers, etc.
- 4. Funding models should support the use of modern communication technology (for example, telemedicine and videoconferencing facilities) to assist in efficient and optimal management of complex problems, including obstetric, social (for example, child protection) and neonatal care.

- d. Community issues
- 1. Access to efficient emergency transport services are critical to provision of high quality rural maternity services.
- Women who must relocate to access appropriate pregnancy care and/or care for their newborn babies should have access to travel and accommodation assistance to minimise the burden imposed by the need for relocation.

Reference

 Grzybowski S, et al. Planning the optimal level of local maternity service for small rural communities: A systems study in British Columbia. *Health Policy* 2009; doi:10.1016/j. healthpol.2009.03.007.

C-Obs 36: Term Prelabour Rupture of Membranes (Term PROM)

Date of this document: July 2010 First endorsed by Council: July 2010 Next review due: July 2013

Term prelabour rupture of membranes (term PROM) is defined as rupture of the membranes prior to the onset of labour at/or beyond 37 weeks gestation. The incidence of term PROM is eight per cent. Spontaneous labour follows term PROM at 24, 48 and 96 hours in 70 per cent, 85 per cent and 95 per cent of women, respectively. Thus, an important proportion of women have significant latency from PROM to delivery if managed expectantly, particularly nulliparous women. Management of term PROM requires a clear discussion with the woman, her partner and caregivers regarding the benefits and risks of expectant management versus active management with induction of labour.

The short-term risks of rupture of membranes include cord prolapse, cord compression and placental abruption. Longer-term risks of delayed delivery include maternal and neonatal infection. The quality of data with which to counsel women has been largely influenced by the randomised term PROM study. The major comparisons between the induction with oxytocin group and the expectant management group (oxytocin) are as follows:

	Induction with oxytocin	Expectant management (oxytocin)
Caesarean section	127/1258 (10.1%)	123/1263 (9.7%)
Neonatal infection	25/1258 (2%)	36/1263 (2.8%)
Clinical chorioamnionitis*	50/1258 (4%)	109/1263 (8.6%)
Intrapartum fever*	46/1258 (3.7%)	93/1263 (7.4%)
Postpartum fever*	24/1258 (1.9%)	46/1253 (3.6%)
Antibiotics before/ during labour*	94/1258 (7.5%)	150/1263 (11.9%)
Neonatal antibiotics*	94/1258 (7.5%)	172/1263 (13.7%)
NICU stay*	83/1258 (6.6%)	146/1263 (11.6%)
Median time to active labour	5 hours	17.3 hours

*denotes outcomes with statistically significant differences

The *Cochrane* review has provided information regarding 6814 women in 12 trials with term PROM managed expectantly or with induction using prostaglandins or oxytocin, but the findings did not differ greatly from term PROM (above).

- No difference in caesarean section rate (RR 0.94, 95% CI 0.82-1.08).
- No difference in operative vaginal birth (RR 0.98, 95% CI 0.84-1.16).
- Active management associated with significant reduction in: – chorioamnionitis (RR 0.74, 95% Cl 0.56-0.97). – endometritis (RR 0.3, 95% Cl 0.12-0.74).
- No difference in neonatal infection (RR 0.83, 95% CI 0.69-1.12).
- Active management associated with significant reduction in NICU/SCN admission (RR 0.72, 95% 0.57-0.92).
- Significantly more women viewed their care more positively with active management (RR for 'nothing liked' 0.45, 95% CI 0.37-0.54).

Neonatal infection is uncommon and the lack of significance between expectant and active management in the randomised trials is likely to represent underpowering, given the other outcomes related to infection were all increased in the expectant management group. Neonatal infection can result in devastating sequelae, including death, chronic lung disease and cerebral palsy. Several case control studies have strongly implicated chorioamnionitis as a cause of loss and cerebral palsy in term and preterm infants. These findings have prompted investigators to question whether PROM at even modest preterm gestation (more than 34 weeks) should also be actively rather than expectantly managed.

Potentially serious maternal morbidity from chorioamnionitis or endometritis is also associated with increasing latency in term PROM. While active management of term PROM was initially thought to be associated with an increased risk of operative delivery and caesarean section, these concerns have not been borne out in randomised studies.

Assessment

Initial assessment of women presenting with term PROM should include confirmation of the diagnosis, confirmation of gestation and presentation and assessment of maternal and fetal wellbeing. Nitrazine (pH-based) tests or Amnisure (detecting placental alpha microglobulin-1 protein in vaginal fluid) may be used where there is diagnostic uncertainty. Digital vaginal examination should be avoided unless immediate induction is planned, as this has been shown to increase the rate of neonatal infection.

Management

Active management of term PROM with induction is associated with reduced maternal infective morbidity without increasing caesarean section or operative vaginal birth. Fewer infants are admitted to NICU and fewer infants require postnatal antibiotics. Nevertheless, a short period (up to 24/24) of expectant management may be considered (following preliminary assessment) at the patient's or clinician's discretion in highly selected and well-supervised cases.

Criteria for expectant management includes:

- Term PROM with fixed cephalic presentation.
- GBS negative.
- No signs of infection (maternal tachycardia, fever, uterine tenderness).
- Normal CTG.
- No history of digital vaginal exam, cervical suture.
- Adequate resource/staffing to provide support as an outpatient or inpatient.
- Commitment to four-hourly maternal temperature, evaluation of vaginal loss and assessment of fetal wellbeing.

Antibiotic prophylaxis

In women known to have vaginal group B streptococcus (GBS) colonisation, prophylactic antibiotics and early administration of oxytocin is recommended. See College Statement *C-Obs 19: Screening and Treatment for Group B Streptococcus in Pregnancy.* For women not known to have GBS, the *Cochrane* review found that antibiotic use significantly reduced the rate of chorioamnionitis and endometritis. Although no statistically significant differences were found for neonatal morbidity, the trials were underpowered to assess this outcome, as the review included only two trials involving 838 women.

Hospital versus home

A sub-analysis of term PROM concluded that expectant management at home was associated with a further increase in the risk of maternal need for antibiotics (OR 1.52) and neonatal infection (OR 1.97).

Oxytocin versus prostaglandins

Induction of labour with vaginal prostaglandins is associated with an increased risk of chorioamnionitis and neonatal infection in comparison to oxytocin induction. Compared to expectant management, vaginal prostaglandins were associated with an increased risk of NICU admission and chorioamnionitis.

Therefore, oxytocin rather than vaginal prostaglandins are preferred for the induction of labour in the presence of term PROM. If the cervix is particularly unfavourable, a risk-benefit assessment may still lead to prostaglandins being preferred. Oral misoprostol may have a future role for this indication, but prior evaluation in clinical trials is recommended.

Conclusion

Randomised controlled trials have concluded that 'planned early birth' (through oxytocin administration) leads to reduced maternal infections, reduced neonatal intensive and special care admissions and greater maternal satisfaction. Mode of delivery is not compromised by choosing either planned early birth or expectant management, with equal rates of caesarean section and instrumental delivery in both groups.

Links to other College Statements

C-Obs 31: Routine Intrapartum Care in the Absence of Pregnancy Complications C-Obs 17: Intrapartum Fetal Surveillance Guidelines

C-Obs 19: Screening and Treatment for Group B Strep

References

- Dare MR, Middleton P, Crowther CA, Flenady V, Varatharaju B. Planned early birth versus expectant management (waiting) for prelabour rupture of membranes at term (37 weeks or more). *Cochrane Database of Systematic Reviews* 2006, Issue 1. Art. No.: CD005302. DOI: 10.1002/14651858.CD005302.pub2.
- Flenady V, King JF. Antibiotics for prelabour rupture of membranes at or near term. *Cochrane Database of Systematic Reviews* 2002, Issue 3. Art. No.:CD001807. DOI: 10.1002/14651858.CD001807.
- Hannah ME, Ohlsson A, Farine D, et al. Induction of labour compared with expectant management for prelabour rupture of the membranes at term. TERMPROM Study Group. NEJM 1996 Apr 18; 334(16):1005-10.
- Wagner MV, Chin VP, Peters CJ, et al. A comparison of early and delayed induction of labour with spontaneous rupture of membranes at term. Obstet Gynecol. 1989 Jul; 74(1); 93-7.

C-Obs 37: Delivery of the Fetus at Caesarean Section

Date of this document: July 2010 First endorsed by Council: July 2010 Next review due: July 2013

Delivery by caesarean section in the fetal interest has become more common as the maternal risks associated with caesarean section have fallen. In the face of safe regional anaesthesia, reliable blood supply, routine antibiotics and sometimes strong patient preference, the fetal risks associated with hazardous vaginal delivery become less tolerable given a relatively safe and accessible alternative. Nevertheless, there is potential for traumatic fetal injury at caesarean section. These injuries include:

- 1. Skull fracture and/or intracranial haemorrhage following disimpaction where the head is deep in the pelvis.
- 2. Brachial plexus palsy following difficult delivery of the shoulders in the presence of fetal macrosomia.
- 3. Cervical spine, spinal cord and/or vertebral artery injury following delivery of the head of a breech presentation.

Continued on page 76.

Caesarean section with the fetal head deep in the pelvis

Consequences

Where delivery needs to be expedited with the presenting part deep in the pelvis, there are added risks of caesarean section including increased risks of:

- 1. Fetal injury including skull fracture and/or intracranial haemorrhage.
- 2. Maternal injury including:
 - a. Tears in the lower uterus.
 - b. Haemorrhage.
 - c. Urinary tract injury.

Delivery principles

The decision for caesarean section in the second stage of labour involves balancing the risks and benefits of a) caesarean section against those of b) an immediate and potentially difficult operative vaginal delivery or c) expectant management with the expectation of achieving a safer station or position for operative vaginal delivery. All options carry some risk and the decision should be made by an experienced accoucheur, preferably with adequate notice of progress in labour, fetal condition and maternal wishes.

If a decision is made to proceed with caesarean section, the following good practice points are recommended:

Pre-operative considerations

- 1. A vaginal examination should be performed immediately prior to commencing the procedure. This is to:
 - a. Exclude the possibility of further head descent such that vaginal delivery would be more easily accomplished.
 - Apply steady, firm upward pressure to assist with disimpaction of the fetal head and assist with the abdominal delivery. Administration of a tocolytic agent may be of benefit.
- 2. An experienced obstetrician should be in attendance where a technically difficult delivery is anticipated.
- 3. The anaesthetist should be appropriately prepared in anticipation of the need for acute tocolysis and management of postpartum haemorrhage.
- The paediatrician should be appropriately prepared for an increased likelihood of additional neonatal resuscitation requirements.

Intra-operative considerations

- The head must be elevated into the abdomen before successful delivery can be accomplished. This may be achieved by either or both of:
 - a. Steady elevation of the fetal head vaginally by an experienced assistant.
 - b. The accoucheur's fingers passing between the head and the uterine wall to below the head and exerting upward pressure.
- 2. The upper uterine segment has invariably retracted, resulting in a reduced intrauterine volume in which to accommodate the fetus as it is displaced upwards. While this is most commonly rectified by physical pressure associated with manual elevation of the fetal head, consideration should also be given to the use of tocolysis to relax the uterus. Commonly used agents for acute tocolysis include glyceryl trinitrate (GTN), salbutamol or terbutaline, or deep general anaesthesia.

3. Occasionally, delivery of the fetal head is impossible despite these measures and delivery of the torso through the abdominal incision is appropriate. This may be particularly encountered in the very preterm fetus. While breech delivery in this setting has been the subject of case reports, it should generally only be performed by those experienced in this technique or where other methods have failed.

Post-operative considerations

The risk of major postpartum haemorrhage is increased with emergency caesarean section in advanced labour, due to the combination of uterine and vaginal trauma, infection, use of tocolysis and atony. Appropriate preparation for such a delivery includes considering the oxytocic and mechanical agents available to control haemostasis, as well as availability of blood and blood products.

Caesarean section for the macrosomic fetus

Consequences

Caesarean section for the macrocosmic fetus may still result in shoulder dystocia and brachial plexus palsy, but with an incidence many times less than with vaginal birth.

Delivery principles

Where shoulder dystocia and fetal injury is anticipated, the abdominal wall and uterine incisions should be sufficiently large to facilitate delivery. Where difficulties are encountered during delivery, these may need to be extended:

- 1. To facilitate access for manoeuvres such as delivery of the posterior arm.
- 2. Converting the uterine incision into a 'J' or 'T' incision.

Delivery of the breech at caesarean section

Consequences

While caesarean section is generally associated with a reduction in fetal trauma when compared with vaginal birth, caesarean delivery of a breech presentation still poses some fetal risk related to trauma and asphyxia, and maternal risk of trauma.

- Cervical spine, spinal cord and/or vertebral artery injury may follow delivery of the after coming head of a breech presentation. These injuries may follow hyperextension of the cervical spine while trying to facilitate delivery of the fetal head through the incision. It should be noted that:
 - a. These injuries may be more likely where the head is hyperextended antenatally producing anomalous development of the cervical spine, or when fetal muscular tone is reduced through a neuromuscular disorder or fetal hypoxia.
 - b. Such injuries may also occur antenatally and are not necessarily the consequence of the delivery itself.
- 2. Maternal consequences of caesarean section can be considerable if the breech is very deep in the pelvis, such that vaginal breech delivery may be recommended. Trials recommending caesarean section for breech presentation have not been powered to examine the subgroup with full cervical dilatation and the breech deep in the pelvis.

Pre-operative

High quality antenatal care is imperative for all women so that the incidence of 'undiagnosed' breech presentations is minimised, thereby enabling appropriate antenatal management of the term

breech to occur, including an ultrasound assessment for fetal normality, hyperextension of the fetal head and an opportunity to offer ECV.

Intra-operative technique

- Where an emergency caesarean section is being undertaken for the breech presentation in labour, a further vaginal examination should always be performed in theatre immediately before embarking on the caesarean section in order to exclude imminent vaginal delivery.
- 2. The key to successful delivery of the after coming head of any breech presentation (whether abdominal or vaginal) is to maintain head flexion during delivery of the limbs and torso. Head extension not only makes head diameters much greater but also incurs the possibility of extension injuries.
- 3. The incision should be sufficiently large to allow access and the necessary manipulations. Head flexion should be maintained during delivery of the limbs and torso by the surgical assistant exerting pressure on the vertex in the appropriate direction.

- 4. When delivery of the after coming head does not occur with simple downward pressure on the uterine fundus, delivery of the after coming head should be effected when the head is low in the uterus by either:
 - a. A modification of the Mauriceau-Smellie-Veit manoeuvre.
 - b. Obstetric forceps.
- 5. Where the fetal head is not sufficiently low or initial attempts at delivery are unsuccessful, the accoucheur may consider:
 - Tocolysis administered by the anaesthetist may assist where there is a uterine retraction ring around the fetal neck, most commonly accomplished with GTN, salbutamol or terbutaline, or deep general anaesthesia.
 - Extension of the uterine incision, most commonly upward in the midline in the form of an inverted 'T' incision. Although undesirable for subsequent pregnancies, this may avoid fetal injury (traumatic or asphyxial) in this technically difficult situation.

C-Obs 38: Planned Vaginal Birth after Caesarean Section (Trial of Labour)

Date of this document: July 2010 First endorsed by Council: July 2010 Next review due: July 2013

A woman with a uterine scar has the option of choosing an elective caesarean section or to attempt vaginal birth. Factors to consider include the material risks in the index pregnancy associated with each approach; plans for further childbearing; the likelihood of achieving a vaginal delivery; and other aspects of individual importance. The decision is one for the woman to make in consultation with her carer, who has an obligation to provide her with all relevant information.

Terminology

This area of practice suffers from misleading terminology. The following terms are recommended and adapted from the National Institutes of Health Consensus Statement (2010):

- Trial of labour (TOL): A planned attempt to birth vaginally in a woman who has had a previous caesarean section. This is also sometimes called a 'trial of vaginal birth after caesarean' (TOVBAC).
- Vaginal birth after caesarean section (VBAC): Vaginal birth following a TOL.
- Elective repeat caesarean section (ERCS): Planned caesarean section in a woman who has had one or more prior caesarean sections, whether or not the caesarean section occurred at a scheduled time. Also may be termed elective repeat caesarean delivery (ERCD).
- **Unsuccessful TOL:** Delivery by caesarean section of a woman who has had a TOL.

Risks associated with a TOL

Uterine rupture

Chauhan *et al* ⁴ reviewed maternal and perinatal complications in 142,075 patients who attempted vaginal birth after caesarean delivery. They reported a uterine rupture rate of 6.2 per 1000 trials of labour. The uterine rupture-related complication rate was 1.8 per thousand for packed red blood cell transfusion, 1.5/1000 for pathologic fetal acidosis (cord pH<7.00), 0.9/1000 for hysterectomy, 0.8/1000 for genitourinary injury, 0.4/1000 for perinatal death and 0.02/1000 for maternal death. These figures concur with a large Australian series where the likelihood of uterine rupture with attempted vaginal delivery after a previous lower segment caesarean section was estimated at five per thousand, hysterectomy 0.5 per thousand and perinatal death from uterine rupture 0.7 per thousand. Landon *et al* ¹⁰ reported 'symptomatic uterine rupture' in seven per thousand in 17,898 TOLs from 19 academic centres in the United States.

Perinatal mortality

Women electing TOL undoubtedly have a significant increase in perinatal mortality risk relative to those who undergo ERCS.¹² However, much of this is attributable to the often understated background rate of perinatal death after 39 weeks gestation. Where 0.4 per thousand may have a perinatal death related to rupture³, a further 1.4 per thousand can be expected to have an antenatal, intrapartum or neonatal death after 39 weeks gestation.¹⁹ This excess of perinatal mortality of 1.8 per thousand (even though mostly not a direct consequence of uterine rupture) must still be acknowledged in counselling about birthing options, as it may be an unacceptable risk for many women and health professionals.²²

Hypoxic ischaemic encephalopathy (HIE)

Landon *et al* ¹⁰ reported 12 cases of HIE amongst 17,898 women undergoing TOL (0.7 per thousand). In the same study, there

Continued on page 78.

were no cases of HIE in 15,801 women having ERCD (p<0.001). Children with long-term neurological impairment following uterine rupture have also been reported^{8,15}, but the frequency is almost impossible to determine, given the absence of long-term follow-up data in these large retrospective series.

Factors associated with increased/reduced risk of uterine rupture

The risk of uterine rupture is increased by induction of labour^{6,11,25}, an interpregnancy interval of less than 18 months¹⁶ and more than one previous caesarean section². Augmentation of labour is also associated with an increase in scar rupture.²³ Fetal weight of greater than 4000 g is associated with an increased likelihood of emergency caesarean birth if vaginal delivery is attempted and a 1.6x (ns) risk of scar rupture.^{6,25}

Maternal risks associated with elective repeat caesarean section

Index pregnancy

This is another area of practice where an extremely low but clinically important frequency of adverse outcomes makes assessment difficult. Epidemiological data attribute higher maternal mortality to ERCS than TOL.¹³ However, women with complex medical and obstetric problems are much more likely to feature in the ERCS than the TOL group, confounding the apparent association.⁹

Subsequent pregnancies

Important in the decision-analysis for many women is the intended future family size. With rising caesarean section rates, the serious complication of placenta accreta is becoming more prevalent. Silver *et al* ¹⁷ found that placenta accreta was present in 0.24 per cent, 0.31 per cent, 0.57 per cent, 2.1 per cent, 2.3 per cent and 6.7 per cent of women undergoing their first, second, third, fourth, fifth and sixth or more caesarean deliveries, respectively. This was a consequence of both an increasing incidence of placenta praevia with repeated caesarean sections and an increased likelihood of placenta accreta where the placenta was located over the uterine scar.

Likelihood of vaginal birth with a TOL

Most series report a likelihood of vaginal birth (if this is attempted) in the range of 60 to 80 per cent (for example, Turner et al, 2006¹⁸). This likelihood is reduced by maternal morbid obesity³ or fetal weight over 4 kg²⁶, but does not appear to be substantially affected by the indication for the previous caesarean section¹⁴.

Interestingly, Victorian perinatal data (2007) suggests a VBAC rate of 56.6 per cent for public and 51.8 per cent for private hospitals in women planning TOL after a primary caesarean section. These lowered figures may be partly because this dataset excludes women who have already delivered vaginally before. Alternatively, it may reflect a higher rate of emergency caesarean section in a more risk adverse TOL population.

Health service requirements for a TOL

All women electing to labour after a previous caesarean section should have ready access to obstetric, neonatal paediatric, anaesthetic, operating theatre and resuscitation services (including availability of blood products), should complications arise (for example, uterine rupture). Where, by virtue of remote location, such on-site services cannot be provided, patients should be informed of the limitations of services available and the implications for care should a rupture occur. In most circumstances, this will result in either an elective repeat caesarean section or, alternatively, antenatal transfer to a centre with more comprehensive services for a TOL.

Antenatal preparation for TOL

All women planning a TOL should be appraised early in the antenatal period with respect to their intrapartum care. The information provided should include:

- The advisability of admission to hospital relatively early in labour.
- The policy with regard to induction and augmentation of labour.
- The importance of intensive maternal and fetal surveillance intrapartum.
- The likelihood of achieving vaginal birth.
- The necessity of emergency caesarean section in the event of poor progress in labour or fetal distress.

Intrapartum care

Admission

A woman undergoing a TOL should be assessed early in labour. As with all women in labour, members of the care team should be notified in a timely manner of the admission and the relevant clinical circumstances.

Fetal surveillance

A uterine scar is an indication for continuous electronic fetal surveillance in labour (see Intrapartum Fetal Surveillance Clinical Guidelines).

Analgesia

There appears little evidence that regional anaesthesia is harmful in a TOL and this should be freely accessible in the absence of other contraindications.

Intravenous fluids, blood sampling and oral intake

Placement of an intravenous line is advisable in a TOL. At that time, blood can be taken for blood group and antibody screen in preparation for possible later complications. Oral intake should be restricted to clear fluids because of a greater than normal probability of needing an immediate caesarean section under general anaesthesia.

Induction and augmentation of labour

These should only be undertaken with caution. Whilst good evidence is lacking, mechanical methods of cervical ripening might be preferred to pharmacological methods and an infusion of oxytocin, whilst not contraindicated, should be used with caution. However, great care needs to be exercised if a decision is taken to augment spontaneous labour with syntocinon.

Assessment of progress in labour and management of failure to progress

A trial of labour mandates vigilant assessment of progress in labour with vaginal examinations at least four-hourly in the active phase of labour and more frequently as full dilatation approaches. The cervix should dilate at least at 1 cm per hour in the active phase of labour and second stage should not exceed an hour in duration, unless birth is imminent.

Contraindications to TOL

Given the spectrum of attitudes with respect to avoiding fetal risk by caesarean section, what may be a contraindication to TOL in a 'fetal risk averse' patient, may be acceptable to a different patient more willing to accept a higher degree of fetal risk in order to achieve VBAC. However, for most women, particularly those not planning a large family, the decision equation for TOL (with the increased perinatal mortality rate [PNMR] of 1.8/1000) versus ERCS will be near equipoise. However, the following conditions are highlighted as being associated with an increased risk of uterine rupture or unsuccessful TOL. These would be contraindications/ relative contraindications to TOL for most women:

- Previous classical or vertical lower uterine segment incision.
- More than one previous caesarean section.
- Less than 18 months since the previous caesarean section.
- Morbid maternal obesity.
- Fetal weight over 4 kg.

TOL in risk-prone circumstances

A TOL may become particularly risk-prone where:

- There is a lack of services for safe provision of emergency care (for example, a TOL conducted at home, birth centre or centre without ready access to obstetric, anaesthetic and pediatric support).
- There is a failure to provide or accept adequate intrapartum maternal and fetal surveillance.
- There are clinical circumstances such as outlined above (for example, more than one previous caesarean section).

While women in these circumstances require the highest level of care that they are able to receive and accept, willingness of a healthcare provider to administer care in risk-prone circumstances cannot be misinterpreted as de facto support for substandard care.

It is suggested that before any healthcare professional agrees to provide care for TOL in risk-prone circumstances, that the women agree to counselling by a senior obstetrician who should:

- Further appraise the woman of the consequences of clinical decisions outside of best practice.
- Acknowledge that while the pregnancy outcome is likely to be favourable, the risks are real and a good outcome does not necessarily equate with best clinical practice.
- Make it clear that care will be provided by the healthcare team to the best of their ability, recognising that any constraints imposed may reduce the likelihood of a good outcome.
- Inform the patient that sudden unexpected complications may impose considerable demands on the limited resources of the health team, with potential adverse consequences not just for her and her baby, but also for other women and their babies.

Clinical audit

Pregnancy after caesarean section should be subject to regular multidisciplinary clinical audit, including an assessment of the numbers of women opting for a TOL versus ERCS as well as the number achieving VBAC, having opted for a TOL. Quality of adherence to agreed protocols should form part of the clinical audit.

Summary

Women with a uterine scar should be counselled as to the risks and benefits involved with both TOL and ERCS. They should be given all pertinent information free of bias, in order to make an appropriately informed decision. If the woman decides to undertake a TOL, there is a need for close fetal and maternal surveillance in labour and immediate access to support staff and an operating theatre, should rupture occur.

Links to other related College Statements

C-Obs 31: Routine Intrapartum Care in the Absence of Pregnancy Complications

C-Obs 17: Intrapartum Fetal Surveillance Guidelines

C-Gen 2: Guidelines for Consent and the Provision of Information Regarding Proposed Treatment

References

- Appleton W, Targett C, Rasmussen M, Readman E, Sale F, Permezel M and the VBAC Study Group. Vaginal birth after caesarean section: an Australian multicentre study. *Aust NZ J Obstet Gynaecol.* 2000; 40: 87-91.
- Caughey AB, Shipp TD, Repke JT, Zelop CM, Cohen A, Lieberman E. Rate of uterine rupture during a trial of labor in women with one or two prior cesarean deliveries. *Am J Obstet Gynecol.* 1999 Oct; 181(4):872-6.
- Chauhan SP, Magann EF, Carroll CS, Barrilleaux PS, Scardo JA, Martin JN Jr. Mode of delivery for the morbidly obese with prior cesarean delivery: vaginal versus repeat cesarean section. *Am J Obstet Gynecol.* 2001 Aug;185(2):349-54.
- Chauhan SP, Martin JN Jr, Henrichs CE, Morrison JC, Magann EF. Maternal and perinatal complications with uterine rupture in 142,075 patients who attempted vaginal birth after cesarean delivery: A review of the literature. *Am J Obstet Gynecol.* 2003 Aug; 189(2):408-17.
- Flamm B, Goings J, Liu Y, et al. Elective repeat caesarean delivery versus trial of labor: a prospective multicenter study. Obstet Gynecol. 1994; 83: 927-932.
- Grobman WA, Lai Y, Landon MB, et al, National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Prediction of uterine rupture associated with attempted vaginal birth after cesarean delivery. Am J Obstet Gynecol. 2008 Jul; 199(1):30.e1-5.
- Impey L, O'Herlihy C. First delivery after cesarean delivery for strictly defined cephalopelvic disproportion. *Obstet Gynecol.* 1998 Nov; 92(5):799-803.
- Jones R, Nagashima A, Hartnett-Goodman M, Goodlin R. Rupture of low transverse cesarean scars during trial of labor. *Obstet Gynecol*. 1991; 77: 815-817.
- Lilford RJ, van Coeverden de Groot HA, Moore PJ, Bingham P. The relative risks of caesarean section (intrapartum and elective) and vaginal delivery: a detailed analysis to exclude the effects of medical disorders and other acute pre-existing physiological disturbances. Br J Obstet Gynaecol. 1990 Oct; 97(10):883-92.
- Landon MB, Hauth JC, Leveno KJ, *et al*, National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Maternal and perinatal outcomes associated with a trial of labor after prior cesarean delivery. *N Engl J Med.* 2004 Dec 16;351(25):2581-9.
- Lydon-Rochelle M, Holt VL, Easterling TR, Martin DP. Risk of uterine rupture during labor among women with a prior cesarean delivery. N Engl J Med. 2001 Jul 5; 345(1):3-8.
- Mozurkewich EL, Hutton EK. Elective repeat cesarean delivery versus trial of labor: a meta-analysis of the literature from 1989 to 1999. Am J Obstet Gynecol. 2000 Nov; 183(5):1187-97.
- National Institutes of Health Consensus Development Conference Statement: Vaginal Birth After Cesarean: New Insights March 8-10, 2010.
- 14. Paul RH, Phelan JP, Yeh SY. Trial of labor in the patient with a prior cesarean birth. *Am J Obstet Gynecol.* 1985 Feb 1; 151(3):297-304.
- 15. Scott J. Mandatory trial of labor after cesarean delivery: an alternative viewpoint. *Obstet Gynecol.* 1991; 77: 811-814.
- Shipp TD, Zelop CM, Repke JT, Cohen A, Lieberman E. Interdelivery interval and risk of symptomatic uterine rupture. *Obstet Gynecol.* 2001 Feb; 97(2):175-7.
- Silver RM, Landon MB, Rouse DJ, et al. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Maternal morbidity associated with multiple repeat cesarean deliveries. Obstet Gynecol. 2006 Jun; 107(6):1226-32.

Continued on page 80.

- Turner MJ, Agnew G, Langan H. Uterine rupture and labour after a previous low transverse caesarean section. *BJOG* 2006 Jun; 113(6):729-32.
- Vashevnik S, Walker S, Permezel M. Stillbirths and neonatal deaths in appropriate, small and large birthweight for gestational age fetuses. *Aust N Z J Obstet Gynaecol.* 2007 47: 302-6.
- Victorian Department of Health. Victorian Maternity Performance Indicators 2007-8. Access at: http://health.vic.gov.au/maternitycare/ matpeform-ind-0708.pdf.
- Walker SP, McCarthy ÉA, Ugoni A, Lee A, Lim S, Permezel M. Cesarean delivery or vaginal birth: a survey of patient and clinician thresholds. *Obstet Gynecol.* 2007 Jan; 109(1):67-72.
- Walker SP, McCarthy EA, Ugoni A, Lee A, Lim S, Permezel M. Cesarean delivery or vaginal birth: a survey of patient and clinician thresholds. *Obstet Gynecol.* 2007 Jan; 109(1):67-72.
- Weimar CH, Lim AC, Bots ML, Bruinse HW, Kwee A. Risk factors for uterine rupture during a vaginal birth after one previous caesarean section: A case-control study. *Eur J Obstet Gynecol Reprod Biol.* 2010 Apr 26.
- Zelop CM, Shipp TD, Repke JT, Cohen A, Caughey AB, Lieberman E. Uterine rupture during induced or augmented labor in gravid women with one prior cesarean delivery. *Am J Obstet Gynecol.* 1999 Oct;181(4):882-6.
- Zelop CM, Shipp TD, Repke JT, Cohen A, Lieberman E. Effect of previous vaginal delivery on the risk of uterine rupture during a subsequent trial of labor. *Am J Obstet Gynecol.* 2000 Nov;183(5):1184-6.
- Zelop CM, Shipp TD, Repke JT, Cohen A, Lieberman E. Outcomes of trial of labor following previous cesarean delivery among women with fetuses weighing >4000 g. *Am J Obstet Gynecol.* 2001 Oct;185(4):903-5.

C-Obs 39: Caesarean Delivery on Maternal Request (CDMR)

Date of this document: July 2010 First endorsed by Council: July 2010 Next review due: July 2013

Definition

The term 'caesarean delivery on maternal request' (CDMR) refers to elective delivery by caesarean section at the request of a woman with no identifiable medical or obstetric contraindications to an attempt at vaginal delivery.

Ethical considerations

Some surgical procedures (for example, cosmetic surgery) are performed on patient request in the absence of a direct physical benefit. Important in the ethical consideration of such surgery would be consideration of: patient autonomy; beneficence (doing good for the patient); non-maleficence (not doing harm to the patient); veracity (providing accurate information); and justice (for example, appropriate allocation of resources).

Clinical advantages of elective caesarean section (over planned vaginal delivery)

When considering the clinical issues related to planned vaginal delivery, the possibility of emergency caesarean section has to be considered in any decision analysis.

Perinatal mortality

Approximately 1.4 per thousand can be expected to have an antenatal, intrapartum or neonatal death after 39 weeks gestation.⁸ This is an unacceptable risk for many women and health professionals.¹⁰ Given the significant morbidity and mortality associated with induction of labour, elective caesarean section may be the most appropriate course of action for a woman for whom a risk of perinatal death of the order of one in 700 is completely unacceptable.

Long-term morbidity

Cerebral palsy can be expected to affect approximately one in 1000 term births. Of these, only ten per cent are felt to have an intrapartum origin², but a further unknown percentage are the

consequence of 'late antenatal' events that might be prevented by elective caesarean section.

Erb's palsy and other birth injuries may occur after caesarean section, but are unequivocally greater after vaginal birth. The rate of Erb's palsy is reported variously between 0.45 and three per thousand births. This is in the range that most women would seem to regard as important in deciding between caesarean section and vaginal birth.¹⁰

Pelvic floor damage

This is a highly contentious area, but there is no doubt a small number of women have continence problems and/or sexual difficulty as a consequence of vaginal birth – at a rate greater than that seen with elective caesarean section. Whilst this number is small and mostly resolving in the months after birth, there is the possibility of long-term sequelae. Nevertheless, it is important to acknowledge that pregnancy, regardless of method of delivery, increases the risk of pelvic floor dysfunction and that caesarean section does not remove the risk of pelvic floor dysfunction completely.

Clinical advantages of planned vaginal birth

Index pregnancy

This is yet another area of practice where an extremely low but clinically important frequency of adverse outcomes makes assessment difficult. Epidemiological data is unable to distinguish a difference in maternal mortality.⁵ In fact, the maternal risks of the index pregnancy are very much related to the likelihood of successful vaginal birth. Because 'emergency' caesarean section is more hazardous than the elective procedure, it can be safer for the mother in the index pregnancy to perform an elective procedure than attempt vaginal birth if the likelihood of achieving vaginal birth is not high.⁴ In most circumstances, elective caesarean section is likely to be associated with a higher maternal mortality than planned vaginal birth, but the absolute number is extremely small.

Subsequent pregnancies

Pivotal in the decision-analysis for many women should be the intended future family size. With rising caesarean section rates, placenta accreta is becomes increasingly common. Silver *et al*⁷ found that placenta accreta was present in 0.24 per cent, 0.31 per

cent, 0.57 per cent, 2.1 per cent, 2.3 per cent and 6.7 per cent of women undergoing their first, second, third, fourth, fifth and sixth or more caesarean deliveries, respectively. This was a consequence of both an increasing incidence of placenta praevia with repeated caesarean sections and an increased likelihood of placenta accreta where the placenta was located over the uterine scar.

Cost

Elective caesarean delivery (ECD) is associated with greater cost than uncomplicated vaginal birth. Nevertheless, the cost of ECD needs to be compared to the cost of ATTEMPTED vaginal birth (therefore, including complicated vaginal deliveries and intrapartum emergency caesarean section). It is for these reasons that many cost-effectiveness models have failed to demonstrate an increased cost of ECD.

Recovery time

There can be no doubt that for most women the recovery after vaginal birth will be quicker, particularly with second and subsequent vaginal deliveries.

Conclusion

When a women requests elective delivery by caesarean section in the absence of medical indication, the obstetrician should acknowledge the legitimacy of the request and explore the reasons underlying it. Accurate information may be sufficient to alleviate concerns and some issues, such as fear of pain, may be satisfactorily addressed in other ways. The expected family size needs to be taken into account and a planned family size of more than three children would be highly significant in the decision matrix.

If, after full discussion, the patient persists with a request for delivery by caesarean section, the obstetrician may:

 Agree to perform the caesarean section, providing the patient is able to demonstrate an understanding of the risks and benefits of the course of action she has chosen;

OR

- 2. Decline to perform the caesarean section in circumstances where:
 - The obstetrician believes there are significant health concerns for mother or baby if this course of action is pursued; or
 - The patient appears to not have an understanding sufficient to enable informed consent to the procedure;

OR

3. Advise the patient to seek the advice of another obstetrician for a second opinion.

Links to other related College Statements

C-Obs 31: Routine Intrapartum Care in the Absence of Pregnancy Complications

C-Gen 2: Guidelines for Consent and the Provision of Information Regarding Proposed Treatment

C-Obs 38: Planned Vaginal Birth after Caesarean Section (Trial of Labor)

References

- Agency for Healthcare Research and Quality. Evidence Report/ Technology Assessment. Number 133. Cesarean Delivery on Maternal Request. March 2006. Available at: www.ahrq.gov/clinic/tp/ cesarreqtp.htm#Report. Accessed December 5, 2007 at: www.acog. org/from_home/publications/press_releases/nr05-09-06-1.cfm.
- Blair E, Stanley F. Aetiological pathways to spastic cerebral palsy. Paediatr Perinat Epidemiol. 1993 Jul;7(3):302-17.
- Doumouchtsis SK, Arulkumaran S. Are all brachial plexus injuries caused by shoulder dystocia? *Obstet Gynecol Surv.* 2009 Sep;64(9):615-23.
- Lilford RJ, van Coeverden de Groot HA, Moore PJ, Bingham P. The relative risks of caesarean section (intrapartum and elective) and vaginal delivery: a detailed analysis to exclude the effects of medical disorders and other acute pre-existing physiological disturbances. Br J Obstet Gynaecol. 1990 Oct;97(10):883-92.
- National Institutes Of Health Consensus Development Conference Statement: Vaginal Birth After Cesarean: New Insights March 8-10, 2010.
- Okumura A, Hayakawa F, Kato T, Kuno K, Watanabe K. MRI findings in patients with spastic cerebral palsy. I: Correlation with gestational age at birth. *Dev Med Child Neurol.* 1997 Jun;39(6):363-8.
- Silver RM, Landon MB, Rouse DJ, et al; National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Maternal morbidity associated with multiple repeat cesarean deliveries. Obstet Gynecol. 2006 Jun;107(6):1226-32.
- Vashevnik S, Walker S, Permezel M. Stillbirths and neonatal deaths in appropriate, small and large birthweight for gestational age fetuses. *Aust N Z J Obstet Gynaecol.* 2007 47: 302-6.
- Victorian Department of Health. Victorian Maternity Performance Indicators 2007-8. Access at: http://health.vic.gov.au/maternitycare/ matpeform-ind-0708.pdf.
- Walker SP, McCarthy EA, Ugoni A, Lee A, Lim S, Permezel M. Cesarean delivery or vaginal birth: a survey of patient and clinician thresholds. *Obstet Gynecol.* 2007 Jan;109(1):67-72.

C-Obs 40: Maternal and Perinatal Data Collection

Date of this document: July 2010 First endorsed by Council: July 2010 Next review due: July 2013

Objective

Data collection, with subsequent reporting and analysis, must underpin an ongoing effort to improve quality of care and clinical outcomes. This cannot occur effectively unless the collection is complete and covers all key aspects of the pregnancy, birth, postnatal and neonatal outcomes.

Uniformity

A perinatal and maternal data set must be collected from ALL pregnancies across Australia and New Zealand.

- 1. The data set must be structured so as to enable BOTH regional and international comparisons.
- 2. Where regional differences exist, additional parameters may be collected with a view to directing specific improvements in care and outcomes.

Continued on page 82.

Specific data to be collected

In addition to the standard demographic, obstetric and neonatal data collection, specific attention must be paid to:

a. Maternal and perinatal morbidity and mortality

The data set collected must include both perinatal and maternal outcomes, reporting both morbidity and mortality. Each parameter must be clearly defined to ensure uniformity of reporting and achieve maximal ascertainment.

b. Clinical indicators

The data collected should enable appropriate clinical indicators to be assessed, such as those mutually agreed by RANZCOG and The Australian Council on Healthcare Standards (ACHS).

c. Model of care

Data must include:

- 1. Intended model of care (therefore, prior to the development of any complications).
- 2. Model of care at birth.
- 3. Duration before birth of transfer of model of care.

d. Place of birth

Data must include:

- 1. Intended place of birth (therefore, prior to the development of any complications).
- 2. Place of birth.
- 3. Duration before birth of transfer of place of birth.

Reporting and analysis

Collection of data alone does not improve outcomes:

- 1. Timely and relevant reporting and analysis of maternal and perinatal data should lead to recommendations for improvements in care, based on that data.
- When comparisons are made between models of care or places of birth, it is important to take steps to ensure that, for the purposes of comparison, each subset had an equivalent obstetric risk profile.
- Reporting and analysis of maternal and perinatal data should be contemporaneous, with agreed timeframes that allow early assessment of any changes to maternity service delivery.
- 4. Reporting must be transparent and available to service providers, relevant authorities and the public.
- 5. Reporting should be accessible to consumers so that their choice in determining models of care and types of service delivery is based on accurate information regarding relevant benefits and risks.

Audit of data collection completeness and quality

Perinatal and maternal data should be subject to regular and random audit and validation to ensure that collection and recording methodologies are sound. Audit of data collection against birth registrations is recommended to ensure completeness of data.

Thinking of retiring from active practice?

If or when you do retire will you be:

- Completely and permanently retired from practice as a specialist obstetrician and/or gynaecologist?
- No longer acting as an expert witness in the field of obstetrics and gynaecology, except in:
- cases for which you have already provided an opinion prior to the date of signing this Retirement Declaration; and
- cases which deal with medical practices current during any time you were in active practice as a specialist obstetrician and/or gynaecologist and prior to signing the Retirement Declaration?

If you answered **YES** to all of the above then why not download the Retirement Declaration form: www.ranzcog.edu.au/fellows/cpdretirement.shtml.

What happens to my Fellowship if I sign the Declaration of Retirement form?

If or when you decide to sign and submit the completed Declaration of Retirement form to RANZCOG, your classification will be changed to Retired Fellow.

As a Retired Fellow of RANZCOG you will not have to:

- Pay annual subscription fees
- Participate in the RANZCOG CPD Program

As a Retired Fellow you will still receive the following from the College:

- O&G Magazine (four issues per year)
- ANZJOG (six issues per year)
- Journal of Obstetrics and Gynaecology Research (if you have elected to receive this)
- RANZCOG Annual Report

What about my patient records?

See College Statement No. WPI-8 on Guidelines for Patient Record Management on the Discontinuation of Practice: www. ranzcog.edu.au/publications/collegestatements.shtml#WPI.

What if I don't want to retire just yet?

If you are not in a situation where you can complete the Retirement Declaration form then you will continue as a Fellow of the College.

For further information or a copy of the Retirement Declaration form, please contact:

Val Spark CPD Senior Coordinator (t) +61 3 9412 2921 (e) vspark@ranzcog.edu.au

AOCOG 2011

The XXII Asian and Oceanic Congress of Obstetrics and Gynaecology

23-27 September, 2011 Taipei, Taiwan

New Frontiers in Women's Health

RANZCOG is seeking Fellows to self-nominate as potential speakers for AOCOG 2011 in the fields listed below. If you wish to put your name forward to be an invited speaker on any of the following topics please send your name, email and topic(s) to Carmel Walker, Asia Pacific Senior Coordinator at cwalker@ranzcog.edu.au.

The deadline for self-nomination is 15 October 2010.

Note: RANZCOG support of your nomination as a speaker does not guarantee a place on the meeting program. Financial assistance is not available from the congress organisers or RANZCOG.

Topics and Subtopics for Symposia

- 1. General Gynaecology
 - Abortion and ectopic pregnancy
 - Diseases of lower genital tract
 - Uterine myoma
 - Pelvic inflammatory disease
 - Contraception
- 2. Gynaecologic Oncology
 - Cervical cancer
 - Endometrial cancer
 - Ovarian cancer
 - Gestational trophoblastic disease
 - Minimally invasive surgery in gynaecologic oncology
- 3. Imaging
 - Breast imaging
 - First trimester fetal ultrasound screening
 - Second trimester genetic ultrasound and fetal malformation
 - 3D/4D ultrasound in obstetrics and gynaecology
 - Imaging in gynaecologic malignancy
 - Fetal MRI
- 4. Perinatology
 - High-risk pregnancy
 - Obstetrical haemorrhage
 - Infectious disease and vaccination in pregnancy
 - Prenatal diagnosis
 - Birth injury

- 5. Reproductive Endocrinology
 - Polycystic ovary syndrome
 - Endometriosis
 - Assisted reproductive technology
 - Cryopreservation of gametes, embryos and ovarian tissues
 - Recurrent pregnancy loss
- 6. Urogynaecology
 - Lower urinary tract dysfunction
 - Urogenital fistula
 - Pelvic organ prolapse
 - Urinary tract infection
 - Urodynamics
- 7. Menopause
 - Women's health and quality of life
 - Cardiovascular diseases
 - Osteoporosis
 - Breast health
 - Alternative medicine
- 8. Minimally Invasive Surgery
 - Laparoscopic management of benign ovarian tumor
 - Laparoscopic pelvic floor reconstructive surgery
 - Endoscopic fertility promoting surgery
 - Endoscopic myomectomy
 - Endoscopic surgery in Müllerian duct anomaly

News from theFetalFrank ForsterSurveLibraryA Pro

Diane Horrigan

RANZCOG Librarian

The Frank Forster Library is fortunate to have acquired the following rare book this year:

Dewees, William P. An essay on the means of lessening pain and facilitating certain cases of difficult parturition. 2nd ed. Philadelphia: Published by Thomas Dobson and Son at the Stone House, No.41, South Second Street, 1819.

This volume was Dewees' published dissertation for the degree of Doctor of Medicine at the University of Pennsylvania in April 1806.

In the first edition, which is only available in microfilm from the National Library of Australia, Dewees dedicated this work to Dr William Shippen, Dr Benjamin Rush, Dr Caspar Winstar, Dr James Woodhouse, Dr Benjamin Smith Barton and Dr Philip Syng Physick. This second edition does not have the dedication noted.

This small-sized volume has 156 pages of text. There are no illustrations. Bibliographical references, some of which are quite detailed in information, are included to illustrate findings and observations. After describing the different kinds of contractions of the uterus in the first part, there are four case studies included at the end of the text giving detailed observation, illustrating the difficulties women present in labour. Dewees quotes: 'A woman must carry her child to the full allotted period...she must be exempt from all and every cause capable of exciting uterine contraction...'. In each case, Dewees describes the use of ergot and its success in advancing or re-establishing full labour contractions.

The Frank Forster Library is the only library in Australia to have this as a printed text; the National Library of Australia has a microfilm holding of the first edition. This title complements another work the library holds by William Dewees:

A compendious system of midwifery, chiefly designed to facilitate the inquiries of those who may be pursuing this branch of study, illustrated by occasional cases. London: John Miller, 1825.

William Potts Dewees (1768-1841)

Dewees is one of the first noted American obstetricians to develop obstetrics as a separate field of medicine in the United States. He was Professor of Obstetrics and Chair of Obstetrics from 1831 to 1841, at the University of Pennsylvania. *Historical review of British obstetrics and gynaecology, 1800-1950* (edited by Munro-Kerr, Johnstone and Phillips) acknowledges Dewees as the 'Father of Midwifery' in America. Dewees was instrumental in the later decades of the 18th century in shaping obstetrics as a specialty.

Women were generally the practitioners of midwifery in the 18th century in America. Dewees played an instrumental role in breaking down the social and educational barriers that prevented physicians from delivering babies, thus greatly enhancing the probability that both mother and infant would survive childbirth.

Fetal Surveillance: A Practical Guide

Reviewed by Dr Anthony Marren RANZCOG Trainee

Dr Jonathan Hyett FRANZCOG

This book articulates the underlying philosophy of the *RANZCOG Intrapartum Fetal Surveillance Clinical Guidelines* by providing a compact yet comprehensive resource for health professionals involved in obstetric management.

Fetal Surveillance: A Practical Guide is divided into four distinct chapters, starting with a succinct description of 'the physiology of fetal surveillance' which provides the reader with the necessary knowledge to appreciate the content of subsequent chapters. The authors continue to discuss the practicalities of fetal heart rate monitoring, describing techniques and potential pitfalls of intermittent auscultation and cardiotocography and listing indications for both antenatal and intrapartum CTGs. The major part of the book is given over to CTG interpretation. This chapter describes the normal CTG and contains clear definitions for the various components that are assessed. The authors continue to differentiate between antenatal and intrapartum CTGs, clearly defining the normal and abnormal CTG. Each point is well illustrated with a series of high quality CTGs placed in a clinical context.

The fourth chapter, entitled 'Other fetal surveillance', discusses the importance of fetal/umbilical cord blood sampling and provides a superficial review of ultrasound-based techniques for antenatal fetal surveillance. Finally, a copy of the current *RANZCOG Intrapartum Fetal Surveillance Clinical Guidelines* is appended.

The authors should be congratulated on managing to define the process of fetal monitoring and the underlying physiology in such a clear fashion. The text is easy to read and will be useful to newcomers to the specialty, as well as those with more experience who will find it a handy point of reference. The main disadvantage and notable omission from the *RANZCOG Intrapartum Fetal Surveillance Clinical Guidelines* is the lack of a grading system for CTG interpretation. Whilst the authors may not want to focus on this approach, it would have been worthy of some discussion, particularly as grading of CTGs has been endorsed by some policymakers in Australia.

FETAL SURVEILLANCE: A PRACTICAL GUIDE

Authors: Baker L., Beaves M., Trickey D. and Wallace E. Year Published: 2009



This book is specifically written to support the RANZCOG FSEP. It is designed to be an easy-to-read resource for all clinicians involved in the care of women in pregnancy and labour. The book contents include:

> The physiological basis for fetal surveillance Fetal heart rate monitoring, including auscultation The abnormal CTG Other methods of fetal surveillance

The **BOOK ORDER FORM** is available from the **FSEP website** at http://www.ranzcog.edu.au/fsep/practical_guide.shtml or **FSEP office** at fsep@ranzcog.edu.au or 03 9412 2958



Multin

s

The Fetal Surveillance Education Program of The Royal Australian and New Zealand College of Obstetricians and Gynaecologists

Women's health in India A personal journey

Prof Ajay Rane FRANZCOG

In January 2010, at the 53rd Annual Federation of Obstetric and Gynaecological Societies of India (FOGSI) Meeting in Gauhati, Assam, the Indian College of Obstetricians and Gynaecologists (ICOG) bestowed me with an Honorary Fellowship for services provided to the specialty.

The President of FOGSI, Dr Sanjay Gupte, said I was the first Australian and the youngest doctor to receive this award from ICOG. Having been thoroughly humbled by such an honour, it was time to reflect on what it all meant.

Being born in the United Kingdom and then uprooted to a small town in India called Jalgaon at the age of six was not a pleasant memory. However, the scene was set, since my father was the only Fellow of the Royal College of Surgeons in his community willing to leave the good life in the UK to serve his people in India.

School was a 50 km round trip on state public transport to the nearest 'English' medium school. It was not difficult to see, even then in my father's hospital, how badly underprivileged women were treated in getting medical care compared to men.

For me, getting into medicine was a rat race competing against tens of thousands of aspirants for 120 seats. Achieving this set the next scene for my exposure to women's health. As a medical student spending endless nights in labour ward, I was exposed to my first maternal death of a 16-year-old primiparous woman with eclampsia and pulmonary odema. With more than 12,000 deliveries a year, my teaching hospital saw every form of morbidity and mortality that the specialty could throw at us. It was quite common for husbands and relatives to refuse to donate blood, even if the woman was haemorrhaging to death, because 'he could get another wife'.

Getting into postgraduate training in obstetrics was another rat race, with only six seats available for our cohort of 200 students. Three years of hard slog, minimal to no leave, on-call 24 hours a day seven days a week, a one in five labour ward roster, over 12,000 deliveries a year, studies, thesis, no epidurals, no neonatal intensive care unit – it was SOLID training – almost like an endurance test.

Most apparent though was the attitude to the birth of a female child. The parents just couldn't hide their disappointment, even if it was a first born child.

After postgraduate training, the next challenge was Membership of the Royal College of Obstetricians and Gynaecologists (MRCOG). This was the ultimate achievement for an Indian trainee. I completed my primary MRCOG in Nepal and experienced my first EVER aeroplane journey of 35 minutes from Calcutta to Kathmandu! (I travelled by boat from the UK to India as a child.) The next ten years in the UK were spent attaining MRCOG, Fellowship of the Royal College of Surgeons (FRACS), Masters in Urogynaecology and then getting a consultant job at the age of 32. India, as a place to serve, only involved a few lectures here and there on holidays and attending the FOGSI meeting in 1996.

The Gosha experience

Having moved to Australia and subspecialised in urogynaecology, again it was time to give back to the 'have nots'.

I was invited to operate at the Kasturba Gandhi (Gosha) Hospital in 2001 to demonstrate the tension-free vaginal tape (TVT) procedure. At once, I realised the cost of one TVT would feed the entire theatre staff for a month and buy much needed essential equipment. In 1885, this hospital was called the Royal Victoria for Women of Caste. Colloquially called the Gosha (*purdah* or veil), it caters for the poorest of the poor women of Chennai.

In 1975, a female urologist was appointed at the Gosha to cope with the ever-increasing demand for repairs of vesico-vaginal fistulas. Professor Rajamaheshwari (Raji), who trained to be a gynaecologist and then did her Masters in Surgery in Urology, has dedicated her life to serving these women in Chennai and all over India.

When I met Raji in 2001 it was a surreal experience. There were 40 patients standing waiting to see me, each with a pelvic pathology bettering the next. Theatres were quite basic but amply substituted by cheerful and willing staff. I was determined to try and make a difference for the women and help Raji, whose dedication, passion and skills are unparalleled.



No running water to scrub when I first started – there was old soap and preboiled and cooled water to get ready to operate.

With the help of my wife Paula, Professor Bob Shull, Associate Professor Malcolm Frazer, Dr George Kaladelfos, Dr Peter Nelmes and many other Fellows of RANZCOG, we set up the Urogynaecology and Reconstructive Pelvic Surgery Society of India (URPSSI) with Raji. This is the only International Urogynecological Association (IUGA) affiliated Indian society in urogynaecology.

The initial desire was to change things. Very quickly we realised we were wrong and that we were there just to help as much as possible and hope for the best. The dedication of the staff resulted in a brand new state-of-the-art theatre suite being built, enabling us to provide an unprecedented quality of care for the underprivileged women of South India.

The government of Tamil Nadu have very generously recognised our contribution by naming the fistula ward the Paula Rane Fistula Ward. We continue our work with Gosha, along with a new orphanage for displaced children with great joy.

The Riwayat experience

In 2006, *The Lancet* published an article estimating the death of 100 million girls worldwide through infanticide, nearly 60 million of these deaths in India alone. This was too much of an issue to be left unexplored. Spurred by the article in *The Lancet* and

my ardent movie-loving, highly creative friend, Professor Sanjay Patole, who is a neonatologist from Perth, we decided to make a true Bollywood film on this issue called *Riwayat*. I met India's first female President, Mrs Pratibha Patil, to discuss the issue of female infanticide, which she strongly condemns. Our movie, *Riwayat*, has four songs sung by famous Indian singers, including Jagjit Singh, Shreya Goshal, Kailash Kher and Shaan.

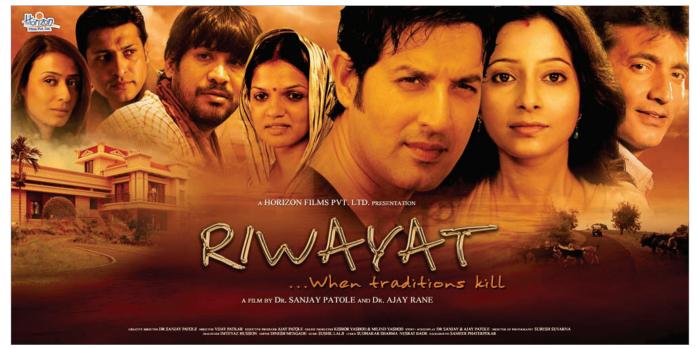
In May, *Riwayat* received the *Award du Merite* at the Monaco International Film Festival for increasing awareness. We continue to showcase the movie worldwide before releasing it at the end of 2010. The expectation is that this movie will save some lives! Read more about *Riwayat* online at: www. riwayatmovie.com.



Professor Rane (left) receiving his Honorary Fellowship of the Indian College of Obstetricians and Gynaecologists.



Waiting room for patients to be seen at Gosha Hospital – no chairs, no appointments!!!



The movie Riwayat will be released at the end of 2010.

Alleviating suffering in Sudan

Dr Alan Hughes FRANZCOG MSF Volunteer

I attended an information evening for Médecins Sans Frontières (MSF) in Alice Springs nearly two years ago and was astonished to learn there was a need for O and G specialists. I had always assumed medical recruitment for this organisation would be limited to trauma surgeons, anaesthetists and orthopaedic surgeons.

Katie Butt

Freelance Journalist

Women's health in the developing world, particularly high causes of maternal mortality, is receiving more attention recently. This is because of the recognised impact on children who lose their mother in places where war, famine and poverty prevail. In countries where many men are either fighting or have died and women are the primary caregivers, without their mother many children will die or may be forced to join rebels, hence women's health has been thrust into the limelight.

In sub-Saharan Africa, women's health is a particularly complex area of medicine. Not only are you working with diseases and clinical issues we don't generally experience first-hand in the western world, but in that setting, you are also contending with extreme poverty, fear, war, hunger, politics and cultural differences.

'The most rewarding aspect of working in Aweil was feeling useful. It was very satisfying to work almost solely on clinical grounds as we had very limited technology.'

In January 2010, I was sent on my first mission to Aweil, South Sudan. I would be the obstetric component of a multinational team of midwives, paediatricians, pharmacists, logisticians and administrators, committed to lowering a maternal mortality rate of 2036/100,000, made huge by lack of infrastructure due to decades of warfare. In countries where most men are either dead or away fighting, the loss of a mother is devastating for a family; it is considered that most children under five years of age would not survive. The three major causes of maternal mortality – eclampsia, haemorrhage and infection – should respond to timely intervention. This would also help reduce the enormous psychological burdens. In a Sudanese colleague's education group of 40 teachers and assistants, only one had both parents alive.

Once accepted for a mission, there are a few hurdles to overcome. For me, the most significant was the reluctance of my wife Chris – her concern for my health and safety and worry about separation after many years of togetherness. Also, it's very difficult to envisage living conditions and what lies ahead, so some degree of anxiety is inevitable, especially on a first mission. However, long talks with two outstanding Australian midwives who had been to Aweil were very useful in surmounting these problems.

The most rewarding aspect of working in Aweil was feeling useful. It was very satisfying to work almost solely on clinical grounds as we had very limited technology. While there was one ultrasound machine, there were no CTGs or IVACs. Biochemistry was limited to Hb (not FBC), syphilis (rapid test) and Parachek (a malaria screen) – there was no bacteriology or histology. There were clinical challenges abound...ruptured uteruses, late obstructed labours (days!) often with fetal death, compound presentation of second twins, placenta praevia (average parity 7 to 8), malaria, syphilis, elephantiasis and maternal tetanus.



Dr Jean-Paul Delain treats a boy for cerebral malaria in Rumaker, Aweil East County.

Also, to be sincerely thanked by the grieving relatives of a dead mother for trying to save her is a profoundly moving experience. The gratitude is overwhelming, as you know as well as the locals, if we weren't there, they wouldn't have a chance.

A major cause of perinatal death in Aweil is neonatal tetanus, perhaps due to a traditional practice of rubbing cow dung on the umbilical stump. Education and opportunistic vaccination at the antenatal clinics helped the women who live in town, but many in outlying areas cannot access these services, so MSF set up a program to administer vaccines to the local people.

I had not been closely involved in the setting up of a mass vaccination program before and was astonished at the logistics. Exhaustive negotiations were undertaken with the bureaucrats at the local Ministry of Health before permission was granted. Then we had to organise a team consisting of Sudanese and international staff – nurses, administrators, logisticians and pharmacists. The biggest challenge would be how to keep the cold chain intact over hundreds of kilometres of desert roads, to arrive in Aweil where the generator power only worked at certain times.

As with any growth experience, it was a bit of a roller-coaster ride, but with many more ups than downs. I couldn't have been luckier in my choice of non-government organisation (NGO). In my view, MSF has impeccable credentials as an employer: remarkable transparency and honesty, excellent infrastructure, lack of potentially compromising dependence on governmental assistance, as well as a proud history and a very sympathetic and egalitarian philosophy. Despite being in a potentially dangerous area, I felt safe as our security is the number one consideration. Also, it's truly international. One of the most exciting aspects of working with MSF is the interaction with colleagues with disparate backgrounds but united in purpose.

I had always wanted to work with an NGO in my retirement. At MSF, the placements are usually only three months for consultants, which is short compared to other NGOs. I'm now looking forward to further projects and new challenges. Perhaps this is what all those past decades of hard work and sleepless nights have been in preparation for!

To volunteer with Medecins Sans Frontiere or to make a donation go to: www.msf.org.au .

Are you looking to obtain further PR&CRM points?

Are you looking to obtain further PR&CRM points?

This three stage process can earn you numerous points.

Stage I: This involves handing out 100 PSQs to your patients and returning them to College House for analysis. Completion of Stage I is worth 2 PR&CRM points. Please note Stage I questionnaires must be returned within 12 months of beginning this project.

Stage 2: After receiving your comprehensive report from the College, outlining the results of your patient satisfaction questionnaires, you then develop an action plan, highlighting any changes that you may incorporate into your practice to promote future patient satisfaction. Completion of Stage 2 is worth 5 PR&CRM points.

Stage 3: Following implementation of the action plan for approximately 12 months, you will be provided with a second kit of 100 questionnaires to re-audit patient satisfaction. A brief comparative report will be provided. Completion of Stage 3 is worth 8 PR&CRM points.

Download the PSQ application form from the website at: www.ranzcog.edu.au/fellows/prcrmactivities.shtml

For queries contact: **Jason Males** CPD & Curriculum Coordinator (t) +61 3 9412 2962 (e) prcrm@ranzcog.edu.au

Queen's Birthday Honours List

Three RANZCOG Fellows achieved awards in the 2010 Queen's Birthday Honours List.

Member (AM) in the general division:

Associate Professor John Svigos, Adelaide, SA

For service to medicine, particularly in the field of obstetrics and perinatology, through executive roles with national and international professional organisations and to medical education.

Dr Christine Tippett, Hawthorn, Vic

For service to medicine, particularly through executive roles with professional organisations, to improved healthcare standards for women and their families, and to obstetrics and gynaecology as a clinician and mentor.

Dr Nic Jools, Walsh Bay, NSW

For service to the community through philanthropic donations of Australian art and financial support for a range of educational and medical organisations, as a benefactor to developing artists, and to medicine in the field of gynaecology.

Anatomy of Complications Workshops 2011, Perth

Dates:

18-19 February 2011 6-7 May 2011 24-25 June 2011 7-8 October 2011

For queries and registrations please contact:

Wendy Rutherford (e) Wendy.Rutherford@health.wa.gov.au

(t) +61 8 9340 1393 (f) +61 8 9340 1063

RANZCOG Research Foundation

Collaborative Bachelor of Medical Science Research Scholarships

Professor David Healy

Chair, Board of Directors, RANZCOG Research Foundation

G_

In 2008, the RANZCOG Research Foundation offered its first Collaborative Bachelor of Medical Science Scholarship. Under this scholarship scheme, open to the O and G medical faculties of each university in Australia and New Zealand, the RANZCOG Research Foundation provides A\$5000, matched by the university department, to assist an undergraduate student with their Bachelor of Medical Science research year. Those participating in 2010 are the University of Adelaide, the University of Melbourne, the University of New South Wales, the University of Western Australia and Monash University. These Collaborative Scholarships continue to grow in popularity and are an important means for supporting the next generation of researchers in our field. The Foundation is pleased to provide you with the following summaries of the research funded in 2009.

Collaborative Bachelor of Medical Science Research Scholarship, 2009 (Monash University)

Ms Susannah Broughton (Supervisor, Professor Euan Wallace)

The Experiences of Ethiopian Women with Ileal Conduits Following Obstetric Injury

In 2009, I undertook a year-long Bachelor of Medical Science research degree, which involved spending four months collecting data at the Addis Ababa Fistula Hospital in Ethiopia.

Obstetric fistula is a devastating condition that affects thousands of women around the world. Although the majority of obstetric fistulae can be repaired surgically, some are irreparable. In such cases, ileal conduit urinary diversion may be considered. My research project aimed to assess the psychosocial impact of a urostomy in the Ethiopian context. This procedure has been performed at the Addis Ababa Fistula Hospital in Ethiopia since 1989 as a last resort for women in whom fistula closure could not be achieved, or who continued to experience incontinence per urethrum despite successful fistula repair.

The findings of my project demonstrated that while most women felt that their life had improved since their ileal conduit, many reported negative effects on aspects of their life, such as relationships and mental health.

I found my time in Ethiopia to be an enriching experience, through which I learnt much about working in a crosscultural environment. My experiences also increased my interest in pursuing a career in women's health. I would certainly encourage future medical students to pursue their interest in obstetrics and gynaecology by undertaking a year of research training and urge specialists to support them in doing this.

Collaborative Bachelor of Medical Science Research Scholarship, 2009 (Monash University)

Ms Patricia Vosdoganes (Supervisor, Professor Euan Wallace)

Investigating the Role of Human Amniotic Epithelial Cells in the Treatment of Inflammation-induced Preterm Lung Injury

Intrauterine infection (IUI) is a major risk factor for chronic lung disease of the newborn – bronchopulmonary dysplasia (BPD). Infection induces lung inflammation that accelerates lung maturation and leads to a disrupted alveolar structure with arrested development, the hallmarks of BPD. There is presently no treatment for BPD. Human amnion epithelial cells (hAECs) are known to mitigate inflammation and aid tissue repair. Using an ovine model of IUI, during my Honours year, I assessed the efficacy of hAECs in preventing BPD.

IUI and pulmonary inflammation was induced in preterm fetal lambs at 117 days gestation (term \sim 147) by the intra-amniotic administration of E. coli lipopolysaccharide (LPS, 20 mg). Fetuses received concurrent hAECs intravenously (IV, n=4), intratracheally (IT, n=4) or in combination (IV+IT, n=4). Controls received saline (n=6), LPS alone (n=5) or hAECs alone (n=2). Fetal lungs were collected at 124 days for assessment.

Following LPS, lungs displayed enhanced functional and structural maturation with increased compliance, septal-crest density and fewer, larger alveoli. Amnion cells decreased septal-crest density (all, p < 0.01), tissue-airspace ratio (IV+IT, p < 0.05), and compliance (IV+IT, p < 0.05) akin to immature controls. Furthermore, hAECs elevated serum IL-10 (IV, IV+IT p < 0.05) and lung CD45+cells (IV, IV+IT p < 0.05).

Human amnion epithelial cells modulate lung changes in an ovine model of intrauterine inflammation. A combination of IV and IT administration appears most effective. We believe that these data suggest that hAECs may be a useful cell-based therapy for the prevention of BPD in preterm neonates born secondary to chorioamnionitis.

Collaborative Bachelor of Medical Science Research Scholarship, 2009 (University of Melbourne)

Ms Cheryl Tang (Supervisor, Dr Penelope Sheehan)

Progesterone Metabolism in Adipose Tissue from Pregnant Women with Raised BMI Compared to Women with Normal BMI at Term

The prevalence of obesity in Australia continues to rise. Obesity is a risk factor for postdates induction of labour and caesarean section for dystocia. Adipose tissue expresses many progesterone metabolising enzymes, thought to be important in maintaining uterine quiescence. We hypothesised that alterations in progesterone metabolism in obese women may contribute to labour complications. We investigated mRNa and protein expression of two main enzymes responsible for progesterone metabolism, 20ahydroxysteroid dehydrogenase (20aHSD) and 5a-reductase.

Omental, subcutaneous adipose tissue and placental samples were obtained from 42 women undergoing elective caesarean section at term, 18 women with a prepregnancy BMI greater than 35 and 24 women with a BMI between 20 and 30 as controls.

Results show a significantly higher 20aHSD protein in women with raised BMI in adipose tissue. 20aHSD was not identified in placenta. No significant difference in 5a-reductase was found.

Increased 20aHSD in adipose tissue from pregnant women with raised BMI may result in decreased circulating progesterone or, conversely, increased 20a-hydroxyprogesterone. This metabolite has been proposed to play a role in human cervical ripening. Increased cervical progesterone may explain the increase in labour complications in obesity.

Despite previous studies demonstrating 20aHSD activity in placental homogenates, 20aHSD protein was not identified in placenta.

Tissue	Cases	Controls	p-value
Omental fat	31 ± 7	14 ± 7	0.03
Subcutaneous	140 ± 19	86 ± 16	0.04



Nuchal Translucency Online Learning Program



Purpose

The Nuchal Translucency Online Learning Program (NTOLP) is designed to replace the theoretical course that is conducted for operators who wish to become credentialed to perform Nuchal Translucency scans.

Content

The NTOLP covers eight topics:

- 1. Principles of screening
- 2. Practicalities of NT measurement
- 3. NT and chromosome abnormality
- 4. Biochemical screening
- 5. 12-week anomaly scan
- 6. Screening test results and informed choice
- 7. Screening and multiple pregnancy
- 8. Increased NT and normal chromosomes

Features

This site uses many elements to engage and interest the learner. Some examples are:

- · Interactivity mouse over, prediction tasks and multiple choice questions
- · Customised images graphs, detailed diagrams, flash animations and ultrasound scans
- Illustrations and text
- Discussion Forums

The course is now live and costs A\$165.00 incl. GST per individual. Please visit www.nuchaltrans.edu.au/ for further details or to enrol. This program is co-located with The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) and development has been funded by the Australian Department of Health and Ageing.

Council Meeting Report 16 July 2010

Penelope Griffiths

Director of Corporate Services

Welcome and announcements

The President welcomed Councillors and non-Councillors to the meeting. Dr Weaver then formally acknowledged the New Zealand Mace, which had been presented to the College from the New Zealand Committee and was being used at the July Council meeting for the first time. The New Zealand Mace will be used alternately with the Australian Mace.

Queen's Birthday Honours List

The President congratulated the following Fellows for their recent awards.

Members (AM) in the General Division

Associate Professor John Svigos, Adelaide, South Australia

For service to medicine, particularly in the field of obstetrics and perinatology, through executive roles with national and international professional organisations, and to medical education.

Dr Christine Trevella Tippett, Hawthorn, Victoria For service to medicine, particularly through executive roles with professional organisations, to improved healthcare standards for women and their families, and to obstetrics and gynaecology as a clinician and mentor.

Dr Nic Jools, Walsh Bay, New South Wales

For service to the community through philanthropic donations of Australian art and financial support for a range of educational and medical organisations, as a benefactor to developing artists, and to medicine in the field of gynaecology.

Report from the President

The President presented his report, including the following major items for the information of Council:

- Release of the National Health and Medical Research Council (NHMRC) National Guidance on Collaborative Maternity Care document.
- Executive Committee Meeting, May 2010, Perth, Western Australia.
- Analysis of Practice Profile of RANZCOG Fellows is complete and available on the RANZCOG website.
- PROMPT (Practical Obstetrics Multiprofessional Training).
- RANZCOG 2010 ASM, 21 to 24 March, Adelaide, South Australia.
- GP Procedural Training Support Program.
- Holders of the New Zealand Diploma of Obstetrics and Gynaecology have been invited to convert their New Zealand qualification to the RANZCOG Diploma.
- Medical Workforce Advice and Coordination Queensland Health.
- Society of Obstetricians and Gynecologists of Canada (SOGC) Meeting, 2 to 6 June 2010, Montreal, Canada.

- Breathing New Life into Maternity Care Conference, 1 to 3 July 2010, Alice Springs, Northern Territory.
- 2010 RANZCOG Provincial Fellows ASM, 6 to 9 May, Tamworth, New South Wales.
- New Council Week format under development.
- Australian and New Zealand Journal of Obstetrics and Gynaecology (ANZJOG) Editorship – the new Editor will be Professor Jan Dickinson from September 2010. An acknowledgement to retiring Editor, Professor David Ellwood, was made.
- FRANZCOG Training Program Review Working Party.
- RANZCOG consideration of nomination for Presidency of the International Federation of Gynecology and Obstetrics (FIGO).
- International relations with other bodies to be monitored on Executive agenda.
- National Maternity Plan update and RANZCOG input via the Maternity Services Advisory Group (MSAG). It has been requested that RANZCOG review proposed pregnancy information hotline material. This is a considerable amount of information and documents will be shared among Councillors for review.
- Joint meeting with the National Association of Specialist Obstetricians and Gynaecologists (NASOG) Executive to be held 11 August 2010.
- Council elections underway, encouragement of new nominations for Council was requested.
- The President passed a formal minute of appreciation to retiring Councillors.

Report from the CEO

The CEO presented his report, including the following major items for information of Council:

- Election of members of the inaugural RANZCOG Board.
- FRANZCOG Training Program Review Working Party.
- Fees.
- Commonwealth Government projects:
 - Selection support grants for GPs located in rural and remote areas to complete DRANZCOG Advanced.
 - Funding the Specialist Training Program (STP).
- Guidelines associated with the Rural Health Continuing Education (RHCE) program.
- New Zealand Parliamentarians' Group on Population and Development – Maternal Health in the Pacific.
- Engagement with jurisdictions in relation to training.
- National Registration and Accreditation Scheme (NRAS) standards.
- CPD Program.
- Australian Medical Council (AMC).
- Staff Organisational Survey.

Executive Committee Report

Public Relations – Porter Novelli

Porter Novelli has been engaged to manage the College's public relations profile and prospective media planning for a period of 12 months. Reviews will be conducted by the College Executive Committee/Board at six and 12-month intervals. Key performance indicators will be utilised to monitor performance and value to the College.

Diploma Reciprocity

The College has instituted a certification process for holders of the New Zealand Diploma to enable them to apply for membership of the College as Diplomates. The recertification aspect will be considered by the Training, Accreditation and Recertification (TAR) Subcommittee of the Conjoint Committee for the Diploma of Obstetrics and Gynaecology (CCDOG).

Strategic Planning Day

The College Strategic Planning Day 2010-2012 will be held on 23 October 2010 for outgoing Executive and incoming Board of Directors.

Regional Committee Chairs Forum

The Regional Committees Forum will be held at College House on 20 August 2010.

UroGynaecological Society of Australasia

A Memorandum of Understanding between RANZCOG and the UroGynaecological Society of Australasia (UGSA) has been established for the provision of support for UGSA.

Education and Assessment Committee

Subspecialty oral examinations

It was approved by Council that as from the 2012 subspecialty trainee intake onwards, the subspecialties oral examinations be removed as a requirement of the subspecialty training programs.

Assessment tools to complement subspecialty written examinations

It was approved by Council that, in conjunction with the Education and Assessment Committee, the subspecialty committees continue to develop further assessment tools to complement the subspecialty written examinations.

Training Accreditation Committee

Amendments to RANZCOG Regulations

Regulation 10.7 – Full-time versus Part-time Training The Chair of the Training Accreditation Committee provided background information to the amendments to the regulations regarding part-time training. Council approved the following amendments to Regulation 10.7 (amendments in bold):

'Year 1 of ITP training must be completed **on a continuous** full-time basis and ideally at the Trainee's home or base hospital. In subsequent years, part-time training may be approved. For the purposes of credited training, the College defines part-time training as halftime training, therefore, 50 per cent (0.5) of the full-time training (1.0) required at the relevant site for the relevant year of training. While Trainees may undertake fractional time if they wish, such time will not generally be credited by the College. Anything less than 1.0 training time will be credited as 0.5, unless exceptional circumstances apply. Anything less than 0.5 training will not be credited. Requests on the basis of exceptional circumstances for fractional training between 0.5 and 1.0 to be credited must be made in writing to the Chair of the relevant Regional/New Zealand Training Accreditation Committee. These requests may be approved by the Chair after appropriate consultation with the Committee and with the Chair of the College Training Accreditation Committee.

Such approval must be obtained prospectively. The approval process must include consideration of the effect any pro rata training arrangement will have on the Trainee's completion of the required months of training for the ITP and/or Elective program. [Delete the previous wording, which was unclear: 'Such a part-time commitment should not be less than half-time. Half-time training must represent 50 per cent of the expected full-time training requirements.']

The [*delete: 'This'*] part-time (therefore half-time) training arrangement defined above must include a range of obstetric and gynaecological experience appropriate to the Trainee's year level, as well as appropriate supervision.

All part-time ITP and Elective training must be completed within 11 years of commencement in the program (as per Regulation 10.11).'

Regulation 10.1.3 – Obtaining Prospective Approval of Training

The Chair provided background information to the amendments to the regulations regarding prospective approval of training. Council approved the following amendments to Regulation 10.1.3 (amendments in bold):

'All ITP/Elective training must be prospectively approved in every year of training. To do this, Trainees must complete and submit to the relevant Regional Office the RANZCOG application for prospective approval of training, which must be checked and signed (if approved) by the relevant Regional/New Zealand Training Accreditation Committee Chair. This application must be submitted not less than four weeks prior to the commencement of training. Only training which has been prospectively approved by the relevant Training Accreditation Committee Chair (therefore, checked and signed off) will be credited by the College.

If Trainees commence training for the first half of the year before obtaining prospective approval of that training, the first six months will not be credited, irrespective of the length of the relevant rotation. If Trainees commence training for the second half of the year and have still not obtained prospective approval of training, then the entire 12 months will not be credited.

Continuing Professional Development Committee

Change of Dates for RANZCOG 2011 ASM

The RANZCOG 2011ASM is to be held in Melbourne, Victoria, from Sunday 27 to Wednesday 30 November 2011 (with premeeting workshops and Diplomates' Days to be held preceding the main meeting on 26 and 27 November 2011).

Continued on page 94.

RANZCOG 2012 ASM

The RANZCOG 2012 ASM is to be held in Canberra, ACT, from Sunday 9 September to Wednesday 12 September 2012 (with premeeting workshops and Diplomates' Days to be held preceding the main meeting on Saturday 8 and Sunday 9 September 2012).

RANZCOG 2011 Indigenous Women's Health Meeting

The RANZCOG 2011 Indigenous Women's Health Meeting is to be held in Cairns, Queensland, from Thursday 2 June to Sunday 5 June 2011.

New Zealand Committee 2012 ASM

The New Zealand Committee Annual Scientific Meeting for 2012 is to be held in Rotorua from Wednesday 21 March to Saturday 24 March 2012.

RANZCOG 2010 ASM, Adelaide, South Australia

The CPD Committee thanked Dr Chris Hughes, members of the 2010 Organising Committee, Ms Kylie Grose and College staff for their contribution to the successful outcome of the RANZCOG 2010 ASM. Final budget and recommendation for the distribution of profits will be provided to the November CPD Committee meeting.

Medico-legal Workshop, RANZCOG 2010 ASM

The CPD Committee congratulated Dr Michael McEvoy on his organisation of the excellent medico-legal workshop, *Giving O and G Evidence: A Mock Court and Report Writing Workshop*, held at the RANZCOG 2010 ASM in Adelaide. This workshop was held on Sunday 21 March 2010 at the Supreme Court of South Australia. Dr McEvoy had advised that he is willing to repeat this workshop and the CPD Committee will progress this with Dr McEvoy.

Verification Check Report

The 2009 Verification Check has been completed and 44 of the 46 Fellows randomly selected during 2009 successfully completed the process; one Fellow was given an exemption and one Fellow retired.

For the 2010 Verification Check, 16 Fellows have been randomly selected and none of these Fellows have previously been selected. Eight Fellows have completed the Verification Check, four have been advised of their selection and one Fellow has provided documentation.

Provincial Fellows Committee

Rural Health Continuing Education

The Support Scheme for Rural Specialists (SSRS) has been replaced with Rural Health Continuing Education (RCHE). The new program will again provide funding for Continuing Professional Development for rural and remote practitioners. The Provincial Fellows Committee is discussing various project ideas and await further funding information in order to determine what projects may be viable.

Election of RANZCOG Board

A ballot and vote was held for the positions of Vice President (2), Treasurer and Board Members (2). The result of the election and composition of the Seventh RANZCOG Council was confirmed as follows:

President:	Dr Rupert Sherwood (as determined at Council meeting, 5 March 2010)	
Vice President:	Dr Digby Ngan Kee	
Vice President:	Dr Louise Farrell	
Vice President:	Professor Michael Permezel	
Treasurer:	Professor Ajay Rane	
Board Members:	Dr Gino Pecoraro Associate Professor Stephen Robson	

RANZCOG Pacific Midwifery Leaders Program

A Brian Spurrett Foundation success story

The RANZCOG Brian Spurrett Foundation aims to make pregnancies safer in the Pacific by improving the capacity of reproductive health workers in the region to deliver appropriate and quality healthcare.

A key component of the Foundation's work is our Pacific Midwifery Leaders Fellowship Program. We provide opportunities for shortterm observation attachments for Pacific midwives in Australian or New Zealand hospitals, to facilitate exposure to high quality practice in maternity care, and, at the same time, to strengthen research capabilities and professional networks between midwives in the Pacific, Australia and New Zealand. Over the past seven years, the program has offered a unique professional development initiative for Pacific midwives and has contributed in a practical way to local and regional efforts to develop human resources in our neighbouring Pacific Island countries.

In 2010, the College has been fortunate to have the opportunity to expand its Brian Spurrett Foundation fellowship program through funding via AusAID's Australian Leadership Award Fellowship (ALAF) scheme. This scheme will, upon application, provide funding for hospitals wishing to provide a Pacific Midwifery Leaders Fellowship Program for four to six weeks for a limited number of midwives. In August 2010, the AusAID ALAF program will fund four Pacific midwives on short-term observation visits to Liverpool Hospital, Sydney South West Area Health Service (SSWAHS). Liverpool Hospital has a seven-year involvement in the College's midwifery leaders program and has already hosted 14 fellowships funded by the Brian Spurrett Foundation. The new initiative to become involved in an AusAID-supported program is an exciting development and opens the door for future opportunities to expand the Pacific Midwifery Leaders Program. Associate Professor Rajat Gyaneshwar, Supervisor for the Pacific Midwifery Leaders Program at Liverpool Hospital and SSWAHS, and Chairman of the RANZCOG Brian Spurrett Foundation Management Committee, comments: 'The experience of Liverpool Hospital and the SSWAHS in RANZCOG's Brian Spurrett Foundation Pacific Midwifery Leaders Program has been mutually beneficial to both ourselves and our colleagues from the Pacific. Our evaluation demonstrates success in providing professional development and experiences for Pacific midwives that they would not otherwise have had access to. Being able to contribute to human resource development for the Pacific has been rewarding and the interest and commitment of SSWAHS is a good example of what can be done and how we can all contribute to raising the level of reproductive health services in the region. In 2010, the opportunity to expand our RANZCOG Pacific Midwifery Leaders Program is an exciting development to complement the existing work of the Brian Spurrett Foundation.'

The President of RANZCOG, Dr Ted Weaver, adds: 'Over the past seven years, the Brian Spurrett Foundation has been well supported and we are very appreciative of the goodwill and donations from College Fellows and members of the public. These contributions from RANZCOG, our Fellows and the public have enabled the Foundation to build a recognised track record in professional development for Pacific midwives. Most importantly, I would like to acknowledge the SSWAHS administration and staff who provide an excellent midwifery leaders program. This has provided a sound platform for us to continue and expand our fellowship program. We welcome involvement of other hospital networks.'



Networking and learning with Pacific colleagues. A farewell party for visiting Pacific midwives at Liverpool Hospital, May 2010. Sr Sera Witherow and Sr Tagiyaco Druku (far left) from Fiji, Mrs Kerry Spurrett (far right) and Mr Richard Gilfillan, midwifery supervisor (seated), with the Liverpool Hospital midwifery team.

How can your hospital get involved?

For Fellows and hospitals interested in further information about what is required for participation in RANZCOG's Pacific Midwifery Leadership Program and how to work with RANZCOG to access funding to host shortterm observation visits for Pacific midwives, contact:

Carmel Walker Senior Coordinator Asia Pacific Services (e) cwalker@ranzcog.edu.au (t) +61 3 9419 0672

Obituaries

Irwin (Bill) Bruce Faris

1918 – 2009

Irwin Faris, known as Bill, was born in Dunedin in 1918 and, after his secondary education at New Plymouth Boys High School, he was awarded a scholarship to attend the University of Otago in 1936. He graduated MB ChB in 1941.

After graduation, Bill joined the New Zealand Army then transferred to the New Zealand Air Force. He was in an aeroplane that went down into the sea near a remote island in the New Hebrides and survived for four days before being rescued.

After serving as a registrar in obstetrics and gynaecology in Dunedin Public Hospital, Bill went to the Crown Street Women's Hospital in Sydney, followed by postgraduate study in the United Kingdom. He gained the MRCOG in 1949 and the Edinburgh FRCS in 1950.

Returning to New Zealand, he went into general practice in Takapuna, in partnership with his father and, two years later was appointed to the Cornwall Hospital, later to become the National Women's Hospital. Bill started a private practice in central Auckland in 1955 and gained the FRACS and the FRCOG in 1961. He became a foundation member of the RNZCOG and retired from practice in 1990.

During his career, Bill was Head of one of the clinical teams at National Women's Hospital and from 1963 to1983 was medical superintendent at St Helen's Hospital. He was a member of the New Zealand Council of the RCOG between 1965 and 1969 and was an elected member of the Auckland Hospital Board, serving as deputy chairman during the late 1970s. For his services to medicine, Bill was awarded the Queen's Service Order in 1977.

Bill Faris died in October 2009.

Dr Tony Baird FRANZCOG New Zealand Felicity Tompkins (Bill's sister)

Dr Joan Evelyn Storey

1921 - 2009

Joan Storey was born in Randwick, New South Wales, on 2 December 1921. A brilliant student, Joan was educated at Ascham, Sydney, gaining prizes every year of her schooling. She continued to excel at the University of Sydney where she graduated in medicine in 1944, being one of the earliest women to be awarded First Class Honours and the University Medal together with the Susan Sanders Paediatrics Scholarship.

After graduation, Joan worked as House Surgeon at the Royal Prince Alfred Hospital, part of which was spent as RMO to her father. During this time, she acquired an interest in obstetrics and gynaecology.

In 1948, Joan travelled to London as ship's surgeon on the Port Lylleton. After working and studying in London she was awarded the MRCOG in 1952. She furthered her training in several London hospitals before returning to Sydney where she set up a general practice in Penshurst. After several years, Joan entered specialist practice and was appointed to the King George V Memorial Hospital, the Rachel Forster Hospital and St George Hospital, where she became a much respected chairman of the department. She was elevated to the FRCOG in 1973 and later became a Foundation Fellow of the RACOG.

After many years of devoted and selfless service to her patients and colleagues, Joan retired to Blackheath in the early 1980s. She became involved in community affairs and the Red Cross Society sharing this with her brother, Dr David Storey, who became Chairman. She was also interested in music and botany and was an active member of the Blackheath Horticultural Society and subsequently an authority on Australian native plants.

Joan will be remembered as a kind, patient-committed and civicminded person of the greatest integrity. She died on 5 November 2009 after a very full life largely devoted to her patients and the community.

Dr Trevor Hyde

FRANZCOG Sydney, New South Wales

Dr Antony (Tony) Baccarini

1925 – 2010

Antony Livio Pasquale Baccarini was born in Woollahra on 29 December 1925. An only child, he grew up in that area. During World War II his father, a lecturer at the University of Sydney, was interned. Supported by his mother, a French teacher, he completed his secondary schooling at Sydney High School and entered medicine at the University of Sydney graduating MBBS in 1950. On graduation, he was a resident at Prince Henry Hospital and Crown Street Women's Hospital, Sydney.

Tony travelled to the UK and worked at Mile End whilst obtaining his MRCOG in 1954. Elevated to FRCOG in 1970, he was a Foundation Fellow of the Australian College in 1979. On returning to Sydney, he was appointed the initial Honorary Gynaecologist at Liverpool District Hospital when it opened in 1958, remaining on the staff there until retirement. With another appointment at Fairfield District Hospital, he practised as a generalist obstetrician and gynecologist in Sydney's south west. He was a VMO gynaecologist at Sydney Hospital and Westmead Hospital.

A tall man, he walked in an erect and stiff manner due to spinal problems. He appeared rather superior and unapproachable, but neither was true of the man. Impeccably mannered, he was charming and entertaining. He spent an active and stimulating retirement in Bowral playing tennis, reading and gardening.

He died aged 84 on 5 February 2010. He is survived by his third wife Helen, children Belinda and David, stepson Mark and four grandchildren.

Dr Ray Hyslop

FRANZCOG Gwandalan, New South Wales