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SEPSIS REDEFINED

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The College

Sepsis redefined

Women's health

The College

From the President

Dr Vijay Roach
President

This issue of *O&G Magazine* explores the subject of sepsis. As we know, sepsis may arise in pregnancy at any time: before delivery, during labour or postpartum. Its source can vary and the onset can be gradual, subtle, but with very harmful effects: pregnant women with severe sepsis may appear very well before suddenly collapsing, with little or no warning. In gynaecological practice, sepsis is relevant in both surgical and non-surgical settings. Prophylaxis, timely recognition of infection and appropriate management, both antimicrobial and supportive, is complex. We welcome the scholarship and discussion in this issue, which will contribute to our knowledge of, and help us manage, these potentially life-threatening conditions.

Earlier in the year, I was contacted by a bereaved father following the death of his daughter from sepsis in pregnancy. I assured him that the College would address the issue of sepsis; educating and informing our members. While nothing can heal the distress of that family, or any other family's loss of someone they love, I hope that this issue of *O&G Magazine* sends a message of care and compassion, and our determination to reduce the risk of another tragic loss.

In developed countries, such as Australia and New Zealand, we are lucky we have quality healthcare systems that help identify severe sepsis, thus saving lives. However, there are inequities in healthcare within our own countries, particularly among Aboriginal, Torres Strait Islander and Māori communities. Additionally, there are many places across the world that are not as fortunate. Internationally, RANZCOG continues to make significant contributions to the provision of safe, high-quality healthcare. RANZCOG recognises our responsibility in the Pacific and, led by a hugely passionate group of members and trainees, we are committed to improving the health of women and their families in our region. I have attended several conferences in our neighbouring countries this year, meeting remarkable, dedicated and skilled individuals doing what they can to make a difference to their communities, and I look forward to RANZCOG's continued support and collaboration in the years to come.

At the Annual Scientific Meeting in November, I launched the College's first Gender Equity and Diversity Report, which formalises the College's commitment and determination to increase gender equity and diversity within RANZCOG leadership. We acknowledge that barriers, including implicit bias and current stereotyped leadership styles, may have impeded leadership opportunities for women and other groups, including specialist international medical graduates. These barriers have restricted training opportunities for some members of RANZCOG, reduced opportunities for some members to participate in RANZCOG events and participate in their workplace, and, affected participation for some RANZCOG employees. Actions we have committed to include, but are not limited to:

- Consideration for a minimum target of 40 per cent female and 40 per cent male Board representation for all future RANZCOG Boards
- Engage with the Australian Commonwealth Workplace Gender Equality Agency to progress gender equity, inclusion and diversity policies across all areas of the College, directed towards leadership, training, academic events, hospitals and other workplaces
- Identify and respond to barriers to participation in RANZCOG leadership
- Establish an online Gender Equity Resource Kit for all RANZCOG members
- Provide all current Councillors with training on implicit and explicit bias

- Implement a target of 30 per cent female representation for RANZCOG examiners in 2020, and a target of 40 per cent female representation for RANZCOG examiners from 2021
- At College-affiliated meetings, the targets for speakers will be minimum 30 per cent women in 2021, minimum 40 per cent in 2022 and 50 per cent in 2023
- At trainee selection, consider the use of blinded resumes
- Investigate the need, role and impact of quotas or targets at trainee selection

I encourage all of you to read the report on the RANZCOG website: ranzcog.edu.au/our-college/gender-equity-and-diversity. Your feedback is always welcome.

As this is the last issue of *O&G Magazine* for 2019, it is a good time to pause and reflect on the year that has passed. During my 20-year membership of RANZCOG, I have never before witnessed this level of engagement from our membership. Through meetings, emails, phone calls and social media, our membership is calling upon the College to be the voice of women's health in Australia and New Zealand. Our members want their College to maintain high standards in training, accreditation and clinical guidance. But they also want RANZCOG to be an advocate for women, for Aboriginal, Torres Strait Islander and Māori communities, refugees, and the right of all people to access quality healthcare, to address the social and cultural determinants of health.

In NSW, after years of tireless campaigning from consumers, politicians and the medical community, abortion was finally decriminalised in September 2019. This historic change will ensure that women are able to access and receive the healthcare they need in a timely, professional, compassionate and respectful manner. Your College worked in collaboration with AMA (NSW), NSW politicians across the political divide and consumer bodies, and our contribution was acknowledged and appreciated by all involved. The debate continues in New Zealand and South Australia and we remain hopeful for a positive outcome.

Like any organisation, we face challenges. It is how we respond to these challenges that will define us. We need to confidently address issues of sexism, bullying and harassment, and foster a culture of inclusion and respect. We need to be a College that is fit for purpose today, and future-proofed for the challenges ahead of us. I believe that with a supportive and talented Board, the Council and its hard-working Committees, the skilled College staff, and the passion and commitment of our members and trainees, we can be confident in the future prospects of RANZCOG.

As the year draws to a close, reflect on the importance and value of the work that we do, our service to the community. Take time for yourself, caring for your physical health and emotional wellbeing. You matter. Have a safe and restful festive season, and see you in 2020.

From the CEO

Vase Jovanoska
Chief Executive Officer

For this last issue of *O&G Magazine* for 2019, we cover the topic of sepsis, a major health problem and the subject of important research and advocacy efforts around the globe. This issue recognises how high-quality data analysis, evaluation and evidence can support the activities of our members and trainees and, most importantly, improve outcomes for patients.

Accreditation Comprehensive Report

In September, the College submitted its formal Accreditation Comprehensive Report to the Australian Medical Council (AMC). The Report provides an overview of the College's current training program and has provided us with the opportunity to reflect on what we do well, as well as assess those areas for improvement and development.

The AMC will review the various accreditation standards and conditions that we as a College must adhere to, in line with increasing regulatory reporting and compliance requirements with various regulatory bodies, including the AMC and Medical Council of New Zealand (MCNZ).

The College should receive feedback on our report in February 2020. The outcomes of the assessment by the AMC will assist us in continuing to deliver high-quality education and training, with a contemporary and well-structured approach to governance, collaborative engagement between all members, trainees and professional staff and efficient College operations, in line with our vision and mission.

I would like to acknowledge representative trainees, Dr Patricia Vosdoganes and Dr Rebecca Mackenzie-Proctor, for their collective efforts and independent submission, in addition to College staff who worked on this important submission.

Trainee support

RANZCOG has an obligation to provide our trainees with the highest standard of training and services. The Curriculum Review project that is currently underway will assess the current RANZCOG training programs, curriculums, assessments and regulations to ensure that they remain fit-for-purpose and result in graduate outcomes that will provide the appropriate skills, knowledge and attributes for O&G specialists into the future.

Wellbeing is an important issue for everyone. The College will continue to advocate for system change in areas that affect trainee wellbeing. It remains a priority for the College to have the appropriate support structures in place for trainees and members so they can get help and advice when they need it. The College is currently working to enhance our existing support services for trainees and training supervisors.

Values

I am very excited about the Organisation Values Working Group (OVWG), who will commence work in November 2019. OVWG will be tasked with the important job of identifying RANZCOG's overarching organisational values, that is, a set of values that inspire and relate to all members, trainees and staff at RANZCOG.

We share, and are invested in, the same mission and vision for our College. We work together every day and it seems fitting that a set of shared values should underpin our work and provide us the opportunity to be driven by, and exhibit, the same standards and values in collaboration with each other.

Reflection

For everyone at the College, 2019 has been an eventful year. My first ten months as CEO of RANZCOG have been filled with learning and meeting so many Fellows, trainees and stakeholders of the College who all work tirelessly towards the same goal: excellence in women's health.

As we move towards 2020 at great speed, I would like to acknowledge the hard work, leadership and continued support of the RANZCOG Board led by President Dr Vijay Roach; the dedication and commitment of the 11th RANZCOG Council and the College's many committees.

I would also like to extend my thanks to College staff around Australia and New Zealand for the work and support they provide to our members and trainees.

I hope the festive season is one of relaxation and recharging, but I acknowledge that many of our members and trainees will be sacrificing time with their loved ones to work across this busy holiday season, with Christmas and New Year's babies yet to arrive.

My hope for RANZCOG in 2020 is that more of our members and trainees engage with the College; to see the opportunity to be part of an organisation that is dedicated to the mission of excellence and advancement of women's health.

LEADERS IN FOCUS

Dr Kirsten Connan
MBBS(Hons), FRANZCOG, DDU
MMedEd (Gender and Leadership)

This feature sees Dr Kirsten Connan in conversation with RANZCOG members in a broad range of leadership positions. We hope you find this an interesting and inspiring read.

Join the conversation on Twitter
#CelebratingLeadership @RANZCOG @connankf

A/Prof Christine Tippett AM FRANZCOG

A/Prof Tippett's entry into O&G occurred after a nine-year break from medicine, during which time she had three children, Sarah, Jonathan and Bronwyn. She now has eight grandchildren whose company she very much enjoys.

In 1981, Chris was appointed as one of three trainees in obstetrics and gynaecology at Queen Victoria Medical Centre (QVMC) in Melbourne. All three trainees appointed to QVMC that year were women, which caused much comment and some controversy. There, she excelled in her training, achieving the FJ Brown Medal in 1984 for the Royal Australian College of Obstetrics and Gynaecology examinations. She spent two years at St Mary's Hospital in Manchester where she gained invaluable experience in the specialty. At the completion of her training, she was appointed as a specialist at QVMC and Box Hill Hospitals and commenced a solo private practice in East Melbourne. When the QVMC moved to Clayton as Monash Medical Centre in 1987, Chris joined the move and continued her role as specialist obstetrician, being appointed head of the diabetes pregnancy service. At this time, she transferred her private practice to Clayton, and further developed her interest in high-risk obstetrics and, in particular, maternal medicine in both the public and private sectors.

In 2010, she was made a Member of the Order of Australia (AM) and in 2017, a member of the Victorian Honour Roll of Women.

In 2018, Chris was elected Honorary Treasurer of the International Federation of Obstetrics and Gynecology (FIGO) and is enjoying making a contribution to the international community.

Chris was both the first, and today remains the only, female RANZCOG President (2006–2008). I had the pleasure of interviewing Chris about her career at College House, where her Presidential photo is on view.

What words best describe your life?
Rewarding and fortunate!

Who has been the greatest influence in your life?
My mother. She was an amazing lady and an outstanding role model for me. I would describe her as an early feminist and a woman who strongly believed that women could and should be able to do whatever they wanted. Although I was often told by others that medicine was not a career for a woman, I cannot recall either she or my father ever questioning my decision.

Do you see yourself as a leader?
That is a difficult question to answer. I have held a number of leadership positions during which time I have worked with many people to drive change and set high standards with the aim of improving the healthcare that we provide for women.

Why did you choose to specialise in O&G?
I loved both medicine and surgery and it seemed liked the perfect combination of both. It was a fortunate choice as I cannot think of any other specialty that I would have preferred.

What have been your proudest leadership roles?
Being the RANZCOG President was a great privilege. During my presidency, I persuaded my colleagues to support me in holding the first Indigenous Women's Meeting in Darwin. It was extraordinarily successful and I am delighted that has led to RANZCOG having a greater focus on Indigenous women's health. I represented RANZCOG at the Senate enquiry which

led to the removal of RU486 from the 'restricted list' and was very involved in Victoria's abortion law reform. At Monash Medical Centre, I established the maternal-fetal medicine unit, and as I approach retirement, it is very rewarding to see it going from strength to strength.

Was your pathway to RANZCOG Presidency planned?
No, not at all! I've always loved being involved in clinical medicine, as well as hospital and College committees. The opportunity arose after a period of time on RANZCOG Council. I had great support from a number of councillors, as well as many of my senior colleagues at Monash Medical Centre. The role wasn't always easy and there were some individuals who found having a female as president challenging, but it was an amazing platform to engage with College members and provide advocacy for women's health in Australia and New Zealand.

What do you see as the greatest challenges with a career in O&G?
I've loved my career and I have no regrets doing obstetrics and gynaecology, but it's a demanding specialty, particularly obstetrics. The hours can be pretty terrible and the emotional toll very real. Having supportive colleagues with whom one can discuss problems and who understand the challenges is immensely important.

Did you see your gender as a barrier to your career?
No, but it did present some challenges. I was certainly aware I was a 'woman in a man's world', and that it was important to contribute to discussion and ensure I was considered for different roles and committees. Sometimes there was surprise that I really was a specialist and from time to time hostility, but I was determined to be good at what I did and be judged for my performance rather than my gender. Although it is undeniable, there remain challenges for women. However, the progress that has been made during my professional career is extraordinary and I have no doubt the equality for which we strive will be achieved.

Do you feel 'we' are heading in the right direction?
One of our aims is to ensure we contribute to ensuring all women have access to the highest standards of healthcare and that their autonomy is respected. A diverse and well-trained workforce is pivotal in achieving this goal. I hope, over time, we will achieve a better gender balance in the training program so we can maintain gender diversity with the advantages it brings. I also hope that more women will come forward to contribute to the College work and, in time, be prepared to stand for leadership roles.

What do you see as current challenges for trainees?
Overwhelmingly, this must be the reduced working hours and the increased trainee numbers. Although this has created improved work-life balance, it has dramatically reduced opportunities for learning, experience and procedural skills. I'd encourage trainees not to rush through their training years and look for opportunities, both here and abroad, to gain more experience and to ensure that when they have completed their training they have confidence in their skills. Part-time and interrupted training has been a great initiative strongly supported by our College; however, there is no doubt it can negatively impact on training and it is important trainees understand and recognise this when they are planning their training time.

Are you willing to be contacted for career advice?
I think the best mentoring relationships grow organically, but I'm certainly very willing to talk about my experience and provide advice on a career in high-risk obstetrics and College activities.

A/Prof Christine Tippett AM.

Do you have any regrets in your career?
We can always reflect and learn from previous mistakes, but I have few regrets. If anything, I wish I had time to take on more roles and participate in more research! I have had a privileged, fortunate and rewarding career, and on refection, I'm surprised about where my decision to go back to work in 1981 has led me.

I thank A/Prof Tippett for her time and insightful comments. She interrupted her beach holiday specifically for this interview, a reflection of her commitment to inspiring future generations in our specialty.

It has been a huge privilege to be able to share the stories of emerging and established leaders in our amazing profession over the last 12 months. During this time, we have had leaders from almost every state and territory, and from general and subspecialty members. We are looking forward to covering our final state (my home state of Tasmania) and the South Island of New Zealand in 2020. We are also looking forward to bringing you interviews from our Diplomate members and federal councillors.

I am delighted to announce that Victorian councillor, Dr Nisha Knot, will be bringing you our Leaders In Focus column in 2020.

Thank you to those who kindly contributed to interviews in 2019. I am truly delighted to finish this year's Leaders In Focus column with RANZCOG's first and only female past President and Hon. Treasurer for FIGO, A/Prof Christine Tippett.
– Dr Kirsten Connan

Editorial

Dr Fiona Langdon
FRANZCOG

During the witching hours of the night on labour ward there are many ways you can spend your time waiting for a patient to slowly inch their way to fully dilated. Once I am happy my GP correspondence is up to date, results are checked and I have exhausted the social media feeds, my new-found favourite website to trawl is the Coroner's Court Inquest Reports page. I am not sure if it is a morbid fascination with disease and death that the midnight hour brings or the fact it is a great learning tool that will hopefully attract CPD points. Maybe it is the fact that they read quite often as a captivating short story, but whatever the reason, they are extremely interesting and keep the tired obstetrician awake. Once finalised, Coroner's reports are available online and from whatever speciality they originate often have an extremely useful lesson in patient management. Of all the cases I read, far and away those that strike the greatest fear in me, and present not as a case of misadventure or significant failure in medical care, are those that relate to sepsis. In so many of these cases, the signs were ever so subtle in the beginning or, if they were present, were easily overlooked. It is only when the patient's status is so clearly that of sepsis that treatment was often implemented but, in the very fact they have ended as a Coroner's case, started far too late. I read these cases and think so often 'Would I have picked up on those signs?' – even with hindsight, it is very difficult to know if one would have.

And this is the issue with sepsis. In the early stages, particularly in young healthy individuals, as so many of our patients are, the signs of sepsis can be subtle. A high temperature is not an early sign in many of the sepsis algorithms because often a patient will only mount a febrile response very late in the disease process. Once the disease overwhelms them, they will often become febrile, or overtly hypotensive and tachycardiac and suddenly the presence of sepsis becomes abundantly clear – but this is often at a point when it is too late and we may be unable to successfully treat them.

Sepsis remains a significant cause of maternal morbidity and mortality. We have made great headway in treating and preventing other major causative pathologies, yet the rates of maternal deaths secondary to sepsis have remained steady. Across the world, in all branches of medicine, sepsis is recognised as a pathological conundrum in that is difficult to detect early, but vastly important to treat early. The importance of this prompt recognition is inherent in the large campaigns based around 'Think Sepsis' and 'Sepsis Awareness Month' (September, if you were planning on celebrating) ensuring that at the back of all clinicians' minds should be the question 'Could this be sepsis?' The importance of early treatment is emphasised in the 'Act Fast' and 'Golden Hour of Sepsis' campaigns that have also been rolled out through Health Departments internationally.

To ensure sepsis is given the recognition it requires, we have devoted an entire issue to this topic. In the upcoming pages, we have aimed to highlight the different clinical scenarios sepsis may present within our speciality and the important features, investigations and treatments one should instigate in each scenario. The recognition of sepsis and the many diagnostic tools hospitals employ to detect it early are reviewed and it is useful to reflect on measures that are taken in your own practice to ensure that every effort is made to recognise sepsis and recognise it early. Prevention of sepsis has also been a focus, both in our clinical setting and the developing world, as well as for the other patient we have: the fetus or neonate.

We would like to thank the Women's Health Committee for recommending the topic to our Editorial Committee and hope you find the issue informative and that it fulfils its aim to keep the issue of sepsis at the forefront of your mind during your clinical work.

Raising global awareness on maternal sepsis

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Infections and sepsis affect thousands of pregnant and recently pregnant women every year, resulting in many avoidable deaths and near misses with debilitating consequences.[1,2] Maternal sepsis is a 'life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion or postpartum period'.[3] Accurate data on the true burden of maternal infections and sepsis, which are critical information in attempting to curb mortality and morbidity resulting from sepsis, were unknown.

To respond to this knowledge gap, the World Health Organization embarked on an ambitious challenge of implementing the Global Maternal Sepsis Study (GLOSS) and Awareness Campaign in 2017 in 52 countries around the world in a unique, one-week simultaneous enrolment of pregnant and recently pregnant women hospitalised in 713 participating facilities.[4] The objectives of GLOSS were to assess the burden of maternal infections and sepsis, to validate existing screening and diagnostic criteria and to raise awareness on maternal sepsis among healthcare providers.[5] More than 2800 women with suspected or confirmed infections were identified during the week of 28 November to 4 December 2017. Four countries from the WHO Western Pacific region participated in the study: Cambodia, Mongolia, Philippines and Vietnam, contributing with a total of 122 women from 57 facilities.

Raising awareness on sepsis is also at the forefront of the Global Maternal and Neonatal Sepsis Initiative as well as the 2017 World Health Assembly resolution on sepsis.[6,7] GLOSS addressed this quest by developing a campaign to accompany the study to increase healthcare provider awareness on maternal sepsis identification and management. The campaign was intended to be implemented in all participating facilities prior to data collection and to continue throughout study implementation and beyond. Through posters, infographics, fact sheets, a website (https://srhr.org/sepsis/), social media messaging, press releases and an online congress, healthcare providers were sensitised and made more aware of the topic, thus helping identify women with signs and symptoms of infections during the study[4] (Figure 1). While materials developed for the campaign were standardised and translated into several languages, countries were given ownership over its implementation. This resulted in some countries developing different materials to accompany the campaign, such as videos, pamphlets, t-shirts, bookmarks and other giveaways, while some countries expanded the campaign to other locations not participating in the study.[8] For example, Mexico implemented the campaign country-wide, even though the study only addressed Mexico City. The country coordinator explained that this was in response to the pressing need to increase healthcare provider awareness of sepsis since they had identified many women suffering the consequences of infections during, and immediately following, a pregnancy.[9]

Similarly, our colleagues in Philippines, struck by the dire consequences from infections among women during pregnancy, delivery and postpartum/post-abortion, decided to expand on the work from the GLOSS awareness campaign and initiate country-specific actions to address these. This led to the development of a national awareness campaign that ran in October 2019.

Maternal sepsis burden and awareness campaign in the Philippines

The Philippine participation in GLOSS highlighted glaring issues about its hospital system and the quality of care provided to women: 45 per cent of patients who participated in the study had an infection, yet the primary source was not identified; 48 per cent were diagnosed based on clinical examination and only 15 per cent were diagnosed aided by laboratory tests. And while 55 per cent of the cases had infection on the day of admission, 45 per cent developed infection while already in the hospital. A common practice to avoid infection is the provision of prophylactic antibiotics to almost all maternity admissions.

In addition, maternal death reviews of 108 cases conducted in 2016 noted maternal sepsis accounted for 9 per cent of the deaths. A finding of the review is that maternal sepsis could have been prevented, as risk factors and the means to reduce the risk of sepsis are known and simple: access to clean water and sanitation, access to quality care during pregnancy and birth, early recognition of the signs of infection, timely access to the right antibiotics and proper infection prevention and control in birthing centres and hospitals.

Figure 1. Infographic developed for the GLOSS awareness campaign.

An analysis of the information gathered during visits to the participating hospitals in Manila under GLOSS made us realise, at the Safe Motherhood Program, that indeed our vague understanding of maternal sepsis has led us to think that it is a condition that can easily be clinically detected and addressed with antibiotics. It is the 'avoidability' and less costly approach of managing maternal sepsis and the promise of saving at least 161 mothers from dying that inspired the National Safe Motherhood Program to launch a Maternal Sepsis Awareness Campaign with a message to avoid infection during pregnancy and save lives. This campaign is a Department of Health initiative in collaboration with the Philippine Infectious Disease Society for Obstetrics and Gynaecology and the Philippine Hospital Infection Control Society and was inspired by the country's participation in the GLOSS study and analysis of country findings. It is hoped that through the campaign the number of mothers' lives saved can lead the country to a 3–9% annual rate of decline in maternal mortality ratio towards achieving the SDG goal of 70/100 000 live births, or better, by 2030.

Philippines campaign features

The campaign is highlighted by Regional Caravans and prioritises the five regions with reported maternal sepsis deaths. At the primary care level, advocacy campaigns targeting doctors, nurses and midwives in both the public and private sectors will be intensified through displaying posters in hospitals and primary-level birthing centres (Figure 2). With messages like 'Maternal sepsis can lead to death' and 'Practice infection prevention and control at all times in your facility; be a model of cleanliness!' the campaign looks to raise awareness among pregnant women and healthcare workers, including midwives. Likewise, community health education through local government health-system-initiated Buntis (Pregnant) Congress and mothers' classes on safer pregnancy and childbirth, and ways to prevent infection during pregnancy, shall be conducted.

It should be noted that most of the country's doctors at primary level are non-specialists and while they are trained on basic emergency obstetric and newborn care, quality of care is not optimised. On the other hand, private-practising midwives abound in the cities and reports of midwives practising beyond the limits of their profession are common, compromising maternal health and survival. The main feature of the Caravan is the conduct of regional scientific forums that will serve as venue for updates on the clinical features and management of maternal sepsis and public health measures to prevent them. The scientific forums will discuss topics related to maternal sepsis across the various issues that confront primary care maternity and newborn care providers and their referral centres, including interventions to improve survival from maternal sepsis, infection control recommendations during labour and delivery, and early recognition of common maternal infections. Around 800 doctors, nurses and midwives have benefited from the campaign. By 2021, the campaign will have covered the whole country.

Participation in GLOSS has brought about changes both in awareness as well as in how maternal infections are identified and managed at the facility level across the world. Maternal sepsis is life-threatening, but when caught early and treated promptly, it can be stopped.

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Figure 2. Poster developed for the campaign in the Philippines.

Maternal and newborn sepsis worldwide

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Maternal sepsis is a life-threatening condition defined by the World Health Organization (WHO) as 'organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion, or in the postpartum period'.[1] It is a leading cause of maternal death, attributing an estimated 33 330 (11 per cent) deaths globally each year.[2] Neonatal sepsis, defined as sepsis within the first 28 days of life, is a leading cause of newborn death, with an estimated 3 million cases each year, resulting in 180 000 (6.8 per cent) deaths.[3,4] In low- and middle-income countries (LMICs), babies born to mothers with laboratory-proven bacterial infection have a seven-fold increased risk of developing neonatal sepsis.[5] As such, implementing strategies to prevent maternal sepsis will also save newborn lives, especially in settings with high neonatal mortality and where sepsis accounts for a greater proportion of deaths.

Limitations of current data

The true burden of sepsis in LMICs remains understudied with an absence of robust data to quantify burden or to guide effective treatment strategies. Current global estimates and treatment strategies have been largely extrapolated from data generated in high-income countries.[6] In the 2015 Global Burden of Disease statistics, sepsis was considered a 'garbage code' with deaths attributed to the underlying source of infections rather than as a result of sepsis, making it impossible to determine accurate estimates.[7]

Similarly, over the past half-century there has been minimal improvement in the availability and completeness of vital registration data (births, deaths, marriages) and comprehensive routine health information systems at global and national levels are lacking. An estimated one-third of births and a higher number of maternal deaths are unregistered or misclassified with scant data on maternal and newborn morbidity.[8]

The importance of prevention

Strengthening the quality of maternal and newborn care in LMICs is vital to preventing maternal and neonatal sepsis. Improvements to infection prevention and control (IPC) and water, sanitation and hygiene (WASH) measures, such as ensuring access to safe water, hand washing, clean delivery areas, preventing overcrowding in maternity units, promoting evidence-based care of the umbilical cord and kangaroo care for small and/or preterm babies, greatly reduce the risk of infection.[9,10] Despite the importance of simple IPC and WASH measures in preventing infection, a study of 66 101 healthcare facilities from 54 LMICs reported 38 per cent of facilities did not have access to safe water, 19 per cent did not have adequate sanitation and 35 per cent did not have access to water and soap for handwashing.[11]

While antibiotics undoubtedly save lives, in many resource-limited settings they are unavailable, overused or substandard, resulting in inadequate treatment and exacerbating adverse effects and antimicrobial resistance (AMR).[6] With virtually no routinely collected data on AMR in maternity units globally, the risks of using prophylactic antibiotics for women during childbirth should be carefully balanced against potential benefits and restricted

Table 1. Summary of 2015 WHO recommendations for the use of prophylactic antibiotics to prevent maternal peripartum infections.

	Quality of evidence	Strength of recommendation
Prophylactic antibiotics are recommended:		
Intrapartum for women with Group B Streptococcus (GBS) colonisation	Very low	Conditional
Preterm prelabour rupture of membranes	Moderate	Strong
Manual removal of the placenta	Very low	Strong
Third- or fourth-degree perineal tear	Very low	Strong
Elective or emergency caesarean section	Moderate	Strong
For caesarean section, prophylactic antibiotics should be given prior to skin incision	Moderate	Strong
For caesarean section, a single dose of first-generation cephalosporin or penicillin should be used	Very low	Conditional
Prophylactic antibiotics are NOT recommended:		
During the second or third trimester for all women with the aim of reducing infectious morbidity	Very low	Strong
Preterm labour with intact amniotic membranes	Moderate	Strong
Prelabour rupture of membranes at (or near) term	Low	Strong
Meconium-stained amniotic fluid	Very low	Conditional
Operative vaginal birth	Consensus	Strong
Episiotomy	Very low	Strong
Uncomplicated vaginal birth	Very low	Strong

to situations where there is evidence of benefit.[12] Current WHO guidelines include recommendations for the rational use of antibiotics around the time of birth (Table 1). However, the evidence supporting these recommendations is mostly of low, or very low quality.[10] The recent 'Prophylactic antibiotics in the prevention of infection after operative vaginal delivery' (ANODE) multicentre randomised controlled trial reported an 8 per cent reduction in confirmed or suspected infection for UK women assigned to treatment with prophylactic amoxicillin and clavulanic acid or placebo, prompting calls for updates to WHO guidance.[13] However, whether these findings are generalisable to LMIC settings is unclear, and given the vastly different characteristics of sepsis in resource-limited settings (including common pathogens, at-risk populations and clinical conditions), we, and many others, continue to acknowledge that interventions effective in high-income settings may not always be effective in LMICs, and may even cause harm.[6,14]

Improvements in IPC and rational use of antibiotic prophylaxis during labour and delivery may reduce maternal deaths from sepsis; however, this strategy will not be sufficient to eliminate preventable newborn deaths. Newborns are susceptible to other sources of infection, and babies born preterm, growth restricted or both, are particularly vulnerable. All too frequently, sick newborns are admitted to neonatal units that expose them to hospital-acquired infections that can be extremely challenging to manage. The Delhi National Infection Study examined rates of sepsis and AMR in 13 530 neonates admitted to neonatal units in India, demonstrating alarmingly high levels of AMR in the most common organisms isolated, with 38 per cent of *E. coli* demonstrating multidrug resistance, and up to 82 per cent in *Acinetobacter spp.*[15,16] This burden of difficult-to-treat newborn infections, combined with a lack of evidence-based strategies for the management of multidrug resistant infections in mothers and babies, has prompted calls for greater emphasis on prevention and antimicrobial stewardship awareness.

Screening, early detection and treatment

Accurate, timely diagnosis and treatment of maternal and neonatal sepsis are essential to optimise patient outcomes; however, detection remains challenging, particularly in resource-limited settings.

For women, a number of physiological changes may mask the early signs of sepsis during pregnancy and birth. The Society of Obstetric Medicine of Australia and New Zealand developed the obstetrically modified quick Sepsis-related Organ Failure (omqSOFA) screening criteria which include: respiratory rate of 25 or more breaths per minute, any non-alert mental state and systolic blood pressure lower than 90 mmHg. A score of 1 is allocated for each present symptom, with a score of 2 or more having predictive validity for women at increased risk of hospital mortality.[17] The global maternal sepsis study (GLOSS) investigators are developing and validating identification criteria for severe maternal infection and sepsis with the aim of developing a core set of practices for prevention, early detection and management.[18] The results of this study have not yet been published. The Surviving Sepsis Campaign (SSC) Guidelines recommend the administration of empirical antimicrobial therapy within one hour of suspected sepsis, with observational studies supporting adherence to the SSC guidelines in improving survival;[19] however, implementation of guidelines in LMICs will be challenging. A survey of 185 African hospitals reported that only 1.5 per cent of

hospitals surveyed had implemented SSC guidelines, with shortages in facilities, equipment, drugs and disposable materials a barrier to implementation.[20]

Diagnosing sepsis in neonates remains difficult. There is no internationally agreed definition, and the lack of system-specific signs can lead to high rates of antibiotic treatment for a clinical 'suspicion' of sepsis alone. Tuzun et al have called for 'a predictive (neonatal) sepsis definition and rapid bedside point-of-care tests.'[21] Australian researchers at the Burnet Institute are currently undertaking a project to develop a point-of-care test for neonatal sepsis specifically for use in resource-limited settings.[22]

The challenge of remote and fragile settings

In remote and fragile settings, access to healthcare is limited by the physical environment and the availability of skilled healthcare workers and resources. Access by air or foot may be the only options in remote settings, while in fragile settings, health systems are often weak or absent. Around 50 per cent of all internally displaced persons are women and children (under 18 years of age) and an estimated 60 per cent of maternal deaths and 45 per cent of neonatal deaths occur in humanitarian settings.[23] Addressing the root causes of fragility and improving capacity to provide accessible, affordable and innovative healthcare services to people in remote and fragile settings is an urgent priority.

The 'three delays' framework

While there is no universal approach to reducing the burden of maternal and neonatal sepsis, the 'three delays' framework provides a model for healthcare workers to plan targeted interventions in resource-limited settings and has been validated across numerous WHO regions. For maternal deaths, the model proposes that mortality is predominantly due to delays in: patient recognition of an obstetric emergency (type 1 delay); reaching an appropriate obstetric facility (type 2 delay), and; receiving appropriate and adequate care when a facility is reached (type 3 delay).[24] This model has recently been adapted for sepsis, proposing three major areas of delay: sepsis recognition and diagnosis at the time of triage (type 1 delay); initial focused resuscitation (type 2 delay), and; ongoing clinical monitoring and re-evaluation (type 3 delay).[25] A combination of these models targeting maternal and neonatal sepsis in resource-limited settings may be a promising solution, but, to our knowledge, is yet to be developed or tested.

Conclusion

Maternal and neonatal sepsis are preventable conditions that contribute a large proportion of global mortality and morbidity, particularly in resource-limited settings. The true burden of disease in LMICs is likely to be vastly underappreciated, representing an urgent need to improve classification of disease and strengthen vital registration. Prevention initiatives should emphasise the importance of improving basic IPC and WASH prevention measures, ensuring the availability of safe and appropriate antibiotics while simultaneously balancing the emerging threat of AMR. Importantly, initiatives proven effective in high-income settings should be cautiously considered in the context of the vastly different characteristics of sepsis in LMICs, where there is an urgent need for locally driven and contextually relevant research and innovation.

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Diagnosing early-onset neonatal sepsis

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Neonatal sepsis is one of the more feared conditions among paediatricians and neonatologists. It can be devastating; mortality for affected infants is high, especially if treatment is delayed. Worldwide, neonatal sepsis affects 3 million infants per year, of whom between 11–19 per cent do not survive.[1] It is the third-highest cause of global neonatal mortality.[2] This condition affects babies and their families in a multitude of ways: there is the stress of a neonatal intensive care unit admission, the impact of processing an unexpected diagnosis, and intensive medical therapy at a time otherwise expected to be spent bonding with a new family member. Further, for some survivors, neonatal sepsis has effects long beyond the newborn period as it increases the likelihood of developmental disability.[3,4]

Early-onset neonatal sepsis (EONS) refers to sepsis that presents in the first few hours/days of life, usually due to an organism acquired in the intrapartum period. In Australia, the frequency of EONS is estimated at 1.17/1000 livebirths.[5] There are a suite of well-known maternal risk factors for EONS: chorioamnionitis, urinary tract infection, colonisation with Group B Streptococcus (GBS) and prolonged rupture of membrane time are some of the more commonly described of these.[6] For neonates, the most prominent risk factor is prematurity; both incidence and mortality from EONS increase with decreasing gestational age.[6]

Considering EONS: the first step of diagnosis

To diagnose sepsis, it first needs to be identified as a possibility. Thinking about whether a neonate could have EONS is a vital part of the evaluation process for any unwell newborn. However, identifying sepsis in neonates at an early stage is a challenging process. Early clinical signs of EONS can be subtle. They may be as simple as an infant who is quiet and breathing quickly or has become lethargic and lost their capacity to feed well. Further, they lack specificity; neonatal sepsis is aptly described as a 'mimic' of other pathologies. Evaluating whether maternal risk factors are present can add valuable information to the evaluation process. However, while these risk factors are well described, delineating how meaningful they are for an individual neonate is not straightforward. In broad terms, many more neonates are exposed to these risks than those who develop EONS. Further, in settings where widespread intrapartum antimicrobial prophylaxis occurs, the contribution of each of these to the risk of EONS has reduced in impact, at least for neonates who are born at, or close to, term.[7] There are several diagnostic tests frequently used in the evaluation phase of neonatal sepsis. C-reactive protein and full blood examination are two of the more commonly described examples; however, neither of these has sufficient sensitivity to definitively rule out EONS at an early stage of illness.[8,9] While blood cultures are a key diagnostic test for possible EONS,[10] their prolonged time to result means that they cannot direct early decision-making for whether a neonate requires treatment. Given this array of uncertainties in the evaluation process for EONS, the usual course of action is to commence empiric antimicrobial therapy at the point where neonatal sepsis is deemed possible, with re-evaluation of the need for this treatment later.

Guidance for identifying possible EONS

A variety of guidelines have been developed over the last several decades to assist clinicians that evaluate neonates for the possibility of EONS. These have largely been premised on identifying at-risk neonates through the presence of maternal risk factors, with a caveat that neonates with clinical signs of possible infection receive treatment regardless of maternal risk factor status.[11,12] While guidelines such as these provide valuable structure to the identification process for EONS, they also direct clinicians to treat a number of babies who, with the benefit of hindsight, never had EONS.[13] There is thus a situation of tension between clinicians and health services appropriately seeking to ensure that no treatment opportunities for EONS are missed, and the broader aim of limiting antimicrobial exposure in cases where, in retrospect, no antimicrobial treatment was needed. While our understanding of the longer-term effects of early life antimicrobial exposure is still evolving, potential links to later childhood morbidities, such as allergy, highlight the importance of consistently reappraising how antimicrobial use can be optimised among neonates.[14] The development of tools to assist clinicians in safely reducing neonatal antimicrobial exposure for possible EONS has become the aim of a variety of research endeavours, with promising results. A successful example is the data-driven development and validation of the Kaiser Permanente Neonatal-Early Onset Sepsis Calculator, an online risk assessment tool that has now effected substantial reductions in antimicrobial use for possible EONS in a number of neonatal health services across the world.[15]

Confirming EONS: the second step of diagnosis

Moving beyond the initial stage where EONS is identified as a possibility, the next step is to finalise the diagnosis: determining whether the neonate really does have EONS. This is important for a number of reasons: a confirmed EONS diagnosis directs further therapy, such as duration and choice of antimicrobials, and in some cases may prompt additional investigations, such as lumbar puncture, to identify or exclude meningitis. For some neonates where a clear clinical illness is combined with microbiologic confirmation of infection, this is fairly simple. However, a number of infants have no identified pathogen, may have equivocal clinical signs, and the decision of whether they require a treatment and investigation course for EONS is then left to the discretion of their treating clinician.[16] Determining how to discriminate which of these neonates require ongoing antimicrobial therapy is a topic of ongoing discussion and controversy among neonatologists.[10,16]

Moving towards consistency in definition

At present, there is no unified definition for neonatal sepsis (including EONS). In fact, multiple definitions for neonatal sepsis are in use across neonatal networks worldwide.[17] This is in contrast to sepsis in the adult population, where operational consensus definitions are regularly reviewed and published.[18] Efforts have now begun to better define neonatal sepsis for research,[19] and the need to develop a practical consensus definition for clinical use is now being actively discussed across neonatal sepsis literature.[16,20] The overarching aim of these endeavours is to ensure neonatal sepsis diagnostic strategies become increasingly accurate so that treatment can be better targeted to cases with true EONS, where early treatment can be lifesaving. The way in which we identify and diagnose neonates with EONS will likely continue to be refined to achieve improved diagnostic certainty and consistency in the future.

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Maternal care: public health interventions

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Public health interventions are essential in preventing maternal sepsis. Maternal sepsis, during and after pregnancy, may arise from many sources and is not limited to infections arising from the genital tract. Given the diversity of sepsis causation pathways, it is essential that targeted evidence-based interventions are identified.[1]

Management of sepsis is no longer limited to the acute care of individual patients. Prevention and treatment of sepsis is now recognised as a public health challenge requiring population- and systems-based solutions. This article aims to frame maternal sepsis as a public health issue and provides an overview of the primary, secondary and tertiary prevention approaches available using Kempker's conceptual model of prevention (Table 1).[2]

Kempker's model can be used to reframe maternal sepsis from a prevention perspective and identify systematic evidence-based interventions that are relevant to the antenatal, intrapartum and postnatal periods.

In this context, primary prevention refers to the prevention of infection or the sepsis event. Secondary prevention refers to the early recognition and treatment of sepsis. Tertiary prevention refers to in-hospital and post-hospital treatment to reduce the long-term consequences of sepsis.

Primary prevention

Evidence-based interventions that have been shown to prevent infection and subsequently reduce maternal morbidity and mortality include:

Infection control

Measures such as handwashing with soap or other cleansing agents, and the use of barrier protection, are widely acceptable practices for limiting the spread of micro-organisms, particularly within hospital environments.

Pathogen Group A Streptococcus (GAS) is the most common cause of severe maternal sepsis, identified as directly responsible for 13 of the 29 maternal deaths from infection in the UK during 2006–08. Patient hand hygiene, and careful perineal wound care are fundamental in preventing infection with GAS in the puerperium.[3]

Antenatal education

Recognition of the severity of an infection by pregnant or postpartum women, family members and healthcare providers has been identified as a key barrier to reducing sepsis-related deaths. Sociodemographic disparities on maternal severe outcomes related to infection have been shown in high-income countries, particularly for ethnic minorities, as well as low- and middle-income countries.[4] Inclusion of education of infection prevention and recognition is an integral component of standard antenatal care in Australia for patients and their families and it is essential that this be provided with the use of interpreters and translated health information.

Antibiotic prophylaxis

- **Screening for asymptomatic bacteriuria**, which occurs in 2–10 per cent of all pregnancies, is recommended because if untreated, women may develop acute cystitis and subsequent pyelonephritis, with can lead to maternal urosepsis, preterm labour and delivery.[5] Urosepsis accounts for one third of antenatal sepsis events.
- **Caesarean delivery** is the single most important risk factor for postpartum maternal infection. Prophylactic antibiotics at the time of caesarean section reduces the risk of wound infection, endometritis and serious maternal infectious morbidity.[6]
- **Operative vaginal delivery** is also a risk factor in which antibiotic prophylaxis is considered in the literature and clinical practice. The evidence from available Cochrane reviews is insufficient to determine whether prophylactic antibiotics given with operative delivery or following third- or fourth-degree perineal tears reduces infectious postpartum morbidities.[7,8] Even so, the use of antibiotics among women with a third- or fourth-degree perineal tear is recommended by the WHO for prevention of wound complications.[9]
- **Preterm (PPROM) and term prelabour rupture of membranes (PROM)** carries a risk of chorioamnionitis and severe maternal sepsis. Evidence for prophylactic antibiotics with PPROM demonstrated a significant reduction in chorioamnionitis and markers of neonatal morbidity.[10] There is no convincing evidence to support the use of prophylactic antibiotics for PROM,[11] though active management with

Table 1. Primary, secondary and tertiary prevention approaches to sepsis.

Traditional model of prevention	Maternal sepsis
PRIMARY PREVENTION: Prevention of infections and onset of sepsis	
• Hygiene	Infection control » Hand-hygiene and barrier protection » Surgical and perineal wound care
• Public awareness	Antenatal education » Interpreters and translated health information
• Antibiotic prophylaxis	Use of prophylactic antibiotics » Asymptomatic bacteriuria » Caesarean delivery » Operative vaginal delivery » PPROM and PROM
• Risk factor management	Quality of care » Health Infrastructure » Health worker standards in antenatal, intrapartum and postnatal care Quality surgical services » Access to caesarean section » Access to abortion care » Vaginal application of antiseptics
• Immunisation	Vaccination for influenza and varicella
SECONDARY PREVENTION: Early detection and treatment of acute sepsis	
• Provider awareness and triage	PROMPT training
• Sepsis care bundles	'Sepsis 6' In-hospital guidelines
• Sepsis alert and in-hospital response	Choice of antibiotic Identifying cause Mode and timing of delivery
TERTIARY PREVENTION: Limit consequences of sepsis	
• ICU care	Established referral criteria and local escalation pathways
• Rehabilitation	
• Post-sepsis follow up	

induction of labour at term has been shown to reduce infectious maternal morbidity.[12] In the context of prolonged rupture of membranes (more than 18 hours) the use of antibiotics is common clinical practice due to a presumed increased risk of maternal and neonatal infection.

Quality of care

Maternal deaths from sepsis highlight and expose broader health determinants and other underlying issues related to substandard quality of care. Factors relevant to the global context include: infrastructure challenges; overcrowding; limited access to water and sanitation; constraints to safe births by skilled birth attendants; lack or inconsistent use of infection prevention and control measures; inaccurate or delayed diagnosis and poor or late management of infection and complications.[13]

Identification of well-recognised risk factors for maternal sepsis, including the presence of pre-existing medical conditions such as anaemia, febrile illness in the two weeks prior to diagnosis of sepsis, and, most notably, mode of delivery, can make a difference in identifying sepsis and subsequent prompt management, which ultimately affects the outcome.

Quality surgical services

- **Access to safe abortion care**, which includes access to safe, quality operating services with the use of prophylactic antibiotics, reduces morbidity. Maternal mortality for unsafe abortion is largely due to sepsis from endometritis.[14]
- **Access to caesarean section**, and operative vaginal delivery, is central to the management of obstructed labour. Obstructed labour accounts for an estimated 4 per cent of maternal deaths, which are caused by ruptured uterus, haemorrhage and sepsis.[15]
- **Vaginal application of antiseptics** for caesarean delivery has been demonstrated to reduce the risk of postoperative endometritis, but no clear difference was detected in postoperative fever or any wound complications, although the beneficial effects might be greater for women with ruptured membranes.[16] There has been no difference in incidence of chorioamnionitis and postpartum endometritis in women who had vaginal application of antiseptic (chlorhexidine douche) for vaginal delivery.[17]

Vaccination

Pregnant women are at high risk for influenza-related and varicella-related morbidity and mortality, including higher rates of hospitalisation, cardiopulmonary complications and death, compared to the general public, hence, influenza vaccination is a component of standard antenatal care and varicella vaccination can be offered pre- or post-pregnancy.[18]

Secondary prevention

Provider awareness and triage facilitates early recognition and treatment of maternal sepsis. Failure to recognise the severity of an infection is known to be a key barrier in reducing sepsis-related deaths.[19] The most common site of sepsis in the puerperium is the genital tract and, in particular, the uterus; however, more broadly other sites of sepsis to be considered include mastitis, pyelonephritis, pneumonia, skin and soft-tissue infection, gastroenteritis and pharyngitis. The timing of infection correlates with particular sites: antenatally, urinary tract infections cause one third of all cases of maternal sepsis, whereas postnatally, genital tract infections cause one third of sepsis cases.[20] Overall, infections due to *E. coli* are most numerous, although infections with GAS are associated with greater severity of sepsis, morbidity and mortality.[21] Pregnant women are also at higher risk of complications of certain specific infections, such as influenza, varicella zoster and listeria.

Practical Obstetric Multi-Professional Training (PROMPT), developed in the UK, is widely used throughout Australia and New Zealand in training of midwifery, nursing, obstetric and anaesthetic staff, to encourage early recognition and algorithm-led appropriate responses to obstetric emergencies, including maternal sepsis.

Sepsis 6, which is promoted by PROMPT training, aims to identify sepsis and enact the following six steps within 60 minutes:

1. Blood cultures
2. Full blood count and lactate
3. IV fluid challenge
4. IV antibiotics
5. Monitoring of urine output
6. Oxygen administration[22]

Choice of antibiotic is dependent on the likely source of infection, while considering known hospital and individual factors, such as prevalence of antibiotic resistant organisms and mode of delivery, patient response and subsequent culture results.

However, it is also important to consider that broad adoption of early, empiric antibiotic treatment may have consequences that are negating to emerging principles in infection control, such as: the inappropriate use of antibiotics leading to depletion of a limited resource; an increase in adverse drug toxicities; and developing emergence of antimicrobial resistance.

Identifying the cause of the infection and 'source control' is essential in the timely management of maternal sepsis. This may require caesarean delivery, hysterotomy or hysterectomy in women with genital tract sepsis.[23] The UK and Ireland Confidential Enquiry into Maternal Deaths identified several women who subsequently died from maternal sepsis following delayed delivery.[24] In several women, delivery was delayed because the fetus had already died and there was a perceived need to ensure the woman delivered vaginally. Failure to deliver the fetus and placenta early in the setting of chorioamnionitis will lead to a persisting source of infection and progression of sepsis despite adequate resuscitation and antibiotic treatment.[25]

Tertiary prevention

Sepsis is among the leading cause of maternal ICU admission. ICU is a largely centralised resource and often not immediately available. Hence, clear referral criteria and recognition of the need for treatment escalation by maternity staff is essential. ICU involvement is indicated when there is cardiorespiratory compromise, evidence of organ dysfunction or other serious clinical concern.

As described in the SOMANZ Sepsis Guideline[23] management of maternal sepsis in ICU is similar in principle to the non-obstetric patient. Limited evidence regarding ICU management of obstetric patients exists, with pregnant patients typically being excluded from clinical ICU trials. Management focuses on maintenance of physiological parameters, organ support and targeted care. General management includes thromboprophylaxis, analgesia, skin protection, bowel care and nutrition. In the postpartum period, perineal care, breast care and lactation issues need to be attended to, in addition to facilitating contact between mother and baby when possible.

Tertiary prevention focuses on efforts to limit the consequences of sepsis, optimising post-sepsis recovery. Maternal infection around childbirth has been shown to have a significant effect on newborn wellbeing.[26] In addition, infection-related morbidities and prolonged hospitalisation can interfere with mother–infant bonding in the first days after birth. Long-term disabilities, such as chronic pelvic pain, fallopian tube occlusion and secondary infertility, can also occur because of maternal sepsis.

As with sepsis in the general population, the complexity of maternal sepsis precludes an all-encompassing targeted public health policy. Sepsis is not a clearly defined disease entity, rather it's a nonspecific, clinical syndrome resulting from many combinations of pathogens, host responses and organ dysfunction. It is challenging to diagnose and manage,

and uniform strategies do not apply. These challenges are compounded in resource-poor settings where the exact sepsis burden is unknown, but estimated to be substantial. Framing maternal sepsis in a population framework, with primary, secondary and tertiary care principles, can assist in ultimately preventing maternal sepsis and limiting its consequences.

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Managing the septic antenatal patient

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Sepsis is a rare, but important, cause of maternal morbidity in the antenatal period. The physiological adaptations of pregnancy can mask the early signs of sepsis and can predispose to rapid maternal deterioration. A high index of suspicion is required to identify women with sepsis, and allow prompt treatment, including appropriate antibiotics.

The leading antenatal causes of sepsis are urinary tract infection (including pyelonephritis), pneumonia and genital tract infections. Causative organisms depend on the site of the infection (Table 1); however, in a significant proportion of infections, no organism is isolated.

Approach to antenatal presentation of sepsis

A pregnant woman presenting with fever or infective symptoms should be assessed with thorough history and examination to identify the potential source of infection and evaluated for signs of sepsis and septic shock. Screening for causes should evaluate risk factors such as diabetes mellitus with poor glycaemic control, immunomodulating medications, malnutrition, smoking, obesity, unwell contacts, recent travel and animal exposure.

Alarm signs include hypoxia, hypotension, oliguria, hyperglycaemia, decreased capillary refill and impaired mentation. Initial assessment should also include evaluation for metabolic acidosis, coagulopathy, renal and liver dysfunction and fluid balance. Blood cultures and swab or culture samples from probable sources should be sent for culture. Monitoring should include close observation of haemodynamic parameters, fluid balance and consideration of the need for invasive blood pressure monitoring and haemodynamic support. Broad spectrum antibiotic coverage as per local guidelines should be commenced, with the spectrum of therapy narrowed, pending culture results when available. Antibiotics should not be delayed as early administration has been shown to improve outcomes.[2]

Fetal monitoring should be performed with intermittent heart rate or continuous cardiotocographic (CTG) monitoring depending on gestation. CTG changes may serve as an early warning sign for maternal haemodynamic or metabolic decompensation.

Septic antenatal patients should be managed in a tertiary centre with access to intensive care facilities and monitoring; retrieval should be urgently arranged if required. Multidisciplinary supports should include intensivists, anaesthetists, microbiologists, physicians and neonatologists. Consideration should be given to the administration of corticosteroids for fetal lung maturation as delivery may be indicated if beneficial to the woman or her infant. In sepsis from extra-uterine infection, the maternal condition should be stabilised prior to attempting delivery, otherwise maternal and fetal mortality rates are increased.[3] The mode of delivery should be individualised based on gestation and the severity of maternal illness.

Urinary tract infection/pyelonephritis

The physiological changes of pregnancy predispose to urinary tract infections and pyelonephritis,[4] with pyelonephritis being the leading cause of septic shock in pregnancy.[5] Pyelonephritis complicates approximately 2 per cent of pregnancies overall, but in the 5–7 per cent of pregnant women who have asymptomatic bacteriuria, the rates of pyelonephritis are reported at 20–30 per cent.[6] Presenting symptoms are usually fever, tachycardia, flank pain and the typical symptoms of urinary tract infection may or may not be present.

E. coli accounts for 70–80 per cent of cases, with the majority of the remainder being due to *Klebsiella, Proteus* and *Enterobacter* organisms. Pyelonephritis is associated with a 15–20 per cent risk of bacteraemia and, hence, initial evaluation for suspected pyelonephritis should encompass blood cultures.[5] There is also a risk of endotoxin-mediated renal dysfunction and assessment of glomerular filtration should be performed, as dosing of antibiotics may need to be adjusted.

Pyelonephritis has been associated with an increased risk of preterm birth; both spontaneous and iatrogenic.[7] There is also a risk of recurrence

Table 1. Infections that may lead to septic shock and common pathogens in pregnancy. (Adapted from Joseph 2009).[1]

Infections that may lead to septic shock and usual organisms	Likely pathogens in pregnancy
Pyelonephritis[1,4] Pneumonia[5,6] Chorioamnionitis[1,2,7–10] Necrotising fasciitis[2,3,5]	1. *Escherichia coli* 2. *Bacteriodes* 3. *Clostridium* 4. *Klebsiella* 5. *Streptococcus species* 6. *Staphylococcus aureus* 7. *Group B streptococcus* 8. *Enterococcus* 9. *Listeria monocytogenes* 10. *Enterobacter*

and prophylactic antibiotics are recommended for all women who present with an episode of pyelonephritis during pregnancy.

Pneumonia

The physiological changes of pregnancy predispose to the development of pneumonia. The incidence of pneumonia during pregnancy is approximately 1–1.5 per cent.[8] Pre-existing lung disease, most commonly asthma, increases maternal risk of pneumonia, along with anaemia and cigarette smoking. Pneumonia may also complicate severe sepsis from another causes[9] or be caused by aspiration.[10]

Community-acquired pneumonias most commonly present with a productive cough, fevers, pleuritic chest pain and shortness of breath. Bacterial pneumonia is most commonly caused by streptococcus pneumonia, haemophilus influenzae and mycoplasma pneumonia.[5] Viral infections, in particular influenza and varicella, can be associated with a severe acute respiratory distress syndrome, and may predispose to secondary bacterial pneumonia.[4]

Evaluation should include assessment of oxygenation and supplementation if needed. Sputum samples can be cultured, but swabs for viral PCR testing and serologies for atypical infections or viruses should also be considered. Chest x-ray may be performed with abdominal shielding with the estimated fetal dose of absorption well below the level associated with adverse short- or long-term effects.[11]

Chorioamnionitis

Chorioamnionitis is typically an ascending polymicrobial infection and most commonly occurs in the setting of ruptured membranes. Less commonly, procedures such as cervical cerclage or amniocentesis may precipitate infection; haematogenous spread can also rarely occur. The infection may present with fevers and maternal and/or fetal tachycardia. Uterine tenderness and malodorous discharge are commonly late signs of infection.

Causative organisms include genital myocplasmas, *ureaplasma urealyticum*, *Gardnerella vaginalis, E. coli* and group B streptococcus. High vaginal swab culture has been shown to be the best predictor of causative organism; however, antibiotic cover should be broad initially to cover for polymicrobial infection. Chorioamnionitis is an indication for delivery and the mode of delivery should be determined based on the usual obstetric indications.[12]

Listeriosis

Listeriosis is an uncommon infection with significant implications for pregnant women. The illness most commonly presents with flu-like or gastrointestinal symptoms, but may be asymptomatic. Infection during pregnancy is complicated by high rates of intrauterine fetal demise, preterm birth and neonatal meningitis. Listeria can be cultured from blood or genital swabs and prompt treatment with appropriate antibiotics can prevent the associated adverse neonatal outcomes.[13]

Sepsis with unclear origin

In the workup of a septic antenatal patient, other uncommon causes should also be considered (Table 2).

Summary

Sepsis is a severe and life-threatening complication of pregnancy. A broad range of causes should be considered and antibiotic therapy initiated promptly with early consideration of transfer to tertiary centres and monitoring in intensive care settings if required. Sepsis alone does not indicate delivery except in the case of chorioamnionitis.

Table 2. Uncommon causes of sepsis.

	Presentation	Investigations
Appendicitis	Abdominal pain, nausea, vomiting	MRI
Cholangitis	Upper abdominal pain, jaundice, nausea, vomiting	Upper abdominal ultrasound
Pancreatitis	Epigastric pain, radiation to back, nausea, vomiting	Lipase, upper abdominal ultrasound
Meningitis	Headache, photophobia, neck stiffness, rash	Lumbar puncture
Skin infection	Erythema, localised pain and swelling	Consider ultrasound for thrombophlebitis or collection

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Managing the septic patient in labour

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Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection.[1] It is a preventable cause of maternal morbidity and mortality. In Australia, sepsis was the fourth-highest cause of maternal mortality between 2006 and 2016[2] and sepsis-related maternal mortality has been increasing.[3]

In the UK, reviewers identified substandard care as a factor in 63 per cent of sepsis-related maternal mortality cases, most often involving a delay in recognition or management, particularly on obstetric units.[4] The physiological changes of pregnancy may mask the early signs of sepsis, the changes in labour may make the clinical picture more difficult to interpret and disease progression may be more rapid compared to non-pregnant women,[5] making recognition and management more difficult. We explore the recognition and management of the septic patient in labour.

Risk factors

Clinicians should be aware of risk factors for sepsis in labour:[6-9]

- Obesity
- Impaired immunity/immunosuppressant medication
- Anaemia
- Vaginal discharge
- Previous pelvic infection
- Previous Group B streptococcal infection
- Invasive procedures (such as amniocentesis)
- Cervical cerclage
- Prolonged rupture of membranes
- Prolonged labour
- Increased number of vaginal examinations
- Group A streptococcus infection in close contacts/family members
- Minority ethnic group origin
- Nulliparity
- Multiple gestation
- Comorbidities (diabetes, chronic renal disease, chronic liver disease, congestive heart failure)
- Aboriginal or Torres Strait Islander origin[3]

Assessment

Signs and symptoms

Women may experience fevers/rigors, diarrhoea or vomiting, rash, abdominal pain, offensive vaginal discharge, a productive cough or urinary symptoms.[5]

Clinical signs suggestive of sepsis include:[5,10]

- Pyrexia
- Hypothermia
- Tachycardia
- Tachypnoea
- Hypoxia
- Hypotension
- Oliguria
- Impaired consciousness
- Fetal distress
- Failure to respond to treatment

These signs, including pyrexia, may not always be present and are not necessarily related to the severity of sepsis.[5]

Maternal vital signs should be recorded regularly on maternity-specific charts to guide assessment and ongoing management. A thorough neurological, cardiac, respiratory, abdominal, uterine and pelvic examination should be performed to determine the underlying cause.

Scoring systems

The Sequential (sepsis-related) Organ Failure Assessment (SOFA) score has been shown to reliably identify patients who have higher morbidity and mortality,[11] but has not been validated in pregnant women. The score uses clinical and laboratory parameters, the Glasgow Coma Scale and the use of inotropes and/or vasopressors to assess organ dysfunction.

The quick SOFA (qSOFA) only uses clinical parameters and is therefore useful to screen women. We recommend the use of the obstetrically modified qSOFA (omqSOFA) (Table 1) in the first instance. End organ dysfunction is defined as an acute change in the total score of more than 2 points where the baseline score is assumed to be 0 if there were no prior concerns. The obstetrically modified SOFA (omSOFA) (Table 2) should be used subsequently for a more thorough assessment.

Table 1. Obstetrically modified qSOFA (omqSOFA) score.

	Score	
Parameter	0	1
Systolic blood pressure	≥ 90 mm Hg	< 90 mm Hg
Respiratory rate	< 25 breaths per minute	≥ 25 breaths per minute
Altered mentation	Alert	Not alert

Management

Sepsis is a medical emergency. Treatment and resuscitation should begin immediately, ideally within the first hour, the 'golden hour'.[12] Investigations and management should be performed concurrently.

Investigations

First-line investigations include:[12]

1. Blood cultures: at least two sets should be obtained from different sites. Cultures should be obtained prior to antibiotic administration but should not delay antibiotic administration.
2. Other cultures: a urine microscopy, culture and sensitivity (MCS) should be obtained. Amniotic fluid MCS, nasopharyngeal swabs, vaginal swabs and stool cultures should be obtained where clinically indicated.
3. Arterial blood gas: this will detect acidosis, hypoxaemia and provide a lactate.
4. Lactate: increased levels are caused by tissue hypoperfusion and levels greater than 2 mmol/L are associated with an increased mortality risk.
5. Full blood count
6. Coagulation studies
7. Urea, electrolytes and creatinine: abnormal electrolytes, elevated urea and creatinine may be seen in sepsis. These should be measured at baseline and until the patient improves.
8. Liver function test: this should be performed as a baseline test and may be elevated if sepsis is arising from hepatic or perihepatic infections, or affecting hepatic blood flow and metabolism.
9. Chest x-ray: imaging may need to be deferred to the immediate postpartum period depending on the stage of labour. If there is strong clinical suspicion of a respiratory source, targeted treatment should be commenced.
10. Methicillin-resistant *Staphylococcus aureus* (MRSA) swabs should be performed. The MRSA status will facilitate optimisation of the antibiotic regime.

Further investigations (such as lumbar puncture, echocardiogram, imaging of the chest and/or abdomen) should be considered, depending on the stage of labour, but may need to be deferred.

Management

A multidisciplinary approach including obstetricians, neonatologists, intensivists, microbiologists, physicians and anaesthetists is required. The key principles include:[5,10,12]

1. Antibiotics: broad spectrum antibiotics should be administered within one hour. Mortality can increase by 8 per cent for each hour of delay.[13]
2. Fluid resuscitation: initial administration of 1–2 L of crystalloid is vital to restore the circulating volume, treat hypotension and improve tissue perfusion.
3. Vasopressors: these should be used for hypotension that is not responding to fluid resuscitation or where fluid resuscitation is inappropriate.
4. Targeted treatment: once a source has been identified, targeted antibiotic therapy should be commenced.

Fetal wellbeing should be assessed simultaneously with continuous electronic fetal monitoring. Any changes in the CTG should prompt re-assessment of

Table 2. Obstetrically modified SOFA (omSOFA) score.

	Score		
Parameter	0	1	2
Respiration PaO_2/FIO_2	≥ 400	300 – < 400	< 300
Coagulation Platelets x 10^6/L	≥ 150	100 – 150	< 100
Liver Bilirubin (µmol/L)	≤ 20	20 – 32	> 32
Cardiovascular Mean arterial pressure (mm Hg)	MAP ≥ 70	MAP < 70	Vasopressors required
Central nervous system	Alert	Rousable by voice	Rousable by pain
Renal Creatinine (µmol/L)	≤ 90	90 – 120	> 120

the mother. Resuscitation will improve uteroplacental perfusion and the fetal condition.

Anaesthetic considerations for the septic woman in labour include:

- Neuraxial blocks: these should only be undertaken after careful consideration due to the increased risk of complications.
- General anaesthesia: if required, increased haemodynamic instability should be anticipated.

Delivery

Sepsis is not an indication to expedite delivery unless the source is thought to be intrauterine or delivery will facilitate improved management attempts. Otherwise, there is no evidence that delivery improves maternal outcomes. Additionally, delivery in the context of maternal instability increases maternal and fetal mortality rates.[14] Delivery should be expedited for the usual obstetric and fetal indications.

Postpartum management

Women should be cared for in an intensive care setting with infection control measures in place. Ongoing antibiotic treatment should be guided by the clinical response. Thromboprophylaxis with low-molecular-weight-heparin should be administered. If a micro-organism is identified, this should be communicated to the neonatologists to guide the neonate's antibiotic treatment.

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Managing the septic postnatal patient

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Sepsis is a leading cause of maternal death worldwide and occurs most commonly in the puerperium.[1] Maternal mortality due to sepsis has declined in Australia, but is still a leading cause of maternal death with a maternal mortality ratio of 0.6 per 100 000 women giving birth from 2006–16.[2]

Sepsis is broadly defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Septic shock is the subset of sepsis in which profound circulatory, cellular and metabolic abnormalities substantially increase mortality. It is characterised by significant hypotension requiring vasopressors to maintain mean arterial pressure (MAP) of 65 mm Hg or higher and serum lactate of 2 mmol/L or higher, despite adequate fluid resuscitation.[3]

Identifying postnatal patients in the early stages of sepsis who are at risk of progressing to septic shock can ensure timely initiation of vital treatments to prevent progression to irreversible organ dysfunction, disseminated intravascular coagulation and death.

Initial assessment

History and examination should be directed towards identification of the likely source of infection in the postnatal patient.[4,5] Sepsis most commonly arises from the genital tract, with endometritis being the most common source of infection and caesarean section being the single most important risk factor for postnatal sepsis.[4,6,7] Prophylactic intravenous antibiotics 15–60 minutes prior to skin incision at caesarean section greatly reduces infection, but does not eliminate it.[8,9] Multiple vaginal examinations, genital tract trauma and instrumental delivery are additional intrapartum risk factors for postnatal sepsis. Other genital tract sources of sepsis include pelvic inflammatory disease, tubo-ovarian abscess and retained products of conception.[10]

Maternal risk factors for sepsis should also be elicited. Medical comorbidities, particularly anaemia and immunosuppression, were found to be the most important factors driving the association between severe sepsis and death in one study.[6]

In addition to assessment of risk factors (Table 1) a complete medical, obstetric and infectious disease history should be undertaken. Common non-specific symptoms of sepsis in the postnate include fever, diarrhoea, vomiting, vaginal discharge and abdominal pain. Rigours or severe myalgia (especially anterior thigh) can herald severe bacterial infection and should prompt concern in the treating team. Agonising pain out of proportion to clinical signs should prompt consideration of necrotising fasciitis/myositis. A generalised maculopapular rash, especially in combination with conjunctival hyperaemia or suffusion may be an early sign of toxic shock syndrome due to staphylococcal or streptococcal infection. Increasing vaginal bleeding or a history of offensive lochia may suggest endometritis or retained products of conception. However, some infections, particularly Group A Streptococcus (GAS) frequently present with scant, odourless lochia. GAS may also present with other non-specific symptoms including fever, sore throat, vomiting, severe abdominal pain and diarrhoea. Suspected GAS sepsis should be managed aggressively due to its invasive nature and association with a higher maternal mortality rate

Table 1. Risk factors for sepsis in the postnatal patient.[4,6,10]

Maternal risk factors	Pregnancy-related risk factors
Medical comorbidities (such as anaemia, immunosuppression, diabetes, obesity)	Caesarean section
Nutritional status	Instrumental delivery
History of pelvic infection and vaginal discharge, including bacterial vaginosis	Premature or prolonged rupture of membranes
Minority ethnic group, including Aboriginal and Torres Strait Islanders	Frequent cervical examinations
GAS infection in family members and close contacts	Internal fetal monitoring
	Amniocentesis, cervical cerclage and other invasive procedures
	Vaginal and perineal trauma
	Vaginal haematoma

than other organisms.[4,5] Postpartum women have a 20-fold increase in the incidence of invasive GAS and Group B Streptococcus infection compared to non-pregnant women.[11]

Sources extraneous to the genital tract should also be considered: mastitis, breast abscess, urinary tract infection, respiratory tract infection (including pneumonia and influenza), soft tissue and skin infection (including surgical site infection and necrotising fasciitis), gastroenteritis, pharyngitis, infection related to regional anaesthesia and intravenous cannulation are common sources of sepsis in postnatal patients. Less common causes include bacterial meningitis, septic pulmonary embolus, deep vein thrombosis, septic pelvic phlebitis and appendicitis.

Non-infective causes that may mimic sepsis, including acute pulmonary embolism, autoimmune conditions and acute liver failure, should also be considered.[5]

Investigations

Preliminary investigations will be guided by suspected sources of sepsis. Blood cultures are the key investigation; ideally at least two (and, if possible, three) sets should be obtained from separate sites prior to antibiotic administration.[4] Collection of blood cultures prior to antibiotic administration greatly increases the sensitivity of identifying the causative organism and directing antibiotic therapy. Investigations should not unduly delay antibiotic administration when bacterial sepsis is suspected, as antibiotic administration within the first 'golden' hour is crucial for maternal survival. Mortality increases by 8 per cent for each hours' delay in antibiotic administration.[5,12]

Other microbial samples should be guided by clinical suspicion for the focus of infection and may include: throat, nasopharygenal aspirate, high vaginal, placental, epidural site, caesarean or episiotomy swabs; and/or breast milk, urine, stool, cerebrospinal fluid and sputum samples.

The laboratory should be informed where there is clinical suspicion of unusual pathogens such as *Listeria monocytogenes*, typhoid, fungal species or tuberculosis, and expert opinion from a microbiologist sought if there is any uncertainty in tests to be ordered or specimens to be collected.[4]

Routine blood tests should be performed urgently and include: FBC, CRP, UEC, LFT, coagulation studies (or ROTEM) and lactate. An arterial blood gas provides further information regarding acidosis and hypoxia.[4,5,10]

Imaging should occur promptly and be guided by the clinical picture. Imaging should not be withheld due to breastfeeding and may include chest x-ray, pelvic ultrasound and CT scan.[4,5,10]

Management

Early recognition of sepsis and assessment of severity are essential to initiating appropriate and timely management. Postnatal sepsis may have an insidious onset but fulminant course.[4] Of note, fever has not been included in the current diagnostic criteria for sepsis.[5] The Sequential (sepsis-related) Organ Failure Assessment (SOFA) score has been validated to identify patients with a high risk of in-hospital mortality,[3] but is impractical to use at the bedside. Thus, the quick SOFA (qSOFA) can be used to screen for sepsis.[13]

A qSOFA score of 2 or more identifies patients with a high risk of in-hospital mortality.[13] Patients suspected of having sepsis based on screening should be assessed for end organ dysfunction as evidenced by a change in the SOFA score of 2 or more.[3] Due to the physiological changes associated with pregnancy, an obstetrically modified qSOFA (omqSOFA) and SOFA (omSOFA) have been developed.[5] These should be used during pregnancy and for one week postpartum, after which time qSOFA and SOFA should be used, as maternal physiology gradually returns to normal.[5] Of note, the maternal blood pressure often peaks 48 hours post birth, and can be higher than values obtained six months postpartum, which should be kept in mind when assessing postnates for sepsis.[5,14] Once sepsis is diagnosed, it should trigger a coordinated multidisciplinary team approach and discussion with critical care providers.[4]

Antimicrobial therapy

Timely initiation of intravenous antimicrobial therapy is important for maternal survival. Antimicrobial choice should be based on likely source of sepsis and local guidelines. Where no source is apparent, antibiotics for postpartum endometritis should be initiated (gentamicin, metronidazole, amoxicillin OR ampicillin, in this order) given endometritis is the most likely source.[5] Gentamicin should be given first as it is the most effective agent for Gram-negative bacteraemia with the quickest onset of action. Alternatively, if endometritis is considered highly unlikely, empirical antibiotics for sepsis of unknown origin can be considered. If GAS is suspected, consider the addition of clindamycin to switch off exotoxin production, which reduces mortality. Flucloxacillin should be used for wound infections and mastitis.[5] Vancomycin should be considered if MRSA is suspected.[5] Box 1 outlines common pathogens implicated in postnatal sepsis, remembering that genital tract related sepsis is often polymicrobial.[10] Nuraminidase inhibitors, oseltamivir or zanamivir, should be given if influenza is suspected.[5]

Some infections, including GAS and *S. Aureus*, require prophylaxis for the neonate (and household

Box 1. Common organisms causing postnatal sepsis.[4,10]

- Group A-beta-haemolytic *Streptococcus pyogenes* (GAS) – commonest cause of maternal death due to sepsis[4,5]
- *Escherichia coli* – commonest cause of maternal bacterial infection[4,5]
- *Staphylococcus aureus,* including methicillin resistant S. aureus (MRSA) – commonest cause of mastitis and surgical site infection[1]
- *Streptococcus pneumoniae*
- *Clostridium spp*
- *Morganella morganii*
- Anaerobic infections – *Bacteroides sp, Prevotella sp, Prophyromonas sp, Preptostreptococcus sp and Finegolida sp*

contacts) as transmission can occur, including during breastfeeding. The treating team should alert neonatologists and infectious disease physicians to the presence of maternal infection.[4]

Most antibiotics are transferred into breast milk; however, the dose to the infant is relatively small. Infants should be monitored for antimicrobial-associated side effects, including vomiting, diarrhoea, thrush or skin rash. Antibiotic therapy should be de-escalated and ceased as soon as practicable to help maintain normal gut microbiota in the infant and mother.[5]

Source control

The focus of infection should be treated. Evacuation of retained products of conception, surgical debridement of wounds, evacuation of infected haematomas, incision and drainage of breast or pelvic collections may be required to achieve source control. Samples should be taken for microscopy, culture, stain or nucleic acid amplification testing. Further antibiotics may be required to cover procedures.[4,5]

Fluid resuscitation and supportive care

Fluid resuscitation for hypotension and tissue hypoperfusion should be initiated with an isotonic crystalloid (usually normal saline 0.9%)[3,4] at 20 mL/kg, to a maximum of 2 L in the ward setting.[5] An indwelling catheter should be inserted, and strict fluid balance recorded. Postpartum women may be more susceptible to fluid overload and pulmonary oedema than non-pregnant patients, which can make fluid resuscitation exceedingly difficult. Vasopressors are generally indicated if MAP above 65 mm Hg cannot be maintained or serum lactates continue to rise. Central venous pressure monitoring may be required. Thus, it is important to involve critical care teams, anaesthetists and intensive care physicians early, especially if transfer to another healthcare facility, with an ICU, is required.

Supplemental oxygen may be required if saturations are abnormal.[5]

Intravenous immunoglobulin can be considered in invasive streptococcal or staphylococcal infection, as it neutralises super antigen effects of exotoxins and inhibits production of inflammatory cytokines.[4,15]

Nonsteroidal anti-inflammatory drugs should be avoided in GAS sepsis, as they inhibit polymorphs.[4]

Thromboembolism prophylaxis should be initiated, as sepsis and the pureperium are both independent risk factors for venous thromboembolism.[5,15]

Conclusion

Prompt recognition and treatment with appropriate antibiotic therapy and source control are essential to minimise maternal morbidity, and potentially death, in septic postnates. Optimal patient outcomes further rely on a multidisciplinary team approach that can deliver effective supportive therapy and escalate care in the deteriorating patient.

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Early flags of concern and warning scores

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Both internationally and throughout Australasia, sepsis is consistently one of the leading causes of maternal morbidity and mortality. Although pregnancy-related sepsis accounted for only 5 per cent of direct deaths in recent New Zealand and UK Maternal Mortality reports,[1,2] sepsis is a significant and important contributor to maternal morbidity. The New Zealand Maternal Morbidity Working Group (MMWG) recently collated notifications of women admitted to a high dependency or critical care area at any point during pregnancy and in the 42 days post pregnancy, over a two-year period. Sepsis was the third leading cause of admission to a higher care area, after postpartum haemorrhage and hypertensive diseases of pregnancy, at 14 per cent and 15.1 per cent in their 2018[3] and 2019[4] reports respectively.

Unlike many emergencies in obstetric practice, sepsis has a more subtle presentation and may not invoke the same sense of urgency in clinical staff as a cord prolapse, acute haemorrhage or placental abruption. However, sepsis can be life threatening, as this clinical vignette from the 2014 UK MBBRACE-UK report[5] highlights:

> A woman was admitted in preterm labour and delivered rapidly. Three hours after delivery she was noted to be tachycardic and had a low blood pressure. These observations were not plotted on a MEOWS or similar chart. She was not reviewed by an obstetrician and was discharged for low risk postnatal care. Her community midwife saw her 24 hours later. No observations were taken. On day 4 she was admitted to the A&E as an emergency, but found to be dead on arrival. A post mortem revealed Group A Streptococcal sepsis. Further enquiries revealed that investigations taken in the hospital during her labour were abnormal. Blood results indicated sepsis and a high vaginal swab cultured Group A Streptococcus.

Sepsis-related morbidity

Severe acute maternal morbidity has been defined by Mantel et al as being 'a very ill woman who would have died had it not been that luck or good care was on her side'.[6] With falling maternal mortality rates, maternal morbidity is becoming an increasingly important indicator in maternity care and can be used to elucidate where improvements in maternity care systems can be made. The New Zealand MMWG undertook in-depth external multidisciplinary panel reviews of 32 of their 67 sepsis-related notifications of pregnant or recently pregnant women cared for in a high dependency or critical care area for their 2018 report.[3] Reviews were structured on a modified version of Vincent and Amalberti's LONDON framework of contributory factors.[7] The six most common themes contributing to the severity of morbidity in these sepsis case reviews are listed in Box 1.

In response to these findings, the New Zealand MMWG and Health Quality and Safety Commission (the Commission) recommended:

- the development of a maternity-specific national sepsis guideline
- inclusion of early recognition and treatment of sepsis within multidisciplinary team training
- District Health Boards establish clinical pathways and sepsis 'bundles' across primary and secondary care to streamline care in these time-critical situations

To address the poor recognition of severity of sepsis, delay in its treatment and inadequate communication between staff, the New Zealand MMWG, together with the Commission, developed and tested a standardised maternity recognition and response system. This matches a national vital signs chart calibrated to maternity-specific physiology with a locally developed escalation and response pathway. The pathway mandates a response by an appropriately qualified responder within a timeframe appropriate to the degree of physiological derangement. Human factors research[8,9] has been incorporated in the chart's design to maximise ease of detection of abnormalities and to promote action if required. Further information on the New Zealand MEWS is available at www.hqsc.govt.nz/mews.

The New Zealand MEWS is a hybrid scoring system. Each of the eight vital signs contributing to a total

Box 1. Themes identified from the NZ maternal morbidity working group's sepsis reviews.[3]

1. Failure to follow recommended best practice (59%)
2. Lack of policies, protocols or guidelines (56%)
3. Lack of recognition of severity (53%)
4. Delay in treatment (47%)
5. Inadequate communication (47%)
6. Lack of knowledge and skills of healthcare providers (47%)

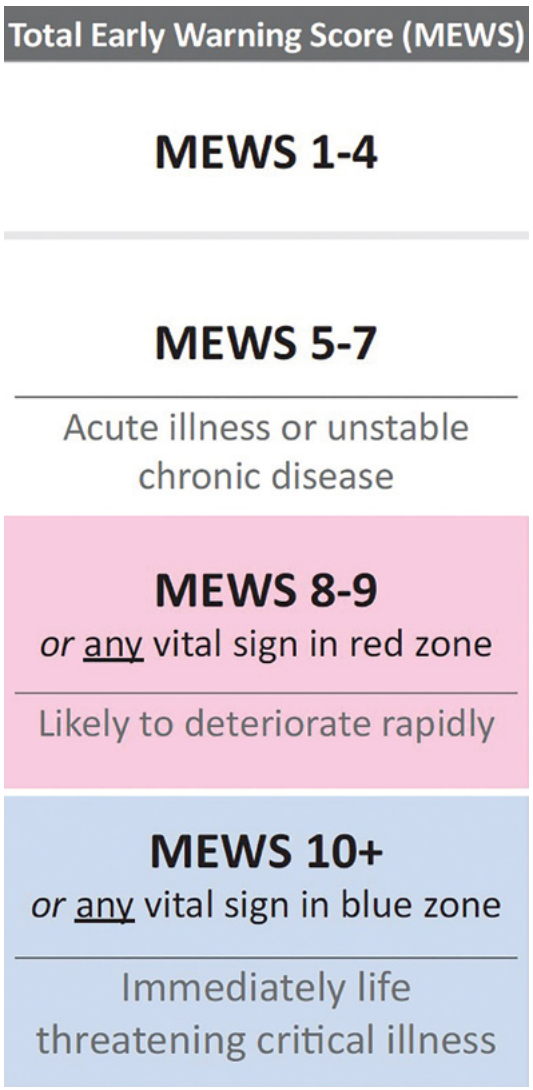

Figure 1. NZMEWS escalation pathway.

score that mandates a response; an extremely abnormal single physiological parameter (pink or blue) can mandate a higher level of response than the associated score. Using this combined recognition and response system, both sepsis and other acute illness in maternity can be detected early in an objective manner, provide a set pathway for response and early appropriate management, which ultimately should reduce the severity of acute maternal morbidity.

Evidence for early warning systems

Standardised recognition and response systems have reduced objective morbidity and mortality outcome measures in adult inpatients. For example, Ludikhuize et al[10] did a study in the Netherlands before and after the introduction of an early warning score system and a structured handover tool (SBAR), in conjunction with a rapid response team in 12 hospitals, with two surgical and two medical wards in each. The study included over a million inpatient bed days and demonstrated a 40 per cent reduction in cardiac arrests and a 20 per cent reduction in hospital mortality, both of which reached statistical significance.

Recognition and response systems in maternity are not able to use hard end points such as cardiac arrest or mortality since they are thankfully rare in this population. However, early experience from using the national NZMEWS in my hospital appears to have improved early recognition of acute deterioration with an associated fall in 'adult code red' emergency calls since its introduction in July 2018 (unpublished data). Having one standard national system is also hugely beneficial to ensure a common language, both between maternity units, and for a mobile workforce.

Sepsis-specific scores

While vital sign scoring systems, such as New Zealand MEWS, can detect acute physiological derangement, they will not necessarily delineate organ dysfunction related to infection (sepsis) from other causes. MEWS does not provide an objective measure of sepsis severity. The Sequential (sepsis-related) Organ Failure Assessment (SOFA) score can determine risk of sepsis-related mortality on patients already in the intensive care unit;[11] however, it uses criteria that are not readily available at the bedside, such as creatinine, platelet count and bilirubin. Quick-SOFA (qSOFA) is a useful bedside screening tool, it prompts consideration of sepsis as a differential diagnosis as well as further investigation of organ dysfunction related to sepsis and consideration of transfer for advanced organ support. (Please see Table 1 on p.31) A qSOFA identifies patients at higher risk of mortality better than SOFA when used outside the intensive care unit.[12]

SOFA has not been validated specifically in the younger pregnant population, so the Society of Obstetric Medicine Australia and New Zealand (SOMANZ) have obstetrically modified the thresholds for scoring within qSOFA and SOFA to account for normal pregnancy physiology, producing the omqSOFA and omSOFA.[13] (Please see Table 2 on p.31) A score of 2 or more in the omqSOFA should prompt a more thorough assessment of severity of sepsis with an omSOFA, while concurrent resuscitation and definitive treatment is instituted. This scoring system is rapidly gaining traction as a useful tool for sepsis assessment in the obstetric population, though it has not been validated in large obstetric populations to date.

Fetus as the canary in the mine

The fetus is a useful early marker of maternal wellbeing. Early physiological deterioration related to sepsis can be masked by younger adults' ability to compensate. In pregnant women, uteroplacental circulation is not autoregulated, therefore maternal sepsis resulting in circulatory insufficiency may lead to compromised fetal perfusion.[14] This could precipitate fetal heart rate abnormalities or reduced fetal movements before overt deterioration in the mother. For this reason, acute fetal concern is included as a trigger for escalation and review in NZMEWS regardless of total vital sign score.

Summary

Maternal sepsis can sometimes be difficult to detect in its early undifferentiated form. Objective scoring systems such as MEWS and omqSOFA are useful screening tools for sepsis. These tools provide a convenient shorthand to convey severity of illness when communicating with senior staff, other medical disciplines and when planning treatment. Early institution of the 'sepsis 6+2' care bundle (Figure 3) in pregnancy-related sepsis, regardless of gestation as well as in the postpartum period, can save lives and reduce both duration and severity of sepsis-related morbidity.

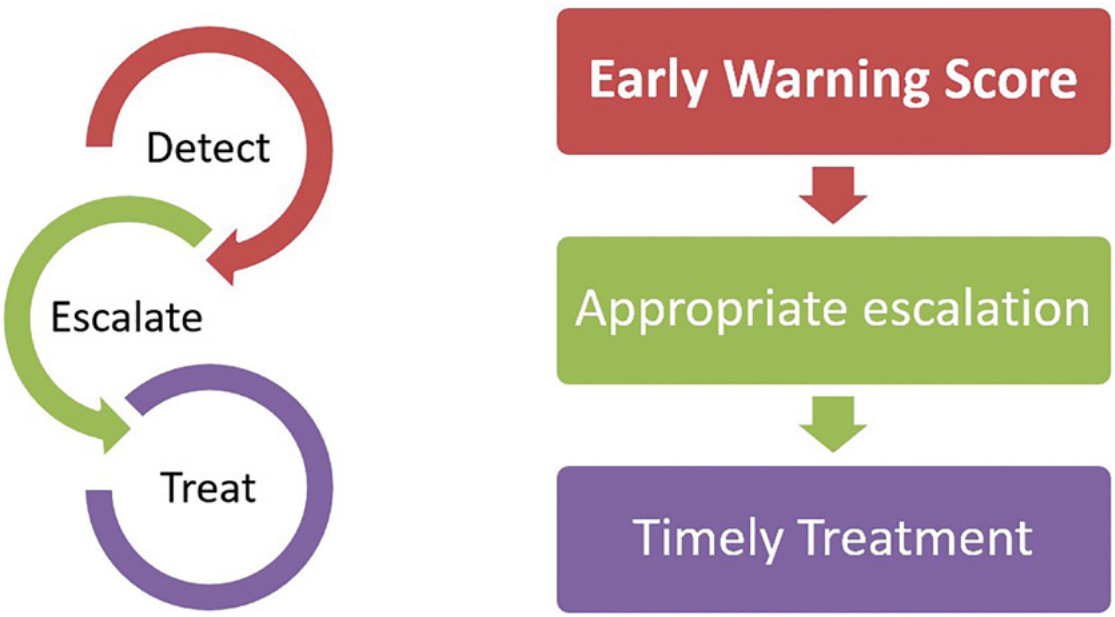

Figure 2. Three essential aspects of an early warning system.

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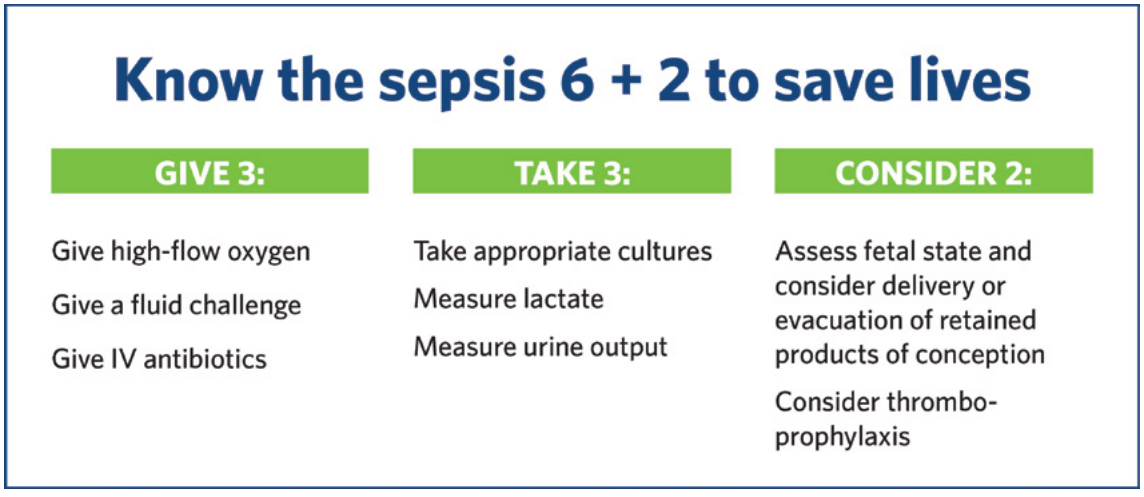

Figure 3. Sepsis 6+2 care bundle, taken from the MMWG sepsis poster, June 2018.

Early recognition and management of sepsis

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Sepsis is a major cause of morbidity and mortality across the world. Over the last two decades, campaigns such as 'SEPSIS KILLS' by Clinical Excellence Commission in NSW and 'Hour-1 bundle' by Surviving Sepsis Campaign have focused on early recognition and management of sepsis to improve outcomes. However, despite advances and emphasis on early recognition and management, mortality from sepsis has remained high.

Introduction

As per the new definition, sepsis is as life-threatening organ dysfunction caused by a dysregulated host response to infection.[1] What differentiates sepsis from infection is an aberrant or dysregulated host response along with organ dysfunction.

A systematic review has estimated the global incidence of sepsis and mortality to be 30 million episodes of sepsis and 6 million deaths per year, many of these preventable.[2]

The incidence and mortality rates of sepsis in Australia have been estimated from studies of adult patients in intensive care units (ICUs). The annual incidence of sepsis among adult patients in Australian and New Zealand ICUs were 77 cases per 100 000, with in-hospital mortality of 37.5 per cent.[3]

Patients with suspected infection, who are likely to have a prolonged ICU stay or to die in the hospital, can be promptly identified at the bedside with qSOFA: quick sepsis-related organ dysfunction assessment score.[1] The score ranges from 0–3 points. The presence of 2 or more qSOFA points near the onset of infection is associated with a greater risk of death or prolonged ICU stay. qSOFA can predict sepsis mortality, with the odds of 5.6 for short-term mortality and 4.7 for long-term mortality.[4]

It uses three criteria, assigning one point for low blood pressure (SBP $\leq$ 100 mm Hg), high respiratory rate ($\geq$ 22 breaths per min), or altered mentation (Glasgow coma scale < 15).[1]

Diagnosis of sepsis

Diagnosis of sepsis relies on a high index of suspicion based on a combination of symptoms, signs, laboratory tests, imaging modalities and recognition of organ dysfunction. None of these in isolation is definitive to make a diagnosis of sepsis.

It is important to recognise that critically ill, malnourished, immunosuppressed and elderly patients may not manifest typical signs of sepsis. Traditional symptoms and signs, such as hypo- or hyperthermia, tachycardia, tachypnoea, altered white blood cell count, are present in most critically ill patients and are unreliable in identifying patients with sepsis.

More than 170 biomarkers have been studied for use in evaluation of sepsis. Most biomarkers have limited ability to differentiate between sepsis and an inflammatory state. Currently, no biological molecular markers are recommended for use in the routine diagnosis or prognosis of sepsis or septic shock.[5] The two most common biomarkers used in clinical practice are C-reactive protein (CRP) and procalcitonin (PCT).

CRP concentration increases 4–6 hours after the start of an infection and reaches a peak at 36–50 hours. It has low specificity (40–67 per cent) but high sensitivity (68–92 per cent). There is no threshold for CRP that helps to discriminate between infected and non-infected patients;

however, elevated levels of CRP correlate with increased risk of organ failure and death.[6] CRP remains useful to assess for sepsis in patients with neutropenia and also to assess for response to antibiotic therapy, as its concentrations fall in 48 hours post appropriate antibiotic therapy.

PCT is a prohormone of calcitonin, normally synthesised by the C cells of the thyroid gland. In sepsis, neuroendocrine cells in the lung and intestine produce PCT. The sensitivity and specificity of PCT vary widely between studies. Its levels rise in 3–6 hours and, as such, can be used for an early predictor of infection. Even though its use may have limited value in diagnosis of sepsis due to its low specificity, it is predominantly recommended for earlier discontinuation of antimicrobial therapy. A recent Cochrane review concluded that the use of PCT to guide initiation and duration of antibiotic treatment results in lower risk of mortality, lower antibiotic consumption, and lower risk for antibiotic-related side effects.[7]

Other potential biomarkers, such as IL-1, IL-6, IL-8, TNF-α, TREM -1, CTLA-4, have unproven use in diagnosis and prognosis of sepsis and are rarely available to clinicians at the bedside.

Early management of sepsis

Early diagnosis and prompt initial resuscitation and management are key to improving outcome. In the absence of definitive treatment for the dysregulated host response, the focus of management is early antimicrobial therapy, prevention of organ dysfunction by aggressive resuscitation and organ support.

The Surviving Sepsis Campaign is a global initiative to reduce mortality from sepsis by collaboration amongst various organisations. The campaign guidelines and bundles of care for prompt recognition and management of sepsis have been shown to reduce mortality. An 'Hour-1 bundle' was created by the campaign guidelines for early intervention in sepsis.[8] This bundle focuses on five interventions to be initiated within the first hour of presentation: measuring lactate, obtaining blood cultures, administration of broad spectrum antibiotics, crystalloid fluid resuscitation for patients who are hypotensive and have elevated lactate levels and administration of vasopressors for maintaining a mean arterial pressure of 65 or more.[9]

Early resuscitation and haemodynamic stabilisation

Septic shock is a medical emergency and early effective resuscitation helps to improve outcomes. All patients with septic shock must be adequately oxygenated to correct hypoxaemia. Even though the type of intravenous fluids has been debated for many years, it is important to correct hypovolaemia rapidly. The surviving sepsis guidelines recommend an initial fluid resuscitation with a dose of 30 mL/kg of intravenous crystalloid fluid with a target of a mean arterial pressure (MAP) of 65 or greater to prevent organ dysfunction and this may be achieved by vasopressors in addition to fluid resuscitation.[9]

The early goal-directed therapy focused on timely optimisation of haemodynamic parameters by continuous monitoring of central venous oxygen saturation ($ScvO_2$, >70%), central venous pressure (8–12 mm Hg), MAP (≥ 65 mm Hg), and urine output (>0.5 mL/kg/h) by interventions such as fluids, vasopressors, blood transfusions and inotropes.[10] However, three subsequent international multicentre trials (Protocolized Care for Early Septic Shock [ProCESS], Australasian Resuscitation in Sepsis Evaluation [ARISE], and Protocolized Management in Sepsis [ProMISe]) have failed to show any significant survival benefit when this protocol was compared to usual care.[11]

Patients needing organ support or vasopressors require ICU admission. Patients with organ dysfunction, requiring high-dose vasopressors, usually undergo invasive haemodynamic monitoring in ICU to assess fluid status and cardiac output so as to intervene and optimise organ perfusion. Surviving Sepsis guidelines recommend noradrenaline and vasopressin as vasopressors for use in septic shock.[8] Stress-dose steroids are used in patients with escalating dose of vasopressors as steroids have shown to have vasopressor-sparing effect, but no mortality benefit.[8]

Early antimicrobial therapy

Appropriate cultures, specifically blood culture, should be obtained if the culture can be performed in a timely manner so as to avoid delays in antimicrobial therapy. Surviving Sepsis guidelines recommend that intravenous antimicrobials are administered within the first hour after recognition of sepsis and septic shock.[8] Studies have shown that each hour of delay in administration of antibiotics results in an increase of 7.6 per cent mortality for septic shock.[12] It is recommended to use empiric broad-spectrum therapy with one or more antimicrobials to cover both Gram-positive and Gram-negative bacteria and, if indicated, against fungi and, rarely, viruses. Local and national guidelines should be sought for specific antimicrobial therapy, depending on source, to avoid inappropriate broad-spectrum antibiotic that may lead to future resistance.

Source control

Identifying source of infection is of crucial importance and additional investigations such as imaging (x-ray, computed tomography, ultrasonography) and acquisition of further diagnostic samples (such as broncho-alveolar lavage, aspirating fluid collections or joints) may be needed.

Source control must be undertaken in a timely manner. Potentially infected vascular access devices, or other infected implantable devices/hardware, should be removed. Intervention, such as abscess drainage (including thoracic empyema and joint), percutaneous nephrostomy, soft tissue debridement or amputation (and cholecystostomy, if indicated), must be considered for the infection control.

Organ support

Patients with sepsis and septic shock usually have organ dysfunction that may need monitoring and support in ICU, including: mechanical ventilation for respiratory failure, continuous renal replacement therapy for renal failure and inotropic therapy for septic cardiomyopathy.

Conclusion

For critically ill patients with sepsis or septic shock, time is of the essence. In all cases, the emphasis must be on early diagnosis and intervention for rapid infection control and organ support to prevent organ failure and death. Increased awareness of sepsis, establishment of local protocols and improved compliance with the Hour-1 sepsis bundle is of paramount importance to improve patient outcomes.

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Antimicrobial stewardship and infection prevention

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The rise of antimicrobial resistance is leading to increased maternal and neonatal morbidity and mortality.[1] Antimicrobials pose a self-defeating conundrum; every dose used contributes to increased resistance and loss of efficacy. Unnecessary antimicrobial prescribing and preventable infections or colonisation with multiresistant organisms (MROs) compound the problem. In recognition of this, antimicrobial stewardship strategies are now mandated in the National Safety and Quality Health Service standards for health service accreditation.[2] In this article, we discuss key strategies of an antimicrobial stewardship program, as well as the role of infection prevention and control (IPC), antibiotic allergy delabelling, and antimicrobial prophylaxis in minimising antimicrobial resistance and harms to mother and neonate. There is also an urgent need for international collaboration between industry, research, government and non-government organisations, to find new ways to support research and development of novel antimicrobials.

Antimicrobial stewardship

Antimicrobial stewardship promotes optimal antimicrobial prescribing (Box 1) while minimising the adverse consequences related to antimicrobial toxicity and resistance, and unnecessary costs. The implementation of an effective antimicrobial stewardship program (Table 1) requires the coordinated efforts of infectious diseases specialists, pharmacists, IPC professionals, microbiologists and hospital or practice administrators to improve and measure the appropriate use of antibiotics (Box 2).

Importance of infection prevention and control

In the 1840s, Ignaz Semmelweis changed modern medicine when he showed that hand hygiene in an Austrian obstetric clinic reduced mortality from more than 10 per cent to 2 per cent. This lesson rings ever true, especially in the face of increasing antimicrobial resistance (AMR). There are high levels of morbidity from multiresistant organisms (MROs) such as methicillin-resistant *Staphylococcus aureus* (MRSA), *S. aureus* with reduced vancomycin susceptibility (hVISA and others), multi-resistant Gram-negative bacilli and vancomycin resistant enterococci. Routine screening for MROs in obstetric patients is not currently recommended,[3] as most colonised mothers do not develop invasive disease. However, undetected MRO colonisation in mothers risks the unintentional introduction of MROs into neonatal units. Awareness of risk factors for colonisation (Box 3) and their detection remain important in the management of symptomatic maternal and neonatal infection. Regardless, strict IPC programs are instrumental in limiting their nosocomial spread. Key elements of IPC programs include measures to reduce inappropriate antibiotic exposure, aseptic technique for invasive procedures, appropriate use of personal protective equipment, screening for MROs when indicated and contact precautions for colonised or infected patients.[4]

Antibiotic allergy delabelling

Antimicrobial stewardship programs provide guidance on antibiotic allergy delabelling and correct second line antibiotic choice when a true allergy exists. False labelling of adverse drug reactions as allergies leads to inappropriate use of second line antibiotics and increased antimicrobial resistance. Correct allergy labelling is further complicated by the fact that up to 80 per cent of patients with true IgE mediated allergic reactions lose these responses over time.[5]

Careful prenatal history-taking can help delineate non-immune-mediated Type A from immune-mediated Type B, drug reaction;[6] (Figure 1). A common clinical scenario is the choice of antibiotic in a pregnant woman colonised with *Streptococcus*

Box 1. Six principles of optimal antimicrobial use.[5]

In prescribing antimicrobials, we need to ensure that we have chosen the:
1. right patient (with [or at risk of] an infection for which antimicrobial therapy [or prophylaxis], is indicated)
2. right time (eg. as soon as possible after onset of sepsis or at appropriate time for prophylaxis [Table 2])
3. right drug choice (with as narrow a spectrum as possible for the likely or known pathogen)
4. right route (orally, as soon as clinically feasible)
5. right dose (to achieve therapeutic level at the site of infection)
6. right duration (no longer than necessary to achieve control of, or prevent, infection)

Table 1. Key components of an antimicrobial stewardship program.[6]

Inpatient setting	Outpatient setting
• Up-to-date antimicrobial guidelines • Formulary restrictions and an approval system for broader spectrum antimicrobials • Prospective audit and direct prescriber feedback • Tailoring of prescribing to the latest local resistance patterns	• Primary Health Network education • Encouragement of auditing and feedback on antimicrobial prescribing at a practice level • Promotion of vaccinations to minimise the need for antibiotics

agalactiae (Group B Streptococcus or GBS), who has a history of penicillin reactions. Women with Type A reactions have low risk of anaphylaxis; first-generation cephalosporins remain the preferred choice. Clindamycin is recommended for women with a high penicillin anaphylaxis risk, if the isolate is known to be susceptible. To facilitate this, sensitivity testing should be requested specifically at the time of GBS culture. Otherwise, vancomycin is now the preferred option in severe penicillin allergy due to rising clindamycin resistance rates globally.[7,8] Australian data showed 4.2 per cent clindamycin resistance in GBS in 2011[9] and, more recently, rates as high as 20 per cent have been reported.[10]

Drug exanthems differ from urticaria by being non-pruritic and often morbilliform, rather than pruritic with a 'wheal and flare' phenomenon. It is usually safe to rechallenge patients who have had drug exanthems, while there is a risk of anaphylaxis with rechallenge of IgE-mediated reactions. In difficult histories, skin testing can be used to determine the likelihood of IgE mediated reactions. It should never be used to evaluate patients with severe non-IgE mediated reactions such as Stevens-Johnson syndrome or toxic epidermal necrolysis, as it cannot predict the recurrence of these reactions.

Ideally, all patients with a history of immune-mediated allergy should be referred to an antibiotic allergy delabelling service for specialist assessment.

Antimicrobial prophylaxis

Correct antimicrobial prophylaxis can prevent infection and reduce morbidity and mortality; however, inappropriate peripartum antimicrobial prophylaxis risks increased antimicrobial resistance and infant gut microbiota dysbiosis.[11] Antimicrobial prophylaxis in the peripartum period targets polymicrobial flora in the genital tract to prevent intra-amniotic infection, postpartum endometritis or surgical site infection, in women at risk. The major ascending cervicovaginal pathogens include group A beta-haemolytic streptococcus (*Streptococcus pyogenes*), GBS, *S. aureus* including MRSA, anaerobic cocci and enteric Gram-negative bacilli.[12-14] Genital mycoplasmas are commonly isolated from patients with intra-amniotic infection, but the clinical significance of these organisms is uncertain.[6]

The World Health Organization (WHO) released guidance on prevention and treatment of peripartum[15] and surgical site infections,[16] in 2015

Box 2. Benefits of an antimicrobial stewardship program.[17]

1. Improvement in patient outcomes (eg. fewer adverse drug effects, decreased length of hospitalisation, fewer readmissions)
2. Optimal (more effective) antimicrobial use
3. Reduction in inappropriate antimicrobial use
4. Reduction in rates of resistant organisms
5. Reduction in rates of *C. difficile* infection
6. Adherence to institutional pathways and protocols
7. Reduction in antimicrobial associated healthcare costs

Box 3. Major risk factors for multidrug resistant organism colonisation.[4]

1. Prolonged hospital admission (with or without antibiotic therapy)
2. Admission to intensive care unit
3. Recent, especially healthcare-related, travel to a high AMR-prevalence country
4. Previous history of MRO colonisation
5. Transfer from long-term care facility
6. Chronic wounds or indwelling medical device
7. Previous prolonged or repeated antibiotic therapy

Table 2. Key recommendations relating to surgical prophylaxis in obstetrics and gynaecology, adapted from eTG[6] and WHO guidelines 2016.[16]

Timing of administration of surgical prophylaxis	Short-acting antibiotics, such as cefazolin, < 60 min prior to incision. Long-acting antibiotics, < 120 min prior to incision. Vancomycin requires a slow infusion; started at least 15 min prior to incision; surgical incision can occur before the infusion is completed.
Prophylaxis duration	Single preoperative dose +/- intraoperative redosing usually adequate in caesarean and gynaecologic surgery. Antimicrobial prophylaxis should not be continued because of the presence of a wound drain for the purpose of preventing surgical site infections.
Intraoperative redosing	Significant delay in starting the operation More than two half-lives of the drug have elapsed since the previous dose (eg. 4 hours for cefazolin) > 1.5 L blood lost during adult procedure

and 2016 respectively. Antibiotic prophylaxis is not recommended for women with prelabour rupture of membranes at more than 36 weeks gestation, for women with meconium-stained amniotic fluid, uncomplicated vaginal births or vacuum- or forceps-assisted operative vaginal births. Antibiotic prophylaxis is recommended for women undergoing manual removal of the placenta and for third- and fourth-degree perineal tears, but not for episiotomy.

Caesarean section is the most important risk factor for maternal infection in the immediate postpartum period, with aseptic surgical techniques and use of prophylactic antibiotics being the cornerstones of infection prevention. WHO recommends vaginal cleansing with povidone-iodine immediately before caesarean section to reduce postpartum endometritis. See Table 2 for key recommendations regarding timing, duration (including in the presence of drains) and intraoperative redosing in preventing surgical site infections. Please refer to Therapeutic Guidelines (eTG)3 for the updated guidelines for prophylaxis and empirical therapy in intrapartum and postpartum infections.

Summary

The world is running out of useful antibiotics in the face of rising antimicrobial resistance. With the increasing implementation of antimicrobial stewardship, along with the principles of antibiotic allergy delabelling, strict IPC and antimicrobial prophylaxis, we aim to empower colleagues to responsibly prescribe antimicrobials, not just for the safety of mothers and neonates, but for our global community.

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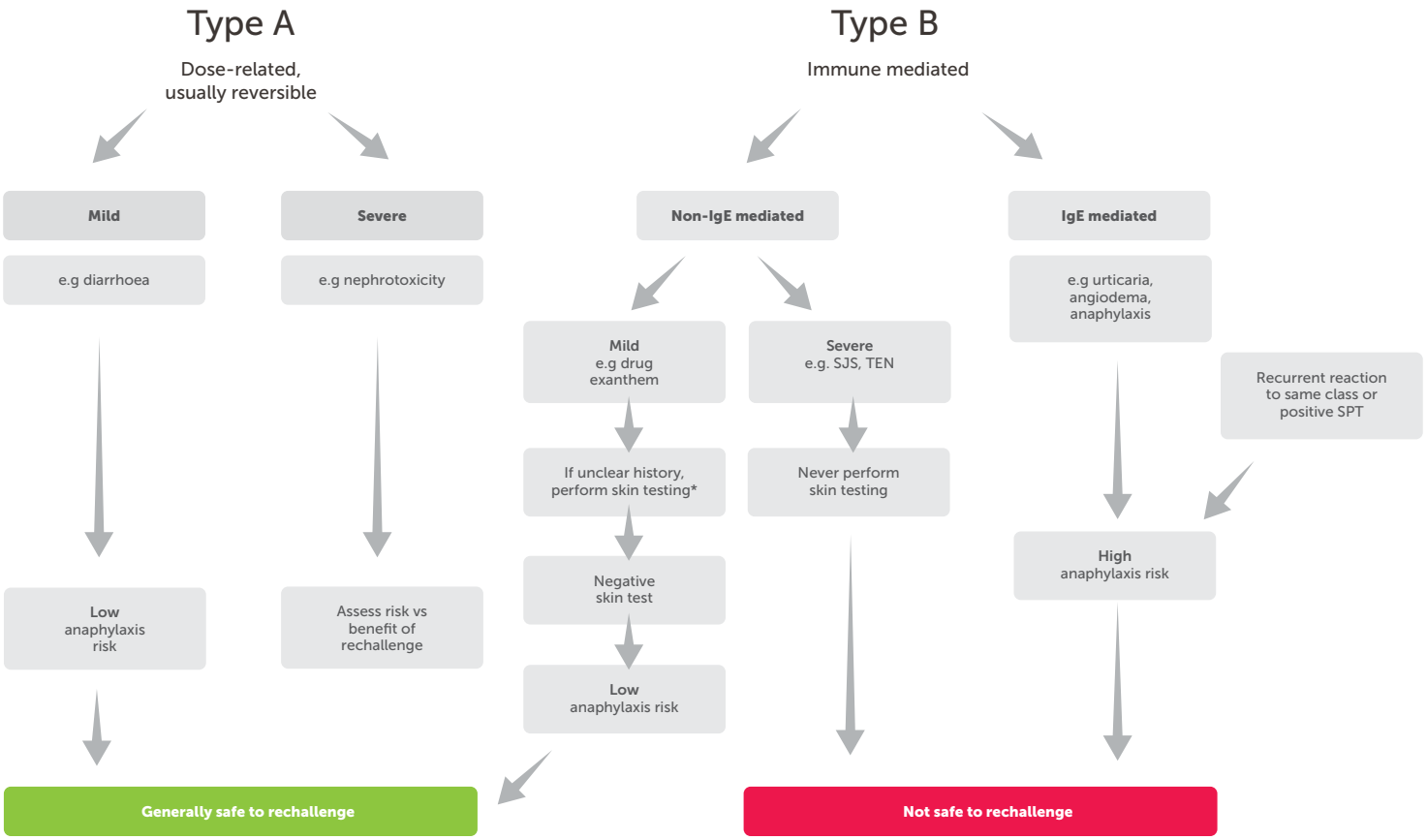

Figure 1. Drug reaction types and implications for drug allergy delabelling. (Adapted from Practical Implementation of an Antibiotic Stewardship Program). [5]

Preventing surgical site infection at caesarean

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The Centers for Disease Control and Prevention define surgical site infection (SSI) as 'infection occurring in the part of the body where the surgery took place within 30 days of the procedure'.[1] In 2016, 34 per cent of Australian mothers gave birth by caesarean section (CS), with more than 106 000 procedures performed.[2] Women undergoing CS have a 5- to 20-fold greater risk for puerperal infectious morbidity compared to vaginal birth.[3]

The most robust strategies for preventing SSI are firstly, to avoid unnecessary CS; secondly, to optimise medical comorbidities (such as glycaemic control) to reduce susceptibility to infection and improve healing; and finally, to maintain best practice in peri-operative management and surgical technique. This review considers the evidence (or lack thereof) for strategies currently employed at CS to reduce the risk of SSI and its consequences.

Pre-operative preparation

Antibiotic prophylaxis

Routine antibiotic prophylaxis at CS is standard practice in Australia, consistent with surgical guidelines internationally. The 2014 Cochrane review on antibiotic administration at CS demonstrated a 60–70 per cent reduction in the incidence of wound infection, endometritis and serious maternal infectious complications with the use of prophylactic antibiotics compared to placebo, for both elective and emergency CS.[3]

Timing of antibiotic prophylaxis

Prophylactic antibiotic administration is generally timed to establish a bactericidal concentration in serum and tissue prior to surgical incision. At CS, a reasonable concern for potential anaphylaxis or the fetal effects of antibiotic administration may lead to delaying surgical prophylaxis until after the fetus is delivered and the cord is clamped, but the well-established benefit of reduced infectious morbidity generally favours antibiotic administration prior to skin incision over these rarer risks. The 2014 Cochrane review supports this, with almost half the rate of combined infections, endometritis and wound infection reported in women with antibiotics administered pre-operatively, compared to those who received antibiotics after neonatal cord clamping.[4]

One meta-analysis and one small randomised controlled trial (RCT) performed in China did show no difference in SSI with pre-incision or post-cord-clamping antibiotic administration in elective CS.[5] However, neither study suggested a benefit to delayed administration, and despite an unusually low incidence of SSI (1 per cent in the control group), the point estimates from this RCT still appeared to favour a (non-statistically significant) benefit of pre-incision antibiotic prophylaxis. By contrast, a systematic review in 2017 reported unequivocally that pre-operative antibiotics reduced infectious morbidity by 28 per cent compared with administration after cord clamping. There was no significant difference in rates of other maternal infections, neonatal sepsis, ICU admission or the need for neonatal antibiotics.[6]

Extended prophylaxis with azithromycin

SSI following CS has a distinct microbial signature, with polymicrobial infection commonly comprising organisms of both skin and vaginal origin.[7] Most studies include trials of first-generation cephalosporins, but extended spectrum antibiotic cover may further reduce infection rates in high-risk patients, particularly from ureaplasma species, which are commonly associated with endometritis and caesarean-related infection.[8,9]

A well-powered RCT from the USA showed that adding a single dose of intravenous azithromycin to routine prophylaxis in women with ruptured membranes for greater than four hours undergoing an unplanned CS significantly reduced the number of women with endometritis, wound infection or other

infectious morbidity up to six weeks after surgery (6.1 per cent versus 12.0 per cent).[9] No increase in adverse outcomes was reported.

The impact of other risk factors, such as obesity, prolonged rupture of membranes and prolonged surgical time, requires more robust evidence, but strategies such as additional intraoperative dosing may further reduce post-caesarean infection rates in these settings.[10]

The neonatal microbiome

While antibiotic prophylaxis provides a clear maternal benefit, any CS must consider the wellbeing of both mother and fetus. Perinatal antibiotics do appear to be associated with potentially important differences in the neonatal gut microbiome;[11] however, a systematic review of 30 studies concluded that the evidence for neonatal impact is inconsistent and at high risk of bias, with most studies not following populations through to clinical outcomes.[12] The actual clinical significance of alteration in the microbiome therefore remains unknown.

There is also limited evidence of the impact of timing of administration on the infant microbiome. One RCT of 1106 women comparing antibiotic prophylaxis at CS pre-incision versus post-cord clamping did measure blood levels of cefazolin in the neonate and confirmed low levels even in the pre-incision group. The significance of this on long-term outcomes and gut microbiota remains unknown.[13]

Interestingly, studies of neonatal meconium microbiota show no difference between those born by CS versus vaginal delivery, with differences in the microbiome not developing until several days after birth.[11] A recent prospective study with 81 mother-infant pairs showed no impact of mode of birth on the microbial community over multiple body sites at six weeks of age.[14]

Hair removal

Most conclusions on hair removal specifically related to SSI following CS are extrapolated from other types of surgery. A 2011 Cochrane review found no statistically significant effect of hair removal to reduce SSI,[15] although the study was underpowered. Current evidence favours the use of clippers over razors, and while hair removal may not directly reduce SSI, it may be beneficial to facilitate the proper application of adhesive surgical dressings.[15]

Vaginal preparation

Particularly in the setting of ruptured membranes, ascending infection is a plausible cause of endometritis is plausible, and vaginal preparation with povidone-iodine has been shown to reduce the number of vaginal organisms.[16]

Several RCTs have assessed the efficacy of pre-operative, vaginally administered antiseptic in reducing endometritis. The related 2018 Cochrane review update showed a reduction in post-CS endometritis from 8.7 to 3.8 per cent with the use of pre-operative vaginal cleansing, with no adverse effects reported.[17] A recent systematic review comparing 23 trials using different vaginal preparations showed that all antiseptic solutions reduced the rates of endometritis with an odds ratio (OR) of 0.48 compared to placebo.[16] Povidone-iodine 1% solution was the most effective in reducing endometritis (OR 0.43), postoperative wound infection and fever.[16] These findings also applied to women undergoing elective CS.[16]

Skin preparation

Many studies have examined pre-operative bathing (predominately using chlorhexidine-based preparations) to prevent SSIs. The Cochrane review's fifth update on this topic showed no clear evidence of benefit.[18]

However, antiseptic preparation of the surgical field with chlorhexidine or povidone-iodine based preparations immediately before surgery is well known to reduce the risk of infection. For CS, SSI does appear to be slightly reduced with chlorhexidine-based preparations versus povidone-iodine, but the evidence remains of low quality.[19]

Intraoperative practices

O-ring retractors

All brands of o-ring retractor consist of two plastic rings connected by a polyurethane sheath, and these have been found to reduce SSI in abdominal surgery.[20] Data for their use at CS remains limited. Some studies suggest infection rates falling from 8 to 1 per cent (RR 7.84) but with large confidence intervals (CI 2.45–70.71).[21]

A systematic review and meta-analysis published this year showed no significant reduction in the rates of SSI with o-ring retractors compared to routine care and retraction.[22] Interestingly, o-ring retractors did have measurable benefit in the subgroup of women with a BMI less than 35 and were associated with better visualisation of the operative field and less need to exteriorise the uterus.[22]

Removal of the placenta

Options for removing the placenta at CS include controlled-cord traction, manual removal or spontaneous delivery. In 2010, a Cochrane review of all RCTs comparing these methods showed that controlled-cord traction results in lower rates of endometritis, less blood loss and shorter duration of hospital stay.[23]

Surgical wound irrigation

There is limited evidence for the role of antiseptic or saline wound irrigation prior to skin closure at CS in reducing SSIs. Much of the surgical data is non-obstetric, and dates from as long ago as 1986. A recent Australian RCT examining betadine wound irrigation prior to skin closure versus no irrigation, showed no difference in the incidence of SSI between the groups.[24] A smaller trial of saline wound irrigation prior to skin closure similarly showed no difference.[25]

Postoperative care

Negative pressure dressings

Post-operative care is critical in wound healing. Despite this, the literature is sparse for care post CS. Prophylactic use of negative pressure dressings (NPDs) has been suggested as a means to reduce surgical wound complications. These dressings use negative pressure applied at the wound site to remove exudate, increase blood flow, stimulate granulation tissue growth and reduce oedema in order to accelerate wound healing.

In a high-risk population of obese women undergoing elective or emergency CS, NPDs have been shown to reduce rates of SSI compared with a standard dressing (RR 0.50, NNT = 22).[26] One systematic review describes a heterogeneous population of mostly obese women where the absolute risk of developing

a SSI was 5 per cent with prophylactic NPDs, versus 11 per cent with a standard dressing.[27] These findings are consistent with the literature on reduction of SSIs with prophylactic NPDs after general surgical procedures; however it is difficult to draw general recommendations from the available data due to heterogeneity of the studies.[28]

Conclusion

There is good evidence for prophylactic antibiotics, as well as preoperative skin and vaginal antiseptic preparation, for reducing SSI at CS. The pre-incision timing of antibiotics for maternal benefit is clear, but research continues as to the potential effects of perinatal administration on the neonatal and infant gut microbiome.

There is unlikely ever to be robust evidence for every step in any specific surgical procedure. It is therefore important that we, as obstetric surgeons, meticulously follow good surgical principles and methodically review our outcomes in order to ensure we provide the best possible care for our patients.

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Surgical gynaecological infections

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Postoperative infection remains the most common complication of gynaecological surgical procedures.[1] A surgical site infection (SSI) is any infection that arises within 30 days after an operation in any part of the body where the surgery took place: superficial at the incision site, deep at the incision site or in other organs or spaces opened or manipulated during an operation.[2]

It is important to consider the likely source of pathogens in each type of surgery. In gynaecological surgery, the source of pathogens can be the endogenous flora of either the patient's skin or vagina. With laparoscopy or laparotomy, where there is no breach of mucosal surfaces, skin organisms (predominantly Gram-positive organisms such as Staphylococci) are likely.[1,3,4] In contrast, with vaginal surgery or hysterectomy, the endogenous flora of the genital tract the likely cause will be polymicrobial, consisting of anaerobes, Gram-negative aerobes and Gram-positive cocci.[1,3,4]

Prior to any surgery, there is preparation with history, examination and appropriate investigations. Prior to gynaecological surgery, screening for genital tract infection is not required; however, women with symptoms or risk factors should be tested and treated for sexually transmitted infections (chlamydia and gonorrhoea) and bacterial vaginosis. These have been associated with an increased risk of infection, endometritis with chlamydia and gonorrhoea following termination and vaginal cuff infection following hysterectomy with bacterial vaginosis.[1,5]

Antibiotic prophylaxis should be given to prevent SSI prior to gynaecological surgery or procedures that enter the reproductive tract, ideally 60 minutes prior to skin incision. For procedures such as hysterectomy, antibiotic prophylaxis is clearly indicated, for others such as insertion of IUD or diagnostic

Table 1. Antibiotic recommendation by procedure.

Procedure	Antibiotic recommendation
Hysterectomy (vaginal/abdominal/laparoscopic)	Cephazolin 2 gm + metronidazole 500 mg IV
Laparoscopy (breach of bowel/uterine/vaginal cavity or conversion to operative laparotomy)	Cephazolin 2 gm + metronidazole 500 mg IV
Urogynaecological procedures (TVT, colposuspension, vaginal prolapse surgery +/- mesh)	Cephazolin 2 gm + metronidazole 500 mg IV
Laparoscopy (diagnostic or operative)	Not recommended
Hysteroscopy or hysterosalpingography or chromotubation with no history of PID and normal tubes on visualisation	Not recommended
Hysteroscopy or hysterosalpingography or chromotubation with history of PID or tubal damage	Doxycycline 100 mg BD for 5 days
Insertion of IUD	Not recommended
Endometrial Biopsy	Not recommended
LLETZ	Not recommended
Surgical termination of pregnancy (if not screened for bacterial vaginosis, chlamydia and gonorrhoea)	Doxycycline 400 mg 10–12 hours prior or azithromycin 1 gm PO and metronidazole 2 gm PO (120 minutes prior)

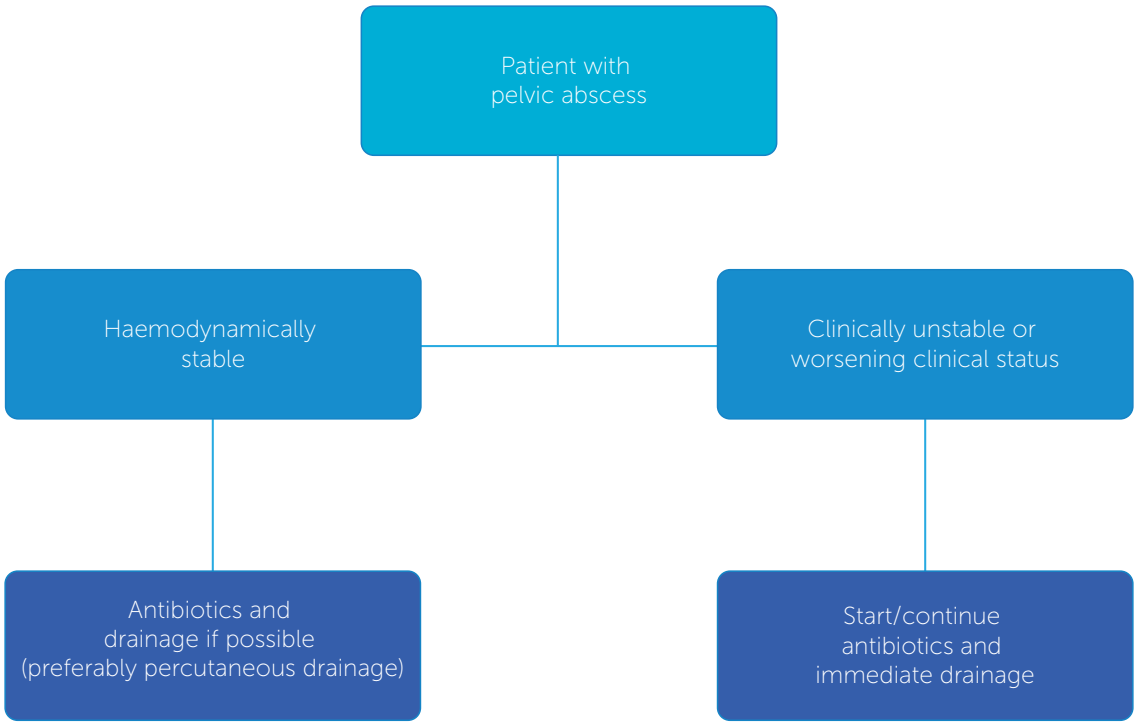

Figure 1. Guiding treatment for pelvic abscess.

laparoscopy, antibiotic prophylaxis is usually not required. For other procedures the evidence is less clear, and recommendations are based on expert agreement until further research evidence becomes available (Table 1).[1,6] Readers should note that these recommendations are correct for non-allergic patients, at the time of writing. Surgeons should consider each patient's individual requirements before prescribing the recommended antibiotic.

Dosage levels above need to be adjusted for the scenarios including obesity, lengthy procedures and excessive blood loss greater than 1500 mL.[1,7]

The patient's risk factors for postoperative infection are predictable and need to be taken into account prior to any surgery, such as smoking status, diabetes, obesity, nutritional status, co-existent infection at a remote body site, vaginal colonisation with micro-organisms and immunodeficiency.[1]

Other practices recommended to reduce the incidence of infection include:

1. Skin preparation: pre-operatively the entire body be washed with soap or an antiseptic agent the night prior. Intra-operatively skin cleansing with chlohexidene-alcohol is superior to povidone-iodine and iodine-alcohol.[7,8]
2. Hair should only be removed at or around the incision site if it will interfere with the operation, preferably with electric clippers. Patients should be advised not to shave the operative site themselves because shaving with a razor increases their risk of infection.[1,7,8,9]
3. Skin preparation: use an alcohol base agent, unless contraindicated.[1,8]
4. Vaginal preparation with either 4% chlorhexidene gluconate or povidone-iodine is acceptable.[1]

In the operating theatre, measures that have shown to reduce the risk of postoperative infections include: maintaining appropriate aseptic technique, preventing hypothermia, maintaining haemostasis while preserving adequate blood supply, gentle handling of tissue, removal of devitalised tissues, use surgical drains and suture material appropriately, keeping operating time to less than 149 minutes and minimising operative room traffic.[1,7]

Clinical features and management of gynaecological surgical site infection

Vaginal vault cellulitis

Vaginal cuff infection of the superficial tissues at the vaginal surgical margin after hysterectomy. Symptoms include increasing abdominal pain and purulent yellow vaginal discharge. Physical examination will review hyperaemia and oedema and tenderness out of proportion to what is expected. Treatment is outpatient oral antibiotic therapy with broad spectrum antibiotics, for example, amoxicillin/clavulanate 875/125 mg orally, twice daily.[10,11]

Superficial skin infection/cellulitis

Wound infection after hysterectomy arises in approximately 1.6 per cent of patients.[12] Patients can present with either cellulitis (erythema around the wound) or an incisional abscess (where purulent discharge arises from the incision itself). Diagnosis can be made by clinical examination of the wound, wound swab and wound aspirate (for microscopy, culture and sensitivity). If there is concern for a deeper collection, ultrasound can help exclude an abscess. With an incisional abscess, the wound should be opened and drained and examination of the fascial layer is vital to ensure it remains intact. Management will be antibiotic therapy; whether this is inpatient or outpatient will depend on patient's clinical status.

Pelvic abscess

Pelvic abscesses arise in less than 1 per cent of patients undergoing obstetric and gynaecological surgery. Patients present with fever, tachycardia, tachypnoea and lower abdominal pain, days to weeks

after the hysterectomy. On examination, there will be diffuse pelvic tenderness and sometimes a fluctuant mass may be palpable in the pelvis or vaginal apex. An elevated white cell count with leukocytosis (left shift) and raised inflammatory markers. Imaging will help delineate the abscess with CT (with contrast) having higher sensitivity than pelvic ultrasound. Treatment needs to be prompt and depends on patient's haemodynamic stability. One possible algorithm to guide treatment is outlined in Figure 1.[11,13]

Broad spectrum antibiotics need to be commenced according to current local guidelines or after consultation with infectious disease physicians. Intravenous antibiotic therapy should be continued until patient is afebrile for 48 hours, the abscess is reducing in size and the inflammatory markers and the patient are clinically improving. Percutaneous drainage can be performed via ultrasound or CT guidance. Patients who do not respond to appropriate antibiotic treatment require either percutaneous drainage (primary or repeat) or surgery.

Endometritis

Any procedure where there is instrumentation of the uterus has the potential for endometritis. The risk of pelvic infection following surgical termination of pregnancy varies from 0.5–3.5 per cent.[14,15] It is, however, relatively uncommon after simple gynaecological procedures such as IUD insertion, hysteroscopy and endometrial sampling.[16]

The patient with endometritis typically presents with fever, lower abdominal pain and foul-smelling vaginal discharge. On examination, the patient will have a high temperature, rapid pulse and lower abdominal tenderness. On vaginal examination, there may be foul-smelling vaginal discharge and bleeding. Vaginal swabs can be taken and sent for microbiology. Pelvic ultrasound may help differentiate retained products of conception from endometritis.

Conclusion

Postoperative infection is the most common complication of gynaecological surgical procedures. Practitioners should maintain a high level of suspicion of patients presenting with symptoms suggestive of SSI. Individual patient factors may substantially affect the course and treatment of SSI and it is important that prophylaxis, diagnosis and treatment is individualised for each clinical situation.

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Group B Streptococcus

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Streptococcus *agalactiae*, commonly referred to as Group B Streptococcus (GBS) is an encapsulated beta-haemolytic Gram-positive organism associated with invasive neonatal disease and maternal sepsis.

Epidemiology

It Is estimated that in 2015, 21 million live births worldwide were exposed to GBS through maternal colonisation, with an associated rate of 205 000 cases of early-onset disease and 90 000 cases of infant mortality under three months of age. Worldwide, at least 57 000 stillbirths, and up to 3.5 million preterm births per annum may be ascribed to GBS disease, though this is likely to be an underestimate, particularly in developing countries.[1] There is significant variation by geographical region, and of note, GBS rates are far lower in neighbouring South East Asian countries where Gram-negative pathogens, particularly *Escherichia coli* and *Klebsiella pneumoniae*, are the predominant cause of early-onset sepsis of the neonate.[2] GBS remains the most common cause of early sepsis of the neonate in Australia, with an incidence of 0.43 per 1000 live births, and mortality rate of 11 per cent.[3]

Clinical manifestations

GBS disease of the infant may be defined as early or late onset. Early-onset disease, occurring in the first six days of life, can manifest as sepsis, respiratory distress, pneumonia or meningitis, and is associated with colonisation of the maternal genitourinary and gastrointestinal tracts. Late-onset disease, occurring between 7 to 89 days of life, often presents with sepsis accompanied by bloodstream infection, meningitis and, in some cases, osteomyelitis, septic arthritis or skin and soft tissue infections. Late-onset disease is attributed to acquisition of GBS after birth. GBS disease of the infant has significant long-term morbidity, particularly if complicated by neurodevelopmental disability.[4] Maternal GBS disease with ascending infection causing fetal infection and chorioamnionitis is complicated by stillbirth and preterm birth. Although uncommon in developed countries, maternal GBS sepsis is associated with significant morbidity, prolonged hospital admission, including the need for intensive care supports and a longer infant admission in neonatal special care units.[5]

Prevention

Intrapartum antibiotic prophylaxis (IAP) reduces vertical transmission, with subsequent reduction in maternal and neonatal morbidity and mortality from invasive GBS disease. This strategy targets women with known GBS colonisation and/or the presence of risk factors including GBS bacteriuria, a previous infant with GBS disease, preterm labour, premature or prolonged preterm rupture of membranes, or maternal fever. Challengingly, up to 50 per cent of neonates with invasive GBS disease have no identifiable risk factors. The risk of early onset GBS varies according to IAP policy. Without an IAP policy, the risk of early onset GBS disease is 1.1 per cent. As IAP coverage increases, the risk of early onset GBS decreases in linear association. Based on regression modelling, the risk of early onset GBS is 0.3 per cent in settings with 80 per cent IAP coverage through universal screening programs, compared with 0.8 per cent in settings with 50 per cent coverage with clinical risk factor-based strategy.[6]

There is no international consensus on whether universal microbiological screening or risk-factor assessment is the superior approach to intrapartum antibiotic prophylaxis. The Australian Government Pregnancy Care Guidelines recommend either routine antenatal testing for GBS colonisation or a risk factor-based approach to prevention, depending on organisational policy.[7] The New Zealand Consensus Guidelines recommend a risk-based GBS prevention strategy as the most clinically and cost effective approach.[8] The RANZCOG guideline, updated in July 2019, recommends 'all maternity services should have an established plan for prevention of early onset GBS. Universal culture-based screening using combined low vaginal plus or minus anorectal swab at 35–37 weeks gestation, or 3–5 weeks prior to anticipated delivery in high-risk pregnancy, such as poorly controlled diabetes, multiple pregnancy, or a clinical risk factor-based approach, are both acceptable strategies for reducing early-onset GBS. Low vaginal and anorectal swabs for GBS screening should be incubated in enriched media to achieve acceptable sensitivities; and intrapartum antibiotic prophylaxis with intravenous

penicillin-G or ampicillin should be offered to all women at increased risk of early onset GBS'.[9]

Similarly, the US guidelines recommend universal microbiological screening and the UK a risk-factor based approach. The lack of consensus on screening relates to a lack of good-quality randomised controlled trials and conflicting evidence.[10] In the UK, the GBS3 trial is approved to commence in April 2020 with three investigation arms comparing rapid test in labour, 35–37 week swab and risk-factor based administration of intrapartum antibiotic prophylaxis.[11]

GBS can cause ascending infection, which is complicated by stillbirth and preterm birth. The pathogenesis for this is not well understood, but it is postulated that intrapartum antibiotic prophylaxis not only reduces colonisation and vertical transmission, but also possibly provides early treatment of fetal infection and chorioamnionitis. Intrapartum antibiotic prophylaxis only reduces early-onset GBS. It does not affect stillbirth or preterm birth rates and has not been shown to have a reduction in late-onset GBS disease.

Exposure to antimicrobials is not without risk. Previously undocumented penicillin allergy may result in intrapartum anaphylaxis, and the implications of broad-spectrum antimicrobial therapy on both the maternal and neonatal microbiome are yet to be fully understood. Initial concerns were raised that intrapartum antibiotic prophylaxis would lead to a rise in non-GBS early-onset sepsis, and an initial trend was seen in the US towards higher rates of Gram-negative early onset sepsis.[12] Longitudinal studies, however, have shown the rates of Gram-negative early onset sepsis have remained stable over time, and this continues to primarily affect very low birth weight preterm infants.[13] Antenatal GBS vaccines are in development and, if efficacious, may be a more successful prevention strategy than intrapartum antibiotic prophylaxis, one which could also reduce the rates of stillbirth, preterm birth and late-onset sepsis attributed to GBS.

Laboratory diagnosis

A major limitation of GBS screening and prevention programs is reliance on accurate laboratory detection of GBS carriage. Women typically collect a combined low vaginal and anorectal swab for testing at 35–37 weeks gestation. The addition of anorectal collection increases the sensitivity by up to 10 per cent and the use of selective enrichment broth, with incubation prior to testing, further improves the yield.

Culture-based methods involve subculture from broth onto selective chromogenic agar plates. These are incubated and growth of colonies are identified as GBS by morphology and confirmed by mass spectrometry. Culture provides reliable testing with standardised susceptibility-testing methods; however, the turnaround time may be up to three days.

Polymerase chain reaction (PCR) with nucleic amplification testing (NAT) assays targeting the CAMP factor or surface immunogenic protein genes of GBS is another approach to screening. NAT has superior sensitivity over culture for the detection of GBS, with the added benefit of shorter turnaround times. Traditionally, PCR testing has occurred in the laboratory, in batched runs, with a turnaround time of 24–48 hours from collection. Culture and PCR testing at 35–37 weeks' gestation will not detect the acquisition of GBS in the intervening period prior to delivery.

Point-of-care (POCT) intrapartum molecular screening is a newer technology that can provide qualitative analysis of the presence of GBS in the genitourinary and gastrointestinal tract at the time of delivery. The benefit of this is 24-hour access to a highly sensitive test, with real-time analysis of the presence of GBS. This is associated with significant decrease in the rate of early onset GBS disease and antibiotic use in neonates. Although POCT is significantly more expensive than traditional laboratory testing, these costs can be offset, at least in part, by the reduction in early onset GBS incidence and disease treatment costs.[14]

PCR testing provides no information about antimicrobial susceptibility, an important disadvantage in the setting of maternal beta-lactam allergy. GBS is almost universally susceptible to penicillin/amoxicillin and cefazolin. In the setting of allergy, the Australian Guidelines recommend intrapartum erythromycin or clindamycin. Australian antibiogram data demonstrate erythromycin resistance in 6.4 per cent and clindamycin resistance in 4.2 per cent of GBS isolates.[15] Thus, antimicrobial susceptibility testing remains essential for pregnant women with known severe and immediate IgE mediated beta-lactam allergy such as anaphylaxis. If susceptibility results are not known and the patient is penicillin allergic, intravenous vancomycin is recommended due to increasing GBS resistance to clindamycin.

Other prevention strategies may include development of a vaccine against GBS, overcoming some of the limitations of intrapartum antibiotic prophylaxis coverage, and lack of efficacy in reduction of stillbirth and late-onset GBS. Future developments may incorporate common resistance mutations in POCT, making this a possible screening modality for the penicillin-allergic patient.

Conclusion

Early-onset GBS is an important cause of neonatal sepsis, and intrapartum antibiotic prophylaxis reduces this burden. What remains to be determined is the best strategy for defining who should receive intrapartum antibiotics. Intrapartum antibiotic prophylaxis does not affect stillbirth rates and has not been shown to have a significant reduction in late onset GBS. Prevention by vaccination is in development and may be a future possibility.

Key points

- Early-onset GBS disease is an important cause of neonatal sepsis
- All maternity services should have an established plan for prevention of early-onset GBS
- Document 'severe penicillin allergy' on the pathology request form to facilitate antimicrobial susceptibility testing
- Point of care testing is a promising, but expensive, technology for intrapartum detection of GBS

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Ogilvie's syndrome: a fourth trimester reality

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Acute colonic pseudo-obstruction, or Ogilvie's syndrome (OS), is a rare condition first described by Sir William Ogilvie in 1948 and characterised by massive colonic distension in the absence of mechanical obstruction.[1] The overall incidence of OS is low (100 per 100 000 admissions), but outcomes can be life changing.[2] OS is rapidly progressive and, if left undiagnosed, can lead to poor outcomes such as bowel ischaemia or perforation followed by sepsis, which carries a mortality rate of 44 per cent in perforated and 8 per cent in nonperforated group.[5,14]

The condition usually arises in patients with underlying predisposing factors, such as severe illness, electrolyte imbalance, use of narcotics, and surgery. It is rarely seen in young women. The most common predisposing factor in this age group is pregnancy, especially post lower segment caesarean section (LSCS). OS has also been reported after normal vaginal delivery.[4,9]

With increasing LSCS rates in Australia, from 19 per cent in 1993[6] to 33 per cent in 2013,[7] the incidence of post-operative complications is also rising. OS can affect one in 1500 deliveries, with significant morbidity.[9] Following an unusually high number of cases of OS in postpartum patients reported to the Consultative Council on Obstetric and Paediatric Mortality and Morbidity (CCOPMM) within the last year, Safer Care Victoria posted an alert in early July 2019 urging clinicians to be vigilant for the signs of this rare condition. In this article, the pathophysiology, epidemiology and treatment options are discussed in association with pregnancy and postpartum period.

Pathophysiology

The pathophysiology of OS is poorly understood and is often multifactorial. Current theory dictates that OS results from an imbalance in autonomic innervation to the colon.[2,14] Various theories have emerged as to the relative overrepresentation of OS in obstetric patients. Some authors have suggested it results from compression of the parasympathetic plexus by the gravid uterus, others that mechanical obstruction of the recto-sigmoid colon occurs as the uterus contracts back into the pelvis. Resting sympathetic tone is increased in the third trimester of normal pregnancy and progesterone, glucagon and prostaglandins, all associated with altered colonic tone, circulate at high levels around the time of delivery.[8] The transition point in OS usually occurs at the splenic flexure, an area where there is a transition of both parasympathetic and sympathetic innervation.[9]

Epidemiology

While OS has been reported after normal vaginal delivery, caesarean section is the single most important risk factor in an obstetric population as 92 per cent of cases reported since 2002 occurred after caesarean section.[10] In particular, emergency caesarean delivery carries the greatest risk.

We have long recognised the inhibitory effects of opiates on gut motility. Given opiate analgesia has been implicated in the pathogenesis of postoperative ileus and bowel dysfunction, it seems likely that opiates contribute to postoperative rates of OS.[12] Use of anticholinergic medications and calcium channel blockers have also been suggested as risk factors.[13]

Diagnosis

Clinical presentation can include abdominal distension (89 per cent), abdominal pain (60 per cent) and vomiting (27 per cent). Constipation is an infrequent feature (15 per cent) and is not required for diagnosis and, conversely, diarrhoea was present in a small number of cases. Bowel sounds are present in almost 90 per cent of patients.[3] Fever, peritonitis and leukocytosis are more common in individuals with perforation or ischemia, but can occur in the absence of these conditions. A perforation and spillage of bowel contents can lead to life-threatening sepsis.

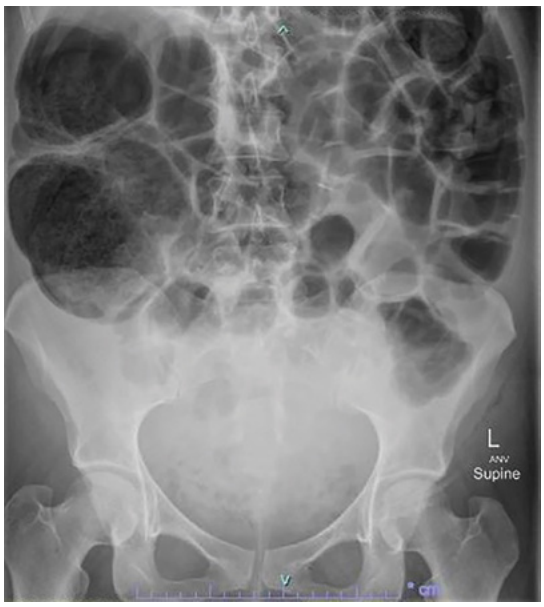

Figure 1. Abdominal radiograph showing dilated colon consistent with OS in a patient post caesarean section.

Presentation may be as early as six hours post-delivery with the majority between days 1–5.[10] OS should be considered in any woman presenting with progressive abdominal distension up to 12 days postpartum.

Plain film imaging demonstrates colonic distension, especially of the caecum and ascending colon. Free air may be present if perforation has occurred, (Figure 1).

Diagnosis of OS mandates exclusion of mechanical obstruction for which CT, with or without rectal contrast, is widely considered the modality of choice with a sensitivity of 91 per cent.[2,5,14] Colonoscopy may be used both as a diagnostic and therapeutic tool for the exclusion of mechanical bowel obstruction and decompression.[5]

Management

Conservative management is recommended for patients without evidence of perforation or ischaemia and a caecal diameter less than 12 cm.[2,5,14] Early consultation with a senior colleague and surgical specialist is highly recommended. This approach mainly involves a trial of bowel rest, nasogastric tube insertion for symptomatic relief, hydration and correction of electrolyte imbalance, early mobilisation, cessation of contributory medications (opiates, calcium channel blockers, anticholinergics) and treatment of underlying infection. Lactulose should be ceased as this can worsen colonic distension. It is reasonable to continue conservative management for a period of 48–72 hours with frequent clinical review and serial plain radiographs every 12–24 hours.[5,13,14]

Early initiation of the Enhanced Recovery After Surgery (ERAS) Program has also shown that a marked reduction in opioid use, both as an inpatient and outpatient, is associated with overall improvement in pain scores post caesarean.[4]

Either pharmacological or colorectal decompression is considered if there is no response to 24–48 hours of conservative management or if caecal diameter reaches more than 12 cm without signs of peritonism and mechanical obstruction has been ruled out. Neostigmine is the only pharmacological treatment for OS. It is an acetylcholinesterase inhibitor that mimics the parasympathetic nervous system and causes colonic decompression.[9] Given its cholinergic side effects, including bronchospasm and bradycardia, caution should be taken in patients with asthma and cardiac conduction diseases. A dose of 2 mg is delivered by slow intravenous (IV) injection over five minutes. IV administration should be in a closely monitored environment where continuous cardiac monitoring is possible and atropine should be drawn up and readily available.[9] In cases where there is initial partial response or recurrence after initial response, a repeat dose may be appropriate, although no consensus has been reached on the optimal timing of repeat dosing.

Subcutaneous administration (0.5 mg twice daily) has recently shown to have a similar success rate of 93 per cent when compared to IV, with no reported adverse events and mitigates the need for continuous telemetry and high-dependency units (HDU).[12] Given its relatively short half-life, and its one-off bolus dosing regime, neostigmine is unlikely to affect breastfeeding.[9]

As neostigmine requires HDU monitoring, colonoscopic decompression appears to be a reasonable alternative and, in some centres, may be more readily available depending upon the skillset of the surgical team. Colonoscopic decompression has proven successful in approximately 88 per cent of cases, but is associated with a perforation risk of 2 per cent.[5]

There are few anecdotal case reports of successful treatment of OS with erythromycin, a macrolide antibiotic known to stimulate gastric and small bowel motor activity by binding to the motilin receptor and inducing smooth muscle contraction through a nifedipine-sensitive mechanism. Its short half-life and the rapid onset of tachyphylaxis restricts its broad application in treatment of

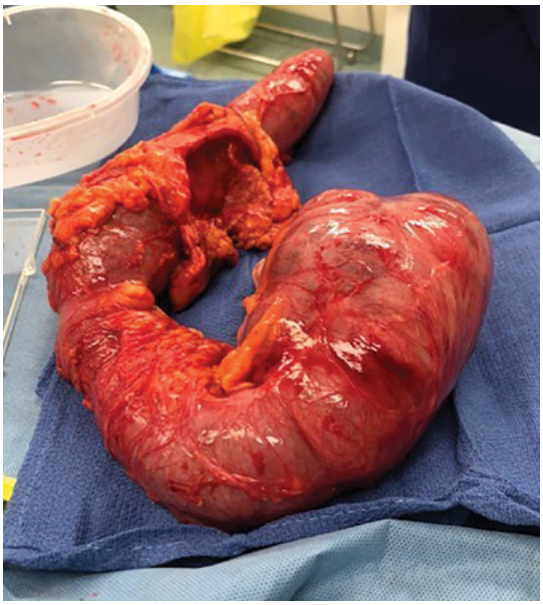

Figure 2. A postpartum caesarean patient required a subtotal colectomy.

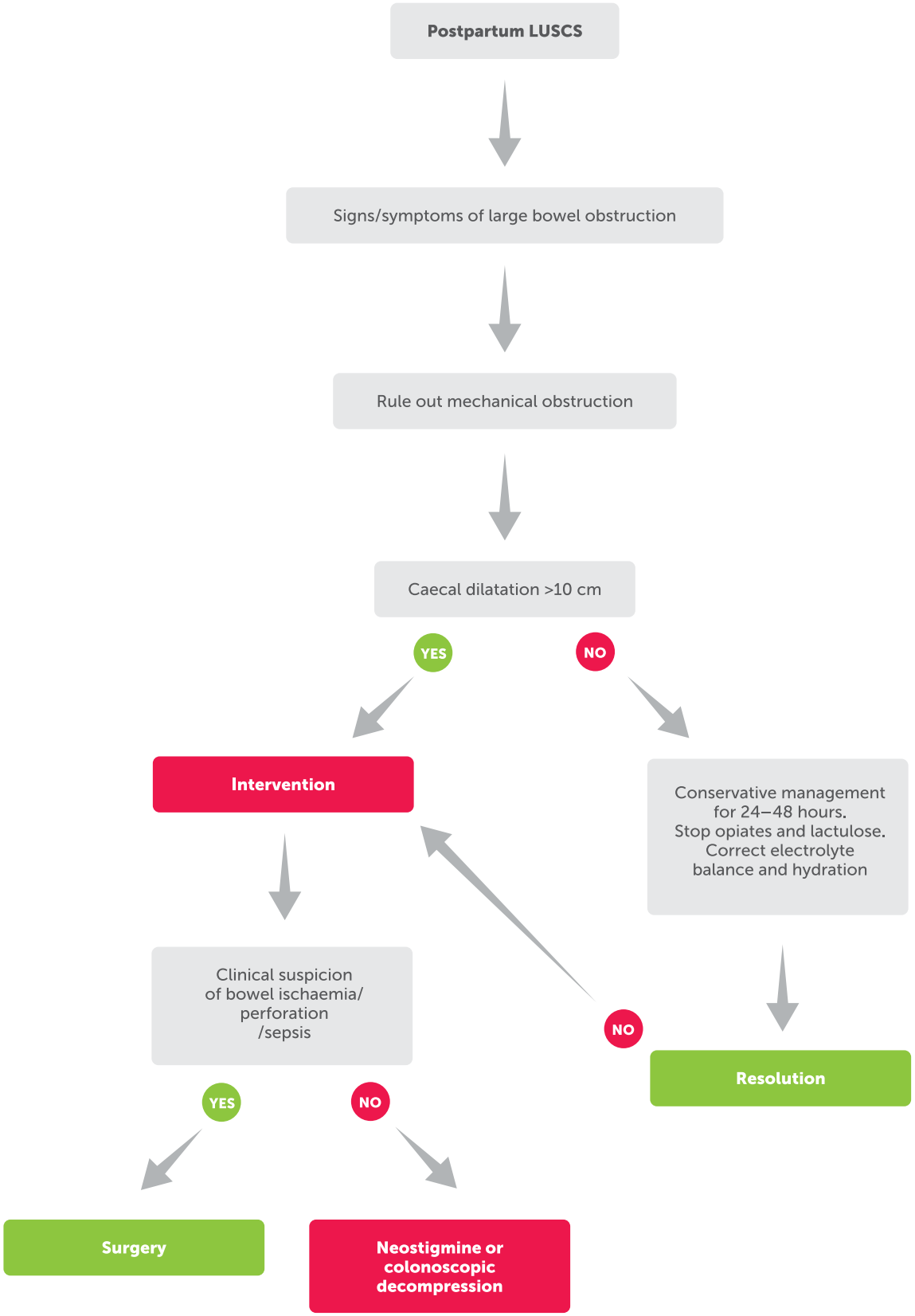

Figure 3. Flow chart for postpartum management of OS.

OS. There is also insufficient data to suggest erythromycin routine use in adults.[15]

Surgical intervention is recommended where OS is complicated by ischaemia/perforation or in cases refractory to prior treatment over the course of 2–3 days[5,9,14] (Figure 2).

We have designed an algorithm to facilitate an earlier recognition of this rare postpartum condition and further management (Figure 3).

Conclusion

OS is a rare postpartum complication with a high morbidity secondary to bowel ischemia, perforation and sepsis. The ERAS program appears promising in improving the surgical outcome in patients with elective caesarean delivery by reducing both inpatient and outpatient use of opioids. Timely recognition of the syndrome, cessation of opioids and lactulose, early consultation with the acute general surgical team, and prompt intervention is necessary to improve outcomes in young postpartum population.

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Q&A

For the broader *O&G Magazine* readership, balanced answers to those curly-yet-common questions in obstetrics and gynaecology.

Q A patient asks about her reproductive potential: when and how should I recommend oocyte cryopreservation?

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A

Australian women now have access to oocyte cryopreservation (egg freezing) as a fertility conservation technique. This is an expanding area of assisted reproductive technology and clinicians are likely to see patients asking about its benefits and limitations. The recent ANZREI consensus statement on elective oocyte cryopreservation is an excellent resource clearly stating the evidence basis and providing practice guidelines.[1] It is recommended reading for practitioners to assist in counselling women.

As women age, oocytes accumulate more DNA damage from daily living activities and their quality declines. This is reflected in lower fertility rates and higher rates of miscarriage as women age.[2] Because many women may not be in a position to reproduce when their natural fertility rates are highest, educating women about when and how their fertility declines is important. Such information enables better decisions about possible family size and postponement of child bearing. Additionally, some women will decide not to have children, use donor eggs or adopt if natural conception is not possible. Access to international donor sperm banks now allows single women or same sex couples the option of conception.

Oocyte cryopreservation is a way for women to freeze their own eggs for a later date; however, it is not a guarantee of live birth and women exploring this option need to be aware of its limitations. Women who embark on a course of oocyte cryopreservation need a baseline assessment of fertility and a discussion about the expected number of eggs to be frozen per cycle. There is no number of frozen eggs that guarantees a live birth and women should be counselled regarding success rates. The number of cycles to be undertaken will be different for each woman depending on age, egg reserve, side effects, cost and desired family size.

All women presenting to women's health clinicians, but particularly those in their late 20s to early 30s seeking fertility advice, should be asked about their menstrual cycle, use of contraception and future pregnancy plans.[3] Clinicians should screen women wishing to delay fertility for any underlying disorders that specifically affect fertility, such as polycystic ovary syndrome, endometriosis or fallopian tube disease. This is also a good time for these women to optimise other systemic health conditions that may affect fertility, such as auto-immune conditions, and document any previous gynaecological surgery (previous salpingectomy for ectopic pregnancy, excision of endometriosis or dilatation/curette). Clinicians should reinforce positive lifestyle habits such as, quitting smoking and illicit drug use, reducing alcohol/caffeine consumption and optimising diet and exercise. Clinicians should obtain a family history including premature ovarian insufficiency and hereditary genetic conditions, and review of medications. For women at risk of low ovarian reserve, reduced fertility, or for those considering elective egg freezing, an assessment of ovarian reserve should be requested, including anti-Müllerian hormone (AMH) level and pelvic ultrasound.

Predicting the rate of reproductive decline in an individual woman is difficult and it should be noted the isolated use of AMH, antral follicle counts and follicle stimulating hormone (FSH) for predicting conception and live birth is controversial.[4] However, AMH, antral follicle counts and FSH levels are used to determine gonadotropin dose for ovarian stimulation and are relatively reliable in predicting oocyte yield during an IVF cycle. Women must have realistic expectations about the number of oocytes required to potentially produce one live birth. Unavoidable oocyte attrition occurs during the process of egg collection, thawing and fertilisation. Intracytoplasmic sperm microinjection (ICSI) is required to fertilise frozen oocytes, due to the outer cumulus layer of the egg being stripped prior to the freezing process. This has additional costs and fertilisation rates are dependent on sperm and egg quality. Embryologists may not deem all eggs collected during an egg pick up to be mature (metaphase II) for freezing purposes; if 10 are collected, only seven may be 'mature' to freeze. When eggs are frozen, only 90 per cent are likely to survive vitrification and the warming process.[1] Only 70–85 per cent of eggs that survive warming will fertilise with sperm through ICSI.[1] Of the eggs that fertilise successfully and form day 5–6 blastocysts, the live birth rate is approximately 29 per cent per embryo transferred.[5] The live birth rate per egg frozen is related to the patient's age and egg

quality at time of freezing and is between 5–8 per cent per egg.[6] Thus, women in their early 30s are the optimal candidates for oocyte cryopreservation and it is best performed before the age of 35 years.[1]

Financial expenses should be disclosed prior to undertaking elective oocyte freezing – particularly the likely need for multiple cycles and the cost of ongoing egg storage. Potential risks must be discussed, including ovarian hyperstimulation syndrome, damage to surrounding structures during oocyte retrieval (bowel, bladder and vessels), and most importantly, that oocyte cryopreservation does not guarantee a live birth. Women should also be aware that studies currently demonstrate no increase in miscarriage or congenital malformations in pregnancies achieved via frozen oocytes.

Now that Australia has its first guideline on elective oocyte cryopreservation, clinicians are likely to see their role expand as more women pursue the technology that enables them to preserve their reproductive potential. To optimise this, clinicians should clearly set out what the process entails, discuss the fact that more than one cycle may be needed and give advice regarding general health measures for fertility, such as to stop smoking and maintain a healthy BMI. With the above information, it is hoped women seeking fertility advice can make empowered decisions about their fertility choices and realistic reproductive potential.

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Pelvic inflammatory disease: a review

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Clinical scenario: A 25-year-old woman presents to the emergency department with lower abdominal pain and a three-day history of abnormal discharge. She has no significant medical history and uses a Mirena for contraception. On examination she is afebrile, with a heart rate of 80 and blood pressure at 124/60. She is tender in both adnexae and has cervical motion tenderness. Her bloods show elevated white cells and neutrophils, and a pelvic ultrasound is normal.

Pelvic inflammatory disease

The above scenario demonstrates a common presentation of pelvic inflammatory disease (PID). PID is an infection-induced inflammation of the upper female genital tract. Infection generally spreads from the lower genital tract to the pelvis. STIs, including chlamydia and gonorrhoea, are implicated in PID; however, other vaginal bacteria can also cause pelvic infection. PID is commonly a polymicrobial infection. In many instances, a single causative organism is not isolated and the absence of a pathogen does not rule out the diagnosis of PID.

Although mortality from PID is rare, the sequalae of infection and inflammation may be serious. Diagnosis relies on a high index of clinical suspicion as symptoms and signs can be subtle and definitive testing for lower genital tract organisms can take time. Early treatment is necessary to prevent long-term consequences, such as infertility and pain. Antibiotic treatment is therefore commonly commenced based on clinical findings alone. In summary, in women with the possibility of PID as their diagnosis, it is prudent to be suspicious and treat early.

Risk factors

Disruption of the cervical epithelium and usual cervicovaginal pH and microbial environment allow lower genital tract microbes to ascend and cause infection and inflammation in the upper genital tract. This disruption may be caused by sexually acquired infections, vaginal microbial imbalances, such as bacterial vaginosis (BV), or mechanically via instrumentation, surgery or pregnancy-related procedures.

Microbiology

The majority of acute PID is caused by sexually acquired infections, such as *Chlamydia trachomatis, Neisseria gonorrhoea* and *Mycoplasma genitalium*, and bacterial vaginosis-related organisms, such as the bacteroides species, *Mycoplasma hominis and Ureaplasma urealyticum*. Additionally, 15 per cent of acute PID is related to bowel or respiratory organisms that have colonised the lower genital tract, such as *E. coli*, Group B Streptococcus, *Haemophilus influenza and Streptococcus pneumoniae*.[2]

Chlamydia is the most common sexually transmitted cause of PID, and approximately 15 per cent of women with either chlamydia or gonorrhoea infections go on to develop PID.[3] The reason that progression to PID occurs for some women and not others is unclear.

BV is a polymicrobial clinical syndrome caused by a change from predominantly lactobacillius organisms to other organisms, including a high number of anaerobes and biofilm formation on the vaginal wall. The pH of the vagina rises and local enzymes that degrade cervical mucous are produced. BV is not sexually transmitted, but may be acquired through sexual activity. Women with BV are more likely to develop PID after termination of pregnancy and IUD insertion, and are 2–3 times more likely to contract other STIs, such as chlamydia and gonorrhoea.[1,2,4]

Mycoplasma genitalium is an established cause of PID and understanding its role is rapidly evolving. Clinical features and risk factors are similar to chlamydia. Patients with *Mycoplasma genitalium* should be referred to a sexual health physician and require additional antibiotic management to the usual PID regimen, with consideration to high rates of antibiotic resistance.[5]

Table 1. Risk factors for PID.[2]

Sexual	Non-sexual
Age <30	IUD insertion in the past 6 weeks
Recent change in sexual partner	Termination of pregnancy
Multiple sexual contacts	Postpartum state
Previous STI	Upper genital tract instrumentation
	IVF

Clinical management of PID

Women presenting with PID may report pelvic or lower abdominal pain, abnormal vaginal discharge, intermenstrual or postcoital bleeding, dyspareunia, dysuria and right upper quadrant pain with a pleuritic nature.

On physical examination, pelvic tenderness and evidence of lower genital tract inflammation together are highly suggestive of PID. Bimanual examination is necessary to check for cervical motion tenderness, adnexal tenderness and masses. The absence of pain has a high negative predictive value. Right upper quadrant tenderness is suggestive of Fitz-Hugh-Curtis Syndrome, a perihepatitis involving inflammation of the liver capsule and peritoneal surfaces, present in approximately 10 per cent of women with acute PID.[6]

Speculum examination allows assessment of the cervix; mucopurulent discharge supports the diagnosis. Cervical friability with contact bleeding also suggests cervicitis. Fever can occur, but systemic illness is not a necessary feature of PID.[2]

Differential diagnosis of PID includes ectopic pregnancy, appendicitis, UTI, complications of an ovarian cyst such as rupture or torsion, endometriosis, irritable bowel syndrome or diverticular abscess.

Investigations

1. **Endocervical swab for nucleic acid amplification testing**
- Testing for chlamydia, gonorrhoea and *Mycoplasma genitalium*
- Urine protein/creatinine ratio for chlamydia is less sensitive than endocervical swab
- Negative sexually acquired infection screen does not exclude PID

2. **High vaginal swab**
- Testing for candida, bacterial vaginosis and trichomoniasis

3. **Bloods**
- FBC: may show elevated white cell count and neutrophilia
- CRP: Elevated inflammatory markers support the diagnosis but are a non-specific finding

4. **Pelvic ultrasound**
- Check for tubo-ovarian abscess
- Rule out other differential diagnoses, such as ovarian cyst events or appendicitis
- May be normal in PID

5. **Rule out concurrent infection and other diagnoses**
- Pregnancy test
- HIV and syphilis serology
- Selective hepatitis B/C screening based on immunity and risk factors

Laparoscopy and endometrial biopsy are not routinely performed for diagnosis of PID.

Inpatient or outpatient management

Hospital admission for intravenous antibiotics, observation and possible surgical intervention should be considered if:
- there is diagnostic uncertainty
- there is clinical failure of, or inability to, tolerate oral therapy
- symptoms are severe or there are signs requiring inpatient treatment
- tubo-ovarian abscess

Management of PID

Antibiotic treatment should start with the provisional diagnosis of PID, without waiting for test results, in women with lower abdominal pain plus cervical, uterine or adnexal tenderness. Pain can be severe, and patients may need admission for analgesia.

Antibiotic choice and dose should be guided by current local guidelines and patient factors. Combinations of a cephalosporin, metronidazole, azithromycin and doxycycline are commonly used.

It is recommended that sexual contacts in the last three months should have a sexual health check and appropriate treatment. If an organism is identified, contacts should be traced and treated as per the sexual health guidelines for that organism. Advise women to avoid intercourse for two weeks after commencing treatment, and one week after contact treatment.

Complications

Complications of PID include tubo-ovarian abscess, infertility, ectopic pregnancy and chronic pelvic pain. Long-term consequences are more likely in women with recurrent or severe PID; however, they may occur despite early diagnosis and successful treatment.

Tubo-ovarian abscesses can be managed either conservatively with intravenous antibiotics, by interventional radiology-guided drainage, or, surgically. There is no consensus on when to attempt conservative versus surgical management, and conservative management will fail in 20–30 per cent of patients. Larger abscesses are less likely to respond to antibiotics alone. Abscess size greater than 5.5–6.5 cm predicts failure of conservative management.[8,9] In women desiring future fertility, early operative management improves future pregnancy outcomes. Early surgical management should also be considered for post-menopausal women who may have associated malignancy.

Infertility due to PID is caused by tubal inflammatory damage, loss of ciliated tubal epithelium and adhesions causing partial or total tubal obstruction. There is higher risk of infertility if PID is caused by chlamydia, if treatment is delayed, in recurrent PID and after severe disease. Tubal damage also increases the risk of ectopic pregnancy.

In the case of PID in the presence of an IUD, the routine removal of an IUD does not hasten clinical resolution;[2] however, removal should be considered if there is no clinical improvement in 48–72 hours.

Summary

PID is a polymicrobial upper genital tract infection that may be sexually or non-sexually acquired. High clinical suspicion is required in women presenting with potential PID, although some may be asymptomatic or have mild symptoms. Treatment should be commenced based on clinical findings as delay increases the risk of long-term negative sequelae.

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Influenza in pregnancy

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Influenza in pregnancy poses significant risks to pregnant women and their babies. In 2009, there were four maternal deaths due to influenza in New Zealand.[1,2] Influenza is a potentially preventable disease with free vaccination available to pregnant women in Australia and New Zealand. In New Zealand there is a vocal anti-vaccination lobby and as health professionals it is our role not only to understand the disease process, understand the vulnerability of pregnant women and know how to recognise, diagnose and treat influenza but also to promote vaccination and enable women to easily access it.

Long ago

One hundred years ago, the Spanish Flu spread throughout the world. Commonly referred to as the black flu due to the bodies becoming so cyanosed, they would turn black upon death. It resulted in the deaths of nearly 60 million people, three times that of World War I.[1]

In the October of 1919, Marlartic reported in the *Lancet* on the maternity experience in Paris. Influenza in pregnant married women had resulted in a 46 per cent maternal mortality. In the 73 per cent of women that had pulmonary complications, 17 per cent resulted in premature delivery, with a perinatal mortality rate of 50 per cent. Simply summarised, 'Woe unto them that are with child'.[2]

PREGNANCY AND INFLUENZA.

THE fatality of influenza among young married women was a matter of common remark in the second wave of the great epidemic in this country. Figures are now available bearing on the subject in Paris. In his thesis on influenza complicated by pregnancy Malartic (*Thèses de Paris*, 1918–19, No. 286) states that the mortality during the recent epidemic among pregnant women at the Paris Maternité Hospital was 46 per cent. Pulmonary complications were extremely frequent, being observed in 73 per cent., and the mortality among cases with these complications was 58·4 per cent. as compared with a recovery rate of 95 per cent. among women in whom the lungs were not affected. Premature delivery, which occurred in 17 per cent. of the cases with pulmonary complications, proved fatal in six out of 11 cases, or about 50 per cent.; miscarriage, which occurred at an earlier stage of pregnancy in 6 per cent. of the cases with pulmonary complications, proved fatal in three out of four cases, or 75 per cent. "Woe unto them that are with child," might have been written of this influenza epidemic.

Figure 1. Excerpt from Lancet, 1919.[2]

This was the first recognition that influenza complicated by pregnancy carried extra risk for mother and child.

Not so long ago

Ten years ago, in 2009, the H1N1 influenza spread throughout the world, requiring the World Health Organization to announce a maximum, level 6, Global Pandemic Alert.[3]

Data collected during this period furthered the knowledge that pregnant women were at increased risk of complications from influenza.

Pregnant women were three times more likely to be hospitalised than the general population and they accounted for 5 per cent of deaths, despite only representing 1 per cent of the population.[4] Maternal mortality was estimated at 6.9 deaths per 100 000 maternities in New Zealand and Australia during this time.[5]

Babies of the mothers who were severely affected had an increased risk of fetal growth restriction, spontaneous abortion, preterm delivery and subsequent perinatal mortality.[4]

Prior to 2009, serious concern for pregnant women with influenza, was only considered if they also had another risk factor such as asthma, smoking, obesity or diabetes. After 2009, it was now recognised that pregnancy alone is a significant risk factor and prompt treatment should be initiated for all.[4]

Data collected during this period also showed pregnant women of Aboriginal, Torres Strait Islander, Māori and Pacific descent are at higher risk.[6]

Current day

New Zealand and Australia continue to see high numbers of pregnant women admitted to ICU with seasonal influenza during the months of May to October each year.

Table 1. Influenza vaccination rates in pregnancy.

USA (2017–2018)	49.1%
England (2016–2017) England (2017–2018)	44.9% 47.2%
South Korea (2014)	37.8%
Australia (Vic 2015–2017)[9]	39%
New Zealand	Not reported

Box 1. Increased risk of influenza in pregnancy.

- Pregnant women are at higher risk of hospitalisation from influenza
- Pregnant women with comorbidities such as asthma, diabetes and obesity are at further increased risk of complications
- Aboriginal, Torres Strait Islanders, Māori, and Pacific Islanders are at further increased risk of complications
- Influenza in pregnancy complicated by pneumonia is associated with significant risk to both mother and fetus
- Complications from influenza increases with gestation and continues into the postpartum period
- Maternal hyperthermia is associated with congenital anomalies, but can be mitigated by antipyretics
- Influenza does not cross the placenta

Complications include pneumonia, renal failure and encephalopathy, requiring admission to intensive care units (ICU), intubation and occasionally even extracorporeal membrane oxygenation. Their ICU stays are usually longer than non-pregnant women and preterm surgical deliveries are performed to relieve the systemic burden and aid recovery.[5]

Increased risk to pregnant women

All medical personnel involved with the care of pregnant women need to be aware of the risk of influenza to all pregnant women.

The reason influenza is more severe in pregnancy is likely due to a combination of the immunological shift from a cell-mediated response to an antibody-mediated one and physiological cardiorespiratory changes (such as reduced functional residual capacity), which worsens throughout pregnancy.[7]

Given the length of the influenza season and that there is risk at all stages of pregnancy, these messages are relevant to every pregnancy.

Safety and effectiveness of vaccination

Vaccination is well established to be safe and effective in pregnancy.[8] Pregnant women in Australia who received an influenza vaccination in 2012 were 81 per cent less likely to attend an emergency department with an acute respiratory infection, and 65 per cent less likely to be hospitalised.

Most convincing may be the fact that maternal vaccination allows transplacental transfer of IgG, giving the newborn immunological protection for the first six months of life, at a time when they are too young to be immunised.

'Not only for themselves, but also for their unborn child'. M Knight.[5]

Unfortunately, vaccination rates in Australia and New Zealand continue to be poor (Table 1).

Influenza vaccination is free to all pregnant women in New Zealand and Australia, but the usual barriers to healthcare still exist (lack of awareness, information, time, language barriers or lack of adequate counselling).

In 2016, Waitakere Hospital, NZ, a vaccinator was situated in antenatal clinic. This significantly increased immunisation rates demonstrating that pregnant women are excepting of vaccination if given the opportunity. Obstetric departments should campaign to their managers to provide funding for an opportunistic vaccinator to be in antenatal clinic during these months of the year, as prevention is truly the best option.

The cost-benefit has been estimated to prevent one to two hospitalisations per 1000 women vaccinated during the second or third trimester.[10]

Safety and benefit of the use of antiviral treatment

Hospitalised pregnant women who receive a neuraminidase inhibitor within the first two days of onset of symptoms had 84 per cent reduction in ICU admission and were one fifth as likely to die than women who were treated later or not at all.[11]

General advice

Hand hygiene and cough etiquette should be reiterated. Breastfeeding should be encouraged given the immunological benefits passed on from the mother in her milk.

Call to action

Let us not be idle. We now live in a time where women are more frequently accessing medical advice from online social sources than from a health professional. We need to go to women with the health messages they need.

Box 2. Transmission of influenza.

Influenza
Contagious viral respiratory tract infection
Method of spread
Droplets and surface contamination
Incubation period
1–7 days (usually 1–3 days)
Infectious period
1 day prior to symptoms
until day 5 in adults
until day 7 in children (note: can be until day 21)

Box 3. Influenza vaccination in pregnancy.

Influenza vaccine:

- Can be given at any gestation of pregnancy
- Takes 2 weeks to begin to be effective
- Is, at best, only 60% effective – if a woman has symptoms of influenza, she should present to a doctor, even if she has been vaccinated
- Gives immune benefit to the newborn for the first six months of life

Box 4. Antivirals for influenza in pregnancy.

Neuraminidase inhibitors:
- Are safe in pregnancy
- Should be started before/despite lab results
- Are most effective in pregnancy when started within 48 hours of symptoms starting
- Still have benefit when given after 48 hours, therefore should be started anyway
- Should be given to women with influenza symptoms, even if she has been vaccinated, as vaccination is only 60% effective
- Will benefit women up to two weeks postpartum
- Has very low placental transfer of 1–14% of maternal concentration

Rx: Oseltamivir 75 mg BD for five days

We need to get social media savvy; use our Twitter accounts, practice's website and Facebook pages and share when the flu season has begun and the benefits of vaccination.

Prevention is where we are going to win the fight with influenza in pregnancy, and education of the public is how we are going to achieve it.

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Case reports

Group A Streptococcus: the master of disguise

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This case demonstrates the need for prompt, decisive care in a situation where a previously well, young, new mother becomes acutely and life threateningly unwell. The presence and involvement of senior clinicians at all stages allowed for confidence in adopting a conservative approach and avoiding a laparotomy, which may have added to risk. A prompt examination under anaesthesia with the assumption of, the very much more common, retained products as an aetiology of postpartum haemorrhage is a safe approach given the lack of specificity of ultrasound in excluding this in the immediate puerperium, and even had sepsis been suspected at that stage, it would have been important to exclude these were underlying. The postpartum haemorrhage in this situation was due to sepsis, but I would highlight the addition of the antifibrinolytic tranexamic intravenously to uterotonics in the management of any significant postpartum haemorrhage.

Good interdisciplinary communication aiding decision making and ease of access to intensive care support potentially all contributed to the prevention of the tragedy of a maternal mortality.
– Dr Rosemary Reid

A 28-year-old woman, gravida five para four, presented to the emergency department (ED) 24 hours after a normal vaginal delivery with heavy vaginal blood loss and increasing abdominal pain. She reported to have soaked five maternity pads. The estimated blood loss at time of delivery was 450 ml and a second-degree tear was repaired at the time. She attended ED at 11:00 via ambulance and was assessed in ED by gynaecology: heart rate 135, blood pressure 140/88, respiratory rate 20, saturations 99 per cent, apyrexial. Examination revealed heavy vaginal bleeding and a high tender uterine fundus well above the umbilicus. She required high doses of intravenous fentanyl for her pain. A Foley catheter was inserted into the bladder. She was given intramuscular syntometrine, intravenous tranexamic acid, cefuroxime and metronidazole, along with misoprostol rectally and an oxytocin infusion. With a high fundus ongoing vaginal loss, tachycardia and high analgesia requirements, the working diagnosis was of postpartum haemorrhage secondary to retained tissue and she was consented for an examination under anaesthetic (EUA). No imaging was performed prior to transfer.

Bloods: Hb 103, WCC 6.1, CRP 77.

She was transferred to the operating theatre and was given a general anaesthetic. The EUA was performed by a registrar with senior medical officer supervision (SMO); the perineal sutures were intact, the uterus was distended but only a small amount of clot found in the uterus. With fundal massage, the uterus contracted and was below the umbilicus at the end of the procedure.

In recovery, she had ongoing abdominal pain with increasing severity and ongoing tachycardia of 140. Intravenous fentanyl, morphine and ketamine was given. On palpation of the abdomen her fundus was at the umbilicus and she was peritonitic. The question was raised of an alternative diagnosis and a CT scan was requested, which showed mild to moderate intraperitoneal free fluid and diffuse periportal oedema, an enlarged uterus with a trace of endometrial fluid and gas which correlated with recent postpartum status and EUA, but no definite cause for her symptoms found. A transabdominal ultrasound in recovery also did not add to the diagnosis.

At 17:20 she was reviewed by an O&G SMO, the cause for her symptoms was still unclear and a surgical review was requested with no additions to the management plan. In the evening, she developed increasing oxygen requirements, a chest x-ray showed bilateral lower zone atelectasis.

Point of care haemoglobin at this time was 93.

She had ongoing diffuse abdominal pain with signs of peritonitis. A further surgical review was requested, it was felt appropriate investigations had been performed and no surgical cause had been identified.

At this point, the blood cultures taken in ED came back positive for Group A Streptococcus (GAS) sensitive to penicillin, clindamycin and vancomycin.

She was transferred to intensive care after 12 hours in recovery due to ongoing oxygen requirement, tachycardia and high pain requirements. Concern arose over the possibility of a pulmonary embolus due to the oxygen requirement and postpartum status, but a computed tomography pulmonary angiogram did not confirm this. It revealed increasing ascites and bilateral pleural effusions. She continued to describe severe diffuse abdominal pain.

The working diagnosis then became GAS spontaneous bacterial peritonitis.

A differential of uterine perforation and myometritis was raised, however, was not supported by a further ultrasound with no suspicious features and there had been no concerns over perforation at EUA.

On day three, another CT abdomen and pelvis was performed to investigate for any other surgical cause for ongoing pain and peritonitis. With the consideration of surgical washout due to ongoing pain.

Her white cell count and neutrophils remained normal the entire stay, however, her CRP was significantly raised at 324.

She received intravenous clindamycin and cefuroxime during her eight-day stay and was discharged on oral co-amoxiclav.

Discussion

Puerperal sepsis is a major cause of morbidity and mortality for women, accounting for 11 per cent of maternal deaths in Australia between 2008–2012.[1] GAS is a life-threatening cause of puerperal sepsis, accounting for 50 per cent of deaths from sepsis in New Zealand between 2006–2013.[1] New Zealand has higher rates compared to other countries and the rates have been increasing since 2002.[2] The onset of GAS can be insidious and progress rapidly as demonstrated in this case; therefore, early recognition and appropriate management is essential.

There are no reported cases in the literature of postpartum GAS spontaneous bacterial peritonitis. It is a rare and life-threatening infection, one that can be difficult to diagnose. It is different to other forms of primary peritonitis in that it affects mainly young healthy people; therefore, it is assumed secondary peritonitis and a surgical cause looked for.[3]

A previous PubMed literature search found 26 publications of case reports with 35 cases of spontaneous bacterial peritonitis, none of which were postpartum: 29 patients had CT scans showing free fluid and oedema but no surgical cause; 34 cases proceeded to laparotomy despite a negative CT scan.[3]

The question is raised as to whether a surgical procedure in this circumstance would help or hinder. Due to the rare occurrence of GAS peritonitis it is not known whether a procedure and washout is of benefit to the patient or not. In a previous review of three cases, one patient died and two patients remained in hospital for nearly 60 days with multiple laparotomies. Could this case report be an example of avoidance of surgery being beneficial to the patient?[3]

There is ongoing research into the development of a vaccine for GAS, which would hope to reduce one of the leading causes of maternal death having a significant impact on women's healthcare.[4]

Research is currently in progress looking into rapid antigen testing to aid in the early diagnosis of invasive GAS, which is widely used in primary care for pharyngitis diagnosis.[5] In this case, a positive rapid antigen test giving a much quicker result than blood cultures may have streamlined her management, reducing postpartum radiation exposure with multiple CT scans.

Conclusion

Sepsis was not initially suspected in this case as she was not pyrexial and had a normal white cell count; however, antibiotics were given rapidly in the ED as it was thought likely she had retained tissue. It is well documented that women with GAS sepsis can present with acute onset severe chest, abdominal or even limb pain.[3] There has not been a reported case of spontaneous bacterial peritonitis in the postpartum period and this case demonstrates another atypical presentation of invasive GAS disease.

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Heterotopic caesarean section scar ectopic

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Heterotopic pregnancy describes a concurrent intrauterine and extrauterine ectopic pregnancy.[1] It is a rare diagnosis, with an incidence estimated to be 1 in 30 000 spontaneous pregnancies.[2] In pregnancies conceived using assisted reproductive therapies (ART), the incidence increases to 1 in 3900.[3] Furthermore, caesarean section pregnancy (CSP) is also uncommon, occurring in less than 1 in 2000 pregnancies in women with previous caesarean delivery.[4,5]

There is limited evidence to guide management of heterotopic pregnancy. Medical treatment involves using localised or systemic methotrexate, while surgical encompasses procedures to remove the pregnancy tissue such as uterine wedge resection or hysterectomy. A recent study by Ramkrishna et al[6] has shown that the use of intra-sac potassium chloride (KCl) and methotrexate is a successful intervention for management of non-tubal ectopic pregnancies, especially for women wishing to preserve fertility. Clearly, medical management is appropriate only in clinically stable cases.[7] Surgical management is otherwise required.[7]

Case description

A 35-year-old woman, gravida 2 para 1, presented to hospital with vaginal bleeding and pelvic pain at 6 weeks gestation. This pregnancy was planned and spontaneously conceived. Her past obstetric history was of an emergency caesarean section at term, two years prior. She was clinically well and underwent a transabdominal and transvaginal ultrasound that diagnosed a probable early dichorionic-diamniotic (DCDA) pregnancy.

Repeat ultrasound at 7 weeks gestation demonstrated a live heterotopic DCDA pregnancy, with one gestational sac developing in the caesarean scar, and the other pregnancy was developing within the uterine cavity.

Initial management options that were considered included termination of the entire pregnancy with intra-sac and systemic methotrexate, termination of the CSP using ultrasound guided intra-sac KCl, with expectant management of the intrauterine pregnancy (IUP), or expectant management with inpatient observation and ultrasound guidance. The unpredictable nature of this pregnancy, with risks of severe haemorrhage, morbidity and mortality, was conveyed to the patient; however, she initially preferred to preserve the IUP and decided to proceed with intra-sac KCl to the CSP.

Figure 2 shows the pre-intervention ultrasound. Using a 20-gauge needle, 2 mL (30 mmol/mL) intra-sac KCl was injected into the CSP using a transplacental entry. Asystole of the CSP was observed.

Repeat transvaginal ultrasound 10 days post selective reduction of the CSP revealed that the trophoblastic ring of the CSP had enlarged in size, with the trophoblast covered by serosa only, and no visible embryo. The large portion of the haematoma described previously was seen to be bypassing the CSP and reaching the internal os. Twin 2 remained live, now at a growth consistent with 9 weeks plus 1 day. Given the ongoing expansion of the CSP trophoblast and the potential risk of future uterine rupture with growth of the IUP, the patient was counselled to proceed with surgical treatment.

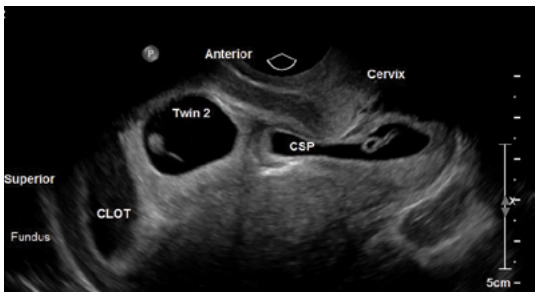

Figure 1. Sagittal view of the cervix and uterus demonstrating fundal clot, twin 2 intrauterine pregnancy and the caesarean scar pregnancy.

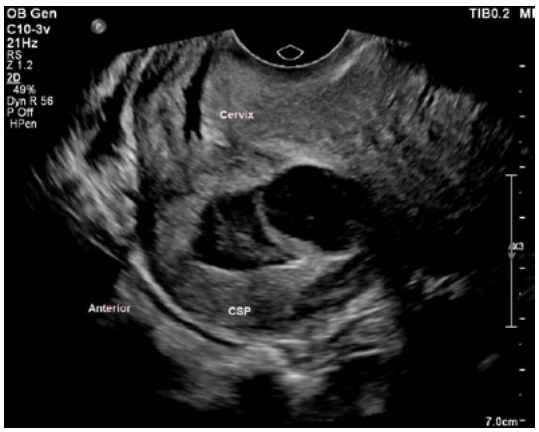

Figure 2. Sagittal view of the cervix and lower uterus demonstrating cervical canal and CSP distending anterior uterine serosa at the level of the caesarean scar. The volume of the CSP had increased subsequent to the KCl injection procedure.

On the 17th day of the patient's admission, the 14th day post elective KCl injection, operative laparoscopy was performed to excise the CSP. After precise and delicate surgical entry onto the uterovesical space and reflection of the bladder peritonium, diathermy was used to create surgical plane proximal to the bulging CSP and a wedge resection was made to remove the CSP using toothed graspers and suction. The defect was then closed in layers using delayed absorbable sutures. No excision of myometrium was required. A cervical dilatation and suction curettage were performed under laparoscopic vision to remove the IUP. Blood loss was moderate due to the vascularity of the gravid uterus; however, the patient remained stable postoperatively and did not require a red cell transfusion. She was discharged home three days later and over the following five weeks her βHCG was tracked down to zero.

Discussion

CSP in heterotopic pregnancy is a rare diagnosis. The number of previous caesarean section deliveries is not correlated to the likelihood of developing CSP, according to Kirk et al.[15] There is a lack of evidence to recommend an ideal management approach and this makes clinical decision making difficult and non-uniform. These cases are clearly challenging to clinicians and distressing for patients. Therefore, multidisciplinary input, particularly from experts in ultrasound and advanced gynaecological surgery, is essential to effective and safe management of these complex cases.

Multidisciplinary input from senior clinicians, including subspecialty experts in laparoscopic surgery and gynaecological ultrasound, were involved in this patient's care, with frequent and in-depth clinical meetings occurring in which this case was discussed and options for management explored. The ultimate decision to proceed with surgical management was challenging, as we respected our patient's desires to conserve the IUP and had explored all conservative management options. Due to the persistent expansion of the ectopic sac, it was felt that on balance, surgical intervention was required to prevent uterine rupture and the resultant significant maternal morbidity.

A review of the literature demonstrates less than 30 published cases of CSP and concurrent IUP. Salomon et al[8] described the first case of a heterotopic caesarean scar pregnancy successfully treated with KCl in the first trimester, with the patient having a 36-week emergency caesarean section for premature rupture of membranes. There are two reported cases in the literature describing successful IUP outcome after surgical management of the CSP. Demirel et al[9] described a case of a heterotopic caesarean scar pregnancy managed with laparoscopic removal of the ectopic mass. They opted for surgical removal of the placental tissue and repair of the myometrium in light of the risks of weakening the lower uterine segment with use of medical management when coexisting with an IUP.[9] The IUP continued without complication, with a healthy baby born at 38 weeks gestation via caesarean section.[9] The other reported case in the literature also describes successful outcomes for the IUP after surgical excision of the CSP with utilisation of laparotomy as their surgical method of choice.[10] In a case report, Gupta et al 16 described suction aspiration as the therapeutic choice in their patient who wanted a successful pregnancy outcome and was also keen to preserve her fertility.

Accordingly, management of heterotopic pregnancy can be medical or surgical. Minimally invasive approaches, such as ultrasound-guided intra-sac injection of methotrexate, have been shown to be associated with high rates of pregnancy termination, without rupture, which may be especially useful in women wishing to preserve fertility.[6] However, this management option is not always appropriate for use in cases of heterotopic pregnancy due to the adverse effects on the IUP. Cases of heterotopic pregnancies with implantation in the caesarean scar are rare, with most heterotopic ectopic pregnancies occurring in the tube. In the more common scenario of the heterotopic pregnancy involving a tubal ectopic, surgical management via salpingectomy is most favourable, as surgical termination of the extrauterine pregnancy can occur, while preserving the IUP.[13] Yet, from the reports discussed here,

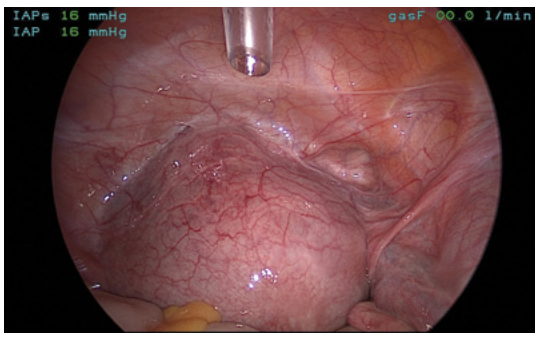

Figure 3. Uterovesical pouch concealing the CSP.

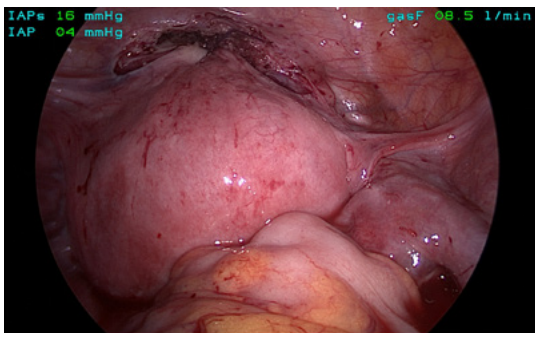

Figure 4. Surgical dissections exploring the CSP.

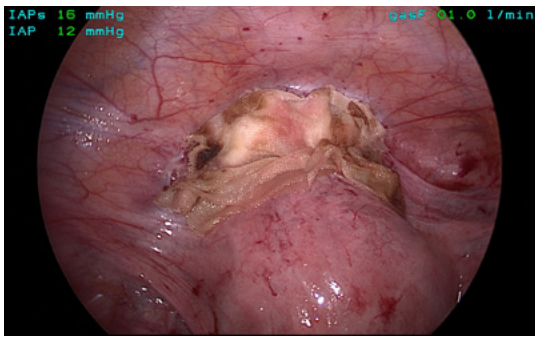

Figure 5. Following the surgical removal of the CSP with applied absorbable adhesive barrier.

consideration of other modalities are beneficial when the extrauterine pregnancies are in unusual locations not easily amenable to surgical intervention, and which may predispose to uterine rupture, such as at the caesarean scar.

Conservative management of CSP is also an option for consideration in certain isolated cases; however, it is often not a clinically preferred option due to the risks of uterine rupture. A recent study by Timor-Tritsch et al[14] determined that both placental implantation in CSP and early (second trimester) placenta accreta share common histopathological features, likely representing different stages in the continuum leading to morbidly adherent placenta in the third trimester. These conditions all implant over the previous caesarean scar and can result in serious obstetric complications.[14]

Most heterotopic pregnancies are diagnosed at five to eight weeks gestation; however, there are reported cases of diagnosis as late as 35 weeks gestation.[11] Delayed diagnosis and management of heterotopic pregnancies can be associated with significant maternal morbidity and mortality, and endanger the IUP. Commonly, the imaging modality of choice for diagnosis of heterotopic pregnancy is transvaginal ultrasonography. Recent literature has concluded that early transvaginal ultrasound performed by an experienced clinician is associated with a sensitivity of 92.4 per cent and a specificity of 100 per cent for detection of heterotopic pregnancy.[12]

This case contributes to the literature regarding the management of CSP as a heterotopic pregnancy. Ultrasound-guided intra-sac KCl may be considered for selective reduction of a CSP when preservation of a coexisting IUP is desired; however, this case demonstrates the need to offer surgical management for those who have failed non-surgical management. Early diagnosis of heterotopic pregnancy is essential to improve the possibility of preserving the IUP and reduce maternal morbidity and mortality, and transvaginal ultrasound adds to diagnostic accuracy. Clearly, with increasing prevalence of advanced maternal age, increased uptake of ART and rising caesarean section rates, clinicians may encounter more cases of heterotopic and CSP. Diagnosis and management of these complex cases should be individualised with appropriate counselling and careful assessment of the patient and a multidisciplinary approach.

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Uterine rupture secondary to placenta percreta

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Uterine rupture is defined as a full thickness separation of the uterine wall and the overlying serosa.[1] It is associated with significant neonatal and maternal mortality and morbidity. It mainly occurs in third trimester;[2] spontaneous uterine rupture in first trimester is rare and very difficult to diagnose.

Placenta accreta is abnormal placental implantation leading to an adherence of the placenta to the uterine wall.[2] It is categorised according to degree of placental invasion into the uterine myometrium. The definition encompasses placenta accrete vera (adherence of the placenta to the superficial myometrium), placenta increta (adherence of the placenta to the body of the myometrium – but not the entire thickness) and the most catastrophic subtype, placenta percreta (penetration and adherence of the placenta through the full thickness of the myometrium, the uterine serosa and potentially nearby organs).[3] The incidence of uterine rupture due to placenta percreta is rare at 1 in 5000 women;[4] previous caesarean section delivery is the predominant risk factor. Here we present to you two concurrent rare occurrences, a case of uterine rupture in second trimester in the setting of placenta percreta.

Case

A 30-year-old woman presented at 20+1 weeks gestation, with post-coital exacerbation of generalised abdominal pain. She did not report vaginal bleeding.

She had had two previous lower segment caesarean sections at term overseas. The morphology scan at 19 weeks and 3 days reported an anterior placenta previa covering the cervical os by 5.1 cm.

On examination, the patient was diaphoretic and pale, with a blood pressure 78/53 and a heart rate 105. She had generalised abdominal tenderness with gross abdominal distension. Blood investigation revealed dropping haemoglobin levels (83 g/L to 61 g/L two hours apart), INR 1.3 and fibrinogen 1.8 mg/dL.

An urgent ultrasound reported large free fluid in the abdomen. The patient was immediately taken to theatre. Laparoscopic entry proved difficult visualisation as blood refluxed into the laparoscopic port and a four-quadrant hemoperitoneum obstructed visualisation of pelvic contents. A large round haemorrhagic mass was seen centrally and thought to be a haemorrhagic cyst (Figure 1).

Decision for conversion to laparotomy through previous caesarean scar found placenta percreta with a ruptured lower uterine segment (Figures 2a and 2b). The central mass seen on laparoscopy was, in fact, the uterus with abruption and large surface vessels.

The fetus was entirely expelled in the abdomen. Due to extensive uterine bleeding and distorted uterine anatomy, the decision was made for subtotal hysterectomy (Figure 3).

Total blood loss was 4000 mL. The patient received 8 units of packed red blood cells, 7 bags of fresh frozen plasma, 1 unit of platelets and 3 L of crystalloid fluids; postoperative care was in ICU. She was discharged home on day six. The fetus weighed 250 g.

Histopathology confirmed placenta percreta with uterine rupture involving the anterior lower uterine segment and adjacent endocervix (Figure 4). β-hCG monitoring found a level of 1149 IU/L at presentation, and came down to less than 1 IU/L three weeks post discharge.

Discussion

In normal implantation, there is a layer of decidua that separates the placental villi from

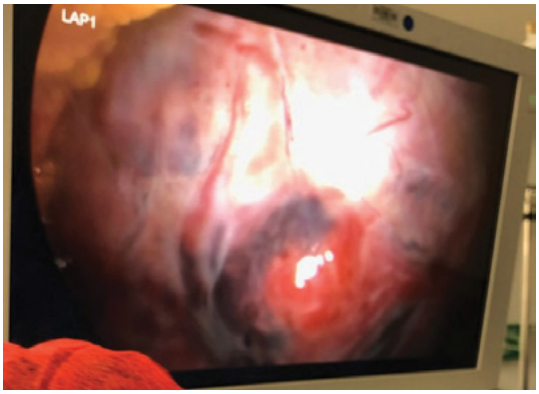

Figure 1. View upon laparoscopic entry of a large central pelvic mass with areas of haemorrhage and prominent large surface vessels.

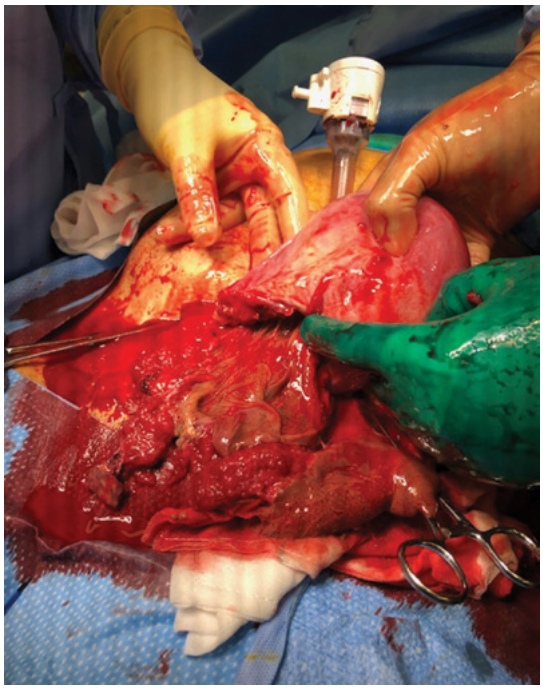

Figure 2a. Lower segment uterine rupture with an adherent placenta.

the myometrium at the area of implantation; in adherent placenta, this is lacking.[3] Adherent placenta is rare, with incidence ranging from 1:500–1:93 000 deliveries.[2] Placental accreta constitutes 78–80 per cent of cases, with placental increta and percreta constituting 15 per cent and 5–7 per cent of remaining cases of adherent placentation respectively.[3,4] Placenta percreta is the most aggressive form of the spectrum, an obstetric complication that can have catastrophic consequences. In adherent placenta, the maternal mortality rate is 7–11.[4] per cent and neonatal mortality is 9.76 per cent, with such rates mostly accredited to placenta percreta complications.

Previous caesarean section is the leading risk factor for uterine rupture as per the presented case. Other risk factors include fetal malpresentation, shoulder dystocia, neglected labour, breech extraction, instrumental-assisted vaginal delivery,[1] previous uterine instrumentation, grand-multiparity and abnormal placentation.[2] Abnormal placentation weakens the area of invasion in the myometrium, predisposing to uterine rupture.[2] Jang et al describe a case of uterine rupture caused by placenta percreta in a patient with a history of dilation and curettage for a spontaneous miscarriage.[4] There are case reports of abnormal placentation and spontaneous uterine rupture in first trimester in patients who underwent assisted reproduction. Norwitz et al[5] report a case of uterine rupture after pelvic radiation causing abnormal placentation (calls upon good history-taking).

Placenta percreta-induced spontaneous uterine rupture more commonly occurs in the second and third trimesters; however, there have been rare cases where it has occurred between 10–20 weeks gestation.[2,4] While the overall incidence of placenta percreta is low, increasing caesarean section rates in modern obstetrics is leading to increasing rates of placenta percreta.[2,3] In women with placenta previa, the frequency of placenta accreta increases with increasing number of caesarean deliveries as per Silver RM et al.[1,6]

Clinical signs of uterine rupture include acute abdominal pain, scar tenderness, vaginal bleeding and maternal tachycardia and hypotension;[5] however, some signs may not be present as our patient had insidious onset of abdominal pain and no vaginal bleeding. There is significant fetal and maternal morbidity and mortality in delayed diagnosis of uterine rupture. Potential complications include fetal death, maternal haemorrhage, injury to nearby organs, emergency hysterectomy and maternal death.[5]

Delayed diagnosis may be attributable to consideration of more common diagnoses, such as a ruptured ovarian cyst. As such, uterine rupture and placenta percreta should be considered in all pregnant women who present with an acute haemorrhagic abdomen at the start of pregnancy.

It is crucial to appreciate the roles of imaging and investigations to minimise morbidity and mortality and allow for early planning and potential conservative treatment.[2] If an adherent placenta is suspected on ultrasound, consider alpha-fetoprotein level, which tends to be elevated, and an MRI for placental mapping when ultrasound findings are inconclusive.[2,6]

Diagnosis of adherent placenta using ultrasound in first trimester is challenging with a sensitivity of 41 per cent; however, ultrasonography in the first trimester should raise suspicion of an adherent placenta in a patient with prior caesarean section if it reveals a placenta previa. 75 per cent of placenta percreta cases are associated with previously known placenta praevias.[1,3,6]

There's the question as to whether our patient with a previous caesarean section and a placenta previa on the morphology scan should have been urgently referred to a tertiary hospital for counselling on further management in light of the complications involved, with utilisation of fetomaternal unit assessment and MRI.

There's the thought that if ultrasound at the morphology scan had questioned placenta percreta, our patient may have been sent in urgently to a tertiary centre to discuss continuation of pregnancy and prolonged hospital admission (with risk of prematurity) versus termination of pregnancy. This raises the question whether there was potential to pick up uterine rupture earlier and whether intercourse triggered the rupture due to further mechanical weakening.

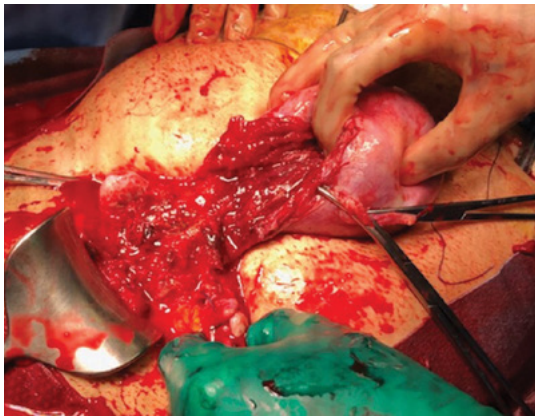

Figure 2b. Significant distortion of the lower uterine segment from uterine rupture.

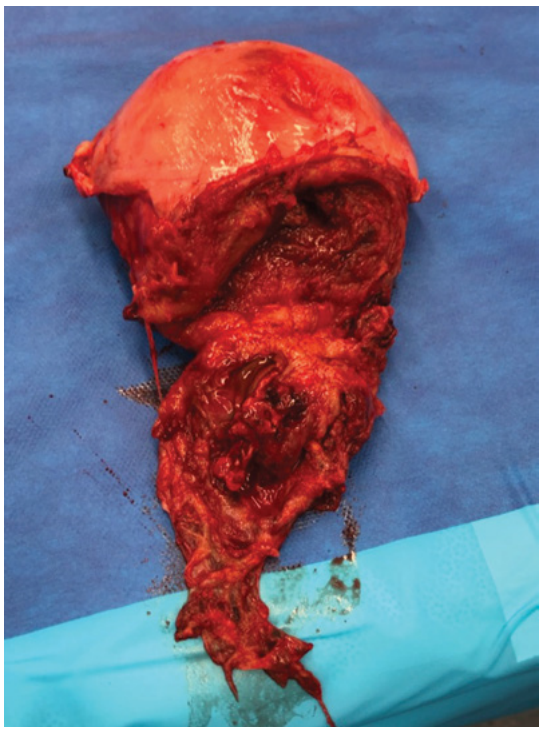

Figure 3. Subtotal hysterectomy specimen with adherent placental tissue..

There are reports of conservative treatment of placenta percreta-induced uterine rupture such as uterine curettage with packing, postoperative chemotherapy, and uterine artery occlusion.[4] The four-fold mortality associated with conservative treatment in comparison to a hysterectomy, however, justifies an emergency hysterectomy to be the preferred approach.[4]

Conclusion

Diagnosis of adherent placenta in early pregnancy is a challenge. This case serves as a reminder to consider uterine rupture as a differential diagnosis in the acute abdomen in early pregnancy, and use of thorough clinical and investigative skills to derive a diagnosis. While a difficult decision, laparoscopy should be considered for investigation of undifferentiated acute abdomen in first trimester of pregnancy.[4]

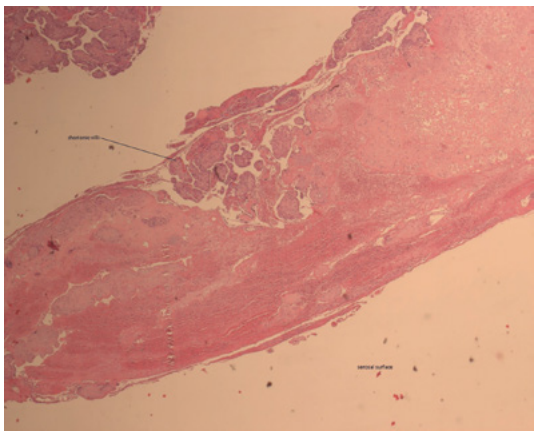

Figure 4. This histopathology slide demonstrates that two key elements of normal placental implantation are not present: there is no decidua between the chorionic villi and the uterus, and there is no myometrium. [H&E stain]. Image Courtesy of Liverpool Hospital Anatomical Pathology and A/Prof Leonardo Santos and Dr Miriam Fewtrell..

Early suspicion for placenta praevia and percreta allows for further assessment with fetomaternal unit referral and consideration of MRI, as well as multidisciplinary team utilisation for delivery planning.

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Brian Spurrett Oration 2019: leave no one behind

Prof Caroline Homer AO
Burnet Institute, Melbourne, Australia

This is an abridged version of the Brian Spurrett Oration delivered at the Pacific Society for Reproductive Health 13th Biennial Scientific Meeting in Port Moresby, Papua New Guinea, 6–11 July 2019. The full Oration is published in the *Pacific Journal of Reproductive Health* 2019;1(10):480-4 and is reproduced here with permission.

Thank you for the opportunity to give this Oration. This is a huge honour and I thank the local organising committee, the PSRH Executive, the RANZCOG Women's Health Foundation Board, the Global Health Committee and the Board. At this, 13th PSRH, we acknowledge the leaders and visionaries who have come before us, in whose paths we walked along, across and between these wonderful islands of the South Pacific.

Today we pay tribute to Prof Brian Spurrett OAM, whose legacy lives on in the scores of Fellows – obstetric doctors and midwives, who have had opportunities to travel, to learn more and to bring skills and capacity back home. Brian was a visionary, he knew that doctors and midwives in this region had enormous capacity and skills, but that mentoring, access to education and networking were needed. Like many of you here today, Brian had a vision to make a difference.

You are here because you want to make a difference. A difference to the communities you live in and serve, a difference to women, mothers, babies, children and adolescents. My oration today is about the difference we all want to make, but none of us can make a difference alone. We need to do it together; however, we need to have systems and processes that let us make a difference and ensure that everyone gets access to the best care, to quality care, to care that not only ensures that people survive, but that they also thrive and can transform their communities.

Access to quality maternal and newborn care will save lives. If every woman had access to educated, regulated and supported midwives for pregnancy, labour and birth and the postpartum period; and if every woman could access specialist care from doctors when she or her baby needed them, lives would be saved. If every child was fully breastfed for six months and had all their vaccinations, lives would be saved. If all women were able to access modern contraceptives and could decide whether and when to have children, lives would be saved.

There is strong evidence that access to midwives in a supported health system will save lives and improve outcomes, but it is not enough to just put a midwife at a health centre and expect everything to be solved. They need good training to start with and this training must include evidence-based knowledge and mentored clinical experiences. The midwife needs to be deployed soon after finishing preservice education, so they do not forget things. They must have the drugs they need – iron tablets, oxytocin, misoprostol, magnesium sulphate, immunisations, contraceptives – and a fridge to put them in along with electricity or a generator to run the fridge. They need basic things like a blood pressure machine, urine dipsticks and a bag and mask to resuscitate a baby.

The midwife needs to be able to provide kind, respectful care so that women will come back – more than just once – and they will come back to give birth. The midwife needs to be in a system that has a nice space for antenatal care, that welcomes women's companions in labour, ensures that women feel supported and safe throughout their labour and birth and, very importantly, are not left alone.

The midwife needs the time and space to do postnatal visits, to make sure women are supported for skin-to-skin, breastfeeding, immunisation and family planning. The midwife needs a phone or radio so they can ring for help or advice if they need. The midwife needs access to a vehicle or a boat if they needs to transfer the woman, especially in labour. The midwife needs someone to debrief with when things go well and when things go badly. The midwife needs continuing education and supportive supervision so they can learn, grow and feel good about their work. The midwife needs to be paid on time and be able to have days off and leave to balance their family life with their work.

At the referral hospital, the midwives and doctors also need a supportive system. This includes drugs, equipment, phones, support and access to an operating theatre, blood bank, and laboratory. The hospital needs enough space to accommodate the mothers, their companions and family (both in labour and postnatally), and their new babies. The hospital needs senior staff who can provide training, advice and support when things are hard or complex, and also for debriefing. The hospital also needs to provide staff with a safe environment to work and to pay them on time. Midwives and doctors need kindness, from their managers and from each other. No one can be kind and respectful to women if they are being scolded or shouted at by their colleagues or they feel frightened to ask questions or admit mistakes.

Having all of these things probably sounds like a lot. For some of you, I am just describing your everyday work – you know these things are important and you already have them. You can reach those most in need in the communities you serve – the poorest and the most disadvantaged. For some of you, you don't have these things, but you know you need them. You are frustrated. You know you need a functional health system to do your job. You need a system that lets

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists

Excellence in Women's Health

ANZJOG

ANZJOG virtual issue available online

In conjunction with the RANZCOG Aboriginal and Torres Strait Islander Women's Health Meeting held in Adelaide, Saturday 15 to Sunday 16 September 2018, ANZJOG together with Wiley has published a virtual special issue devoted to Aboriginal, Torres Strait Islander and Māori women's health. Edited by Dr Marilyn Clarke, Chair of the Indigenous Women's Health Committee, and Dr Leigh Duncan, Chair of He Hono Wāhine, this issue features recent articles from ANZJOG and is open access.

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you be the best midwife, doctor, nurse or community health worker that you can be. You need a health system that can make sure that everyone gets access to care, and no one is left behind.

So, what will it take to build better systems? You know what you require – the workers, the drugs, the buildings and the water. But how do we transform these specifics into resilient and functional systems?

We need knowledge. We need to know what is currently going on – we need data. There is a saying 'no data, no problem; no problem, no solution'. So, we need data to know if we have a problem and to plan and evaluate a solution. We need data that is in real time or close to real time. We need to know when the stocks are low, when the drugs are expired, when the roads are washed away and the vehicle cannot get out or in, when the health workers are sick and cannot be at work and when we need to arrange back up.

We need a well-educated and well-supported health workforce. The workforce needs up-to-date curriculums, education programs that provide quality learning, simulation, supported clinical experiences and a career path. We all need ongoing updates – what we learned 10 or 20 years ago is not enough. We need to do skills and drills, every day or at least most days. These drills will make sure we can respond quickly in an emergency and we know how to work together as a team. Cross-functional and interdisciplinary learning is needed. We will all work better together, and more respectfully, if we understand what we all can do. We need to understand our different scopes of practice and what we bring uniquely to the bedside or to the community and to be clear about our roles.

We need to learn together, support one another and be respectful and kind to one another. This is especially important on the days when things go badly and we are stressed, tired and (maybe) grumpy or scared about what will happen next. Caring for one another also means we are more likely to admit when we make mistakes and learn from these mistakes. Caring for one another also means we will provide better care to women, babies and their communities.

We need to support the gathering of evidence – to show how things could be better, to test out new or different ways to make things better, and to scale up or roll out things that we know work. Many of you will be thinking – that is research, that is for other people, that is not for me. I am just a midwife, doctor or nurse and I just want to do my job. Well, using evidence in our work is part of our job. Scaling up what we know works from the research is part of our job. Changing the way we do things and testing out if this is better is part of our job. Being brave enough to change because of the evidence, this is part of our job.

Then we need to learn how to be advocates. How to take what we know, use our voice and influence policy makers, health service managers and the government. Advocacy is the process of building support for an issue or cause and influencing others to take action. Your advocacy must engage with the community, especially those leaders involved with groups for women and youth.

While you may not have specific resources dedicated to conducting advocacy activities, there may be partners in your country or at the regional and global levels who you can work with. There will also be NGOs you can work with. Local community and village organisations and women's groups who will help you to advocate for change. Working with women and women's groups is essential as they know what is needed.

Media coverage is often a great way to ensure your advocacy message reaches a wide and varied audience. Having your message broadcast increases public awareness of the issue and often generates broad support. There are a number of international days of celebration that might be worth using for the media. International Women's Day, International Day of the Midwife, International Day of the Nurse, World Health Day, International Youth Day, World Contraception Day, International Day of the Girl and the International Day for the Elimination of Violence Against Women. That is a lot of days to use as advocacy for mothers and babies. Another important advocacy time will be 2020, which WHO has designated the Year of the Midwife and the Year of the Nurse.

In all this work to build better systems, keep women at the centre. The systems must not be about us – they must not be designed just to work for us – they must first work for women and their communities. All women deserve access to quality care – especially the poorest, the hardest to reach, the disabled, the most vulnerable and ones who run away from us or do not choose to come to us for care. We need to make sure the systems work for them, so that they feel supported, respected, listened to and engaged in their care.

Universal healthcare will only happen when women are at the centre, gender equity exists and violence against women stops. These are big issues that won't be easy to solve, but we can all do our bit. We can all provide the best quality care that we can. We can be kind to the women and communities we serve and to each other. Kindness is free and you don't have to wait to have a perfect health system to be kind.

Finally, we all need courage. Brian Spurrett had courage and determination to make things better. He could have just stayed at home and done his day job. You could all just stay at home and do your day job, but you are here. You have fundraised, got sponsorship, saved up, gone without or borrowed to get here. Many of you came to workshops over the weekend to learn and share – that takes courage – courage to admit we don't know it all and there is more to gain. Many of you are giving presentations here at PSRH, some for the first time, and that also takes courage. You will go back with new ideas and new practices that you will try and encourage others to take up or you will teach others to do – that takes courage.

We all need a booster vaccination of hope, energy and commitment and a good dose of courage. Because we know that we cannot leave anyone behind. Our countries and our communities will only be strong and powerful when we leave no one behind. When we have gender equity at all levels, when all our girls and boys are educated equally and have equal access to high school and further education, when our women can safely choose if and when to have children, when our mothers can give birth safely and our babies grow up to be strong and confident members of the community. I know we can do it.

Timing of initiation of antenatal care at the PMGH

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Antenatal care is a vehicle for multiple interventions, including health education, recognition of risk factors and family planning counselling. Delayed access to antenatal care reduces opportunity for appropriate screening and management of risk factors resulting in poor maternal and fetal outcomes.[1]

About 65–71 per cent of pregnant women in developing countries receive at least one antenatal visit, while 47 per cent have more than four visits;[2] only 17 per cent book early, compared to developed countries where only 2.8–16 per cent book after 20 weeks.[3]

In Papua New Guinea (PNG), only 44–53 per cent of births are supervised and 33–79 per cent of pregnant women receive some form of antenatal care. A study done in Madang province of PNG noted that 39 per cent of women with bad obstetric outcomes delayed initiation of antenatal care.[4] Although 60–70 per cent of women who delivered at Port Moresby General Hospital (PMGH) in 2015 had attended more than four antenatal visits, the maternal mortality ratio was 95.3 per 100 000 live births, while the perinatal mortality rate was 25 per 1000 deliveries; it was 19.5/1000 for women who had antenatal care and 67/1000 for non-attendants. The HIV rate was 4.3 per cent among non-attendants who were tested during labour versus 1.85 per cent for the attendants. The reduction in vertical transmission of HIV among attendant women has halved since 2010, when ART medications became available in PNG, from 17.7 per cent in 2010 to 8.2 per cent in 2014, a further testimony for the value of antenatal services for PNG.[5]

In most developing nations, it is always a struggle to get women to book early for antenatal care for various reasons including health workers' bad attitude, limited number of staff, poor accessibility to the antenatal clinics (distance and cost), unhappy experience during previous pregnancies and efforts to avoid multiple visits to the clinic.[1] In spite of the value of antenatal care, the low rate of utilisation of facilities and the reasons for this is why this study was initiated.

Methodology

The definition of early 'booking' for antenatal care at the PMGH is first attendance at 20 weeks gestation or less in contrast to the WHO definition of booking before 12 weeks gestation. Between 7 February and 6 July 2017, 821 women who attended PMGH for their first antenatal visit were interviewed to identify the main factors influencing the timing of their initiation for antenatal care. Significant variables were examined by univariate analysis and multiple regression analysis with p-values less than 0.05 and odds ratios whose confidence intervals did not include 1 taken as significant.

Ethical clearance for this study was given by the University of PNG School of Medicine and Health Sciences Ethical Committee and the management of the PMGH.

Results

Using the PMGH definition of early booking, 81 per cent of the patients booked late for antenatal care. Figure 1 shows a total of 860 cases interviewed with 39 excluded as per exclusion criteria.

The mean age of women was 27 years, with a range of 15–45 years of age. Factors associated in univariate analysis with early antenatal booking, as highlighted in Table 1, included: primigravida, Highlands origin, previous bad obstetric history, previous family planning use, planning of this pregnancy, being happy with the pregnancy and those who perceived that it was the right time to initiate antenatal care. 'Bad obstetric history' included previous miscarriage, perinatal death, cardiac disease and ectopic pregnancy.

Factors associated with late booking included the following: no, or less than primary level, education of either the woman or her partner, patient's low unemployment status, women living with an extended family, those avoiding frequent antenatal visits, those with other pressing obligations, hospital costs and those sent away at an earlier booking visit including women who came early but were told to return at quickening, as well as women who missed the 'first 20 women to be enrolled' cut.

The multiple regression analysis has noted significant variables in early booking (Table 2). It confirmed that women who were of Highlands origin, and those who perceived that it was the right time to book, those who were not unemployed and who did not avoid too many hospital visits were all likely to book early for antenatal care.

Table 1. Variables influencing initiation of antenatal booking using early booking as ≤ 20 weeks gestation.

Characteristic	Frequency (n= 821)	≤ 20 weeks	> 20 weeks	OR	95% CI	P-value
Socio-demographics						
Denomination: United Church	218 (26.6%)	30/159 (19%)	188/662 (28%)	0.59	0.38–0.9	0.008
Region of Origin: Highlands Southern	274 (33%) 401 (49%)	67/159 (42%) 67/159 (42%)	207/662 (31%) 334/662 (50%)	1.6 0.7	1.1–2.3 0.5–1.01	0.006 0.036
Patient's level of education: nil or less than primary	267 (32.5%)	15/159 (9 %)	252/662 (38%)	0.17	0.097-0.29	0
Patients unemployment status (yes)	616 (75%)	100/159 (63%)	516/662 (78%)	0.48	0.3–0.7	0.0001
Family size: Extended	348 (42%)	48/159 (%)	300/662 (45%)	1.9	1.3–2.8	0.0003
Partner's level of education: nil or less than primary	119 (14.5%)	15/159 (9%)	104/662 (16%)	0.56	0.3–0.99	0.03
Obstetric factors						
Primigravida	268 (33%)	61 (38%)	207 (31%)	1.4	1.0–2.0	0.05
Previous family planning use	310 (56%)	65 (67%)	245 (54%)	1.7	1.1–2.8	0.01
Past pregnancy complications	166/553 (30%)	63 (54%)	103 (24%)	0.27	0.2–0.4	0
Perinatal death	37/166 (22%)	13 (11%)	24 (6%)	2.1	1.1–4.4	0.03
Miscarriage	66/166 (40%)	26 (22%)	40 (9%)	2.8	1.6–4.9	0.0002
Cardiac disease	2/166(1%)	2 (2%)	0 (0%)	-1	0	0.04
Do you think now is the right time to book for ANC? (n= 821)(yes)	492 (60%)	126 (79%)	366 (55%)	3.1	2.04–4.7	0.00000001
Situational factors						
Was lack of finance an issue to come for ANC?	156 (19%)	19 (12%)	137 (21%)	0.5	0.3–0.9	0.006
Was she avoiding too many antenatal visits?	163 (20%)	10 (6%)	153 (23%)	0.22	0.1–0.4	0.0000001
Did she have other obligations so delayed her visit?	246 (30%)	36 (23%)	210 (32%)	0.6	0.4–0.9	0.01
Was she worried about other hospital costs so came late?	164 (20%)	22 (14%)	142 (21%)	0.6	0.36–0.9	0.02
Did she come earlier but told to come when baby is big/moving? (n= 818)	33 (4%)	1 (0.6%)	32 (5%)	0.12	0.02–0.9	0.007
Did she come earlier but told to come back because she was late? (n= 821)	344 (42%)	41 (26%)	303 (46%)	0.4	0.28–0.6	0.000002
Psychosocial factors						
Is this pregnancy planned: no	299 (36%)	44 (28%)	255 (39%)	1.6	1.1–2.4	0.006
Happy about pregnancy	639 (78%)	136 (86%)	503 (76%)	1.9	1.2–3.01	0.005

Discussion

An analysis of 45 developing countries showed that 81–91 per cent of women start antenatal care late (that is, after 20 weeks) which is very similar to our findings.[6]

Many similar studies have suggested that maternal age, marital factors, religion, ethnicity, level of education and occupation of both partners do have an influence on the timing of antenatal care, while others dispute these findings.[7-9]

This study noted that Highlands' women were more likely to book early while Southern women were likely to book later. Whether this finding was related to the location of PMGH in the Southern region and therefore had the disadvantage of increased numbers of village and slum dwellers of Southern origin to influence socio-economic factors is uncertain.

It is gratifying to note that women with prior history of ectopic pregnancy booked early. These women are usually counselled to do so at the PMGH.

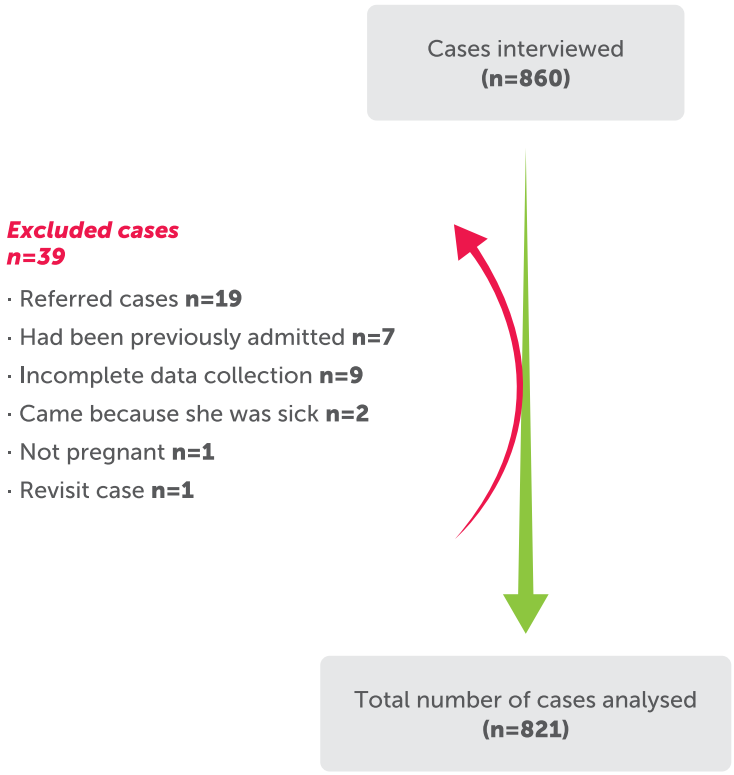

Figure 1. 860 cases interviewed with 39 excluded as per exclusion criteria.

The correct timing of initiation of antenatal care has been a concern in many studies.[6,8] Of note is partners' support playing an important role in maternal and child health. Women with better formal education, those with partners who are also better educated and with skilled occupations and are supportive were more likely to book early.

At PMGH, 33 per cent of maternal deaths have an underlying medical condition.[5] Many of these medical conditions will not be diagnosed and treated unless women book early for antenatal care. In this study, women expressed the need for public health education. When women understand the importance of booking early for antenatal care, and do so, many advantages accrue, such as establishing the gestation as accurately as possible to set the scene for future decision-making. This is so important that in the developed world, early pregnancy units are available to encourage, and eventually reduce, revisits for the majority to pay more attention to high-risk pregnancies.

Acknowledgements

We would like to acknowledge the RANZCOG Foundation Global Health Research Scholarship for funding this project.

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Table 2. Multiple logistic regression analysis of variables that were significantly associated with early booking in univariate analysis.

Variables	Odds Ratio	95%	CI	Coefficient	SE	Z-statistic	P-value
Do you think now is the right time to book (yes)	3.1634	1.7784	5.627	1.1516	0.2938	3.9192	0.0001
Highlands (yes)	1.9058	1.1547	3.1456	0.6449	0.2557	2.5225	0.0117
Patients unemployed (no)	0.488	0.2702	0.8814	-0.7175	0.3017	-2.3786	0.0174
Was she avoiding too many antenatal clinics (no)	0.2314	0.0949	0.5642	-1.4635	0.4547	-3.2187	0.0013

Obituaries

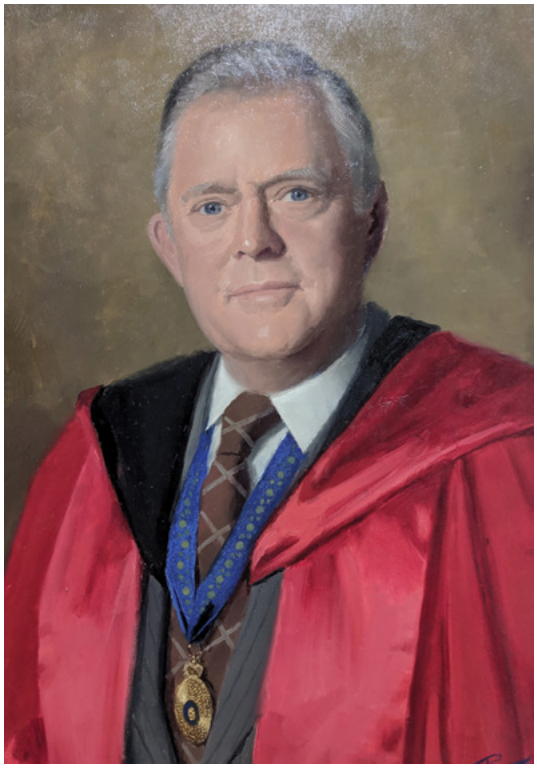
Prof Norman Albert Beischer 1930–2015

Prof Norman Albert Beischer AO, MD BS, MGO, FRCS (EDIN), FRCOG, FRACS, FRANZCOG, DMEDSC (HON) was an intellectual giant and visionary who made an enormous contribution to improving women's health and progressing the science and our knowledge of obstetrics and gynaecology.

Norman was born in Bendigo, Victoria, on 15 August 1930, and attended the Bendigo State and High schools before completing his education at Geelong Grammar. In 1948, he was awarded the Argus Literature Prize and the Geelong Grammar School Council's AH Whittingham Scholarship. This love of language and the written word stayed with him all his life and was evident in his later publications. Norman progressed to the University of Melbourne where he graduated MBBS in 1954. During this time, he achieved numerous honours, including the Fulton Scholarship in Obstetrics and Gynaecology, and the Hubert Sydney Jacobs Prize in Clinical Gynaecology, launching his path to obstetrics and gynaecology. His postgraduate training was at the Alfred Hospital, Royal Children's Hospital and Royal Women's Hospital from where he obtained his initial training in obstetrics and gynaecology. As was the practice in those times, Norman travelled to Northern Ireland where he worked in Lurgan, Portadown and Ballymoney hospitals, obtaining his membership of the Royal College of Obstetricians & Gynaecologists (MRCOG) and subsequently the Fellowship of the Royal College of Surgeons of Edinburgh (FRCS Ed). While in the UK, Norman met Elizabeth Young whom he married in 1961 and was his life-long partner, the mother of his three children and the love of his life.

On his return to Melbourne in 1965, Norman joined the Department of O&G at the Royal Women's Hospital as first assistant to Prof Lance Townsend who immediately recognised his enormous potential as a clinician, surgeon and academic. At the time, the Professorial Unit was responsible for the management of cervical cancers within the hospital. Prof Townsend gave Norman the task of performing the Wertheim hysterectomies so that he could become proficient in surgery of the lateral pelvic wall, this being a prerequisite for dealing with obstetric haemorrhage for which he may have been called upon to deal with in the future as a head of department.

In 1968, Norman was appointed the second Professor of O&G at the University of Melbourne following Marshall Allan, the first Professor of Obstetrics, and Lance Townsend who was the first Professor of O&G within the University. In 1969, he worked at the Johns Hopkins Hospital in Baltimore before taking up his appointment at the newly opened Mercy Maternity Hospital, a position he held for 28 years. Over this time, he established the hospital as a first-class facility providing obstetric and gynaecological care for the women of Melbourne. From the outset, he involved every consultant in the hospital in auditing the outcomes of clinical management and produced the triennial report of the hospital, which was widely distributed and set the standard of excellence for a tertiary institution from which all other maternity units within Victoria could be compared. He applied



Painting of Prof Norman Albert Beischer.

the same meticulous scrutiny to clinical outcomes by sitting on the Consultative Council on Obstetric and Paediatric Morbidity and Mortality, of which he became Chairman from 1984 until his retirement in 1999. Norman was also a member of the National Health and Medical Research Council National Perinatal Statistical Unit, which was responsible for reporting maternal deaths in Australia.

Norman was an exceptional teacher, with students rotating from the Austin Hospital Clinical School being warmly welcomed and enthusiastically taught. He edited several student textbooks, most notably Obstetrics and the Newborn with Eric Mackay from Brisbane, now in its 4th edition, which were easy to read, colourfully illustrated and continue to this day to be standard teaching texts for undergraduates in Australia.

Norman was a passionate researcher, having authored more than 200 publications. He was quick to recognise the need to assess fetal wellbeing in utero in order to reduce perinatal mortality. Utilising the work of Prof James Brown who had developed a bioassay for oestriol, he established a program of routine testing for urinary oestriol excretion in the third trimester to identify those pregnancies at risk of placental insufficiency and intrauterine growth restriction. Innovative in his management, he attempted to improve the intrauterine environment and growth in utero through bed rest and intravenous hyperalimentation, these being the only measures available at the time to allow prolongation of the pregnancy. In order to determine the timing of delivery more precisely for these high-risk

pregnancies, he established the Fetal Monitoring Unit, under the supervision of Frank Chew, which used cardiotocography to assess fetal wellbeing in utero. Through these measures and embracing routine ultrasound scanning, he, in effect, established the foundations of the discipline of maternal-fetal medicine well before this was even considered a subspecialty within obstetrics.

Norman was a pioneer in appreciating the importance and effect of hyperglycaemia in pregnancy and implemented routine testing for gestational diabetes mellitus in the third trimester for all antenatal patients. This was at a time when there was no clear policy on antenatal screening with gestational diabetes having a reported low incidence in our community. His recommendation for routine one-step full glucose tolerance testing was over 40 years later accepted by the World Health Organization as the standard of care in obstetrics. Norman also recognised that gestational diabetes was a marker for the risk of developing type 2 diabetes mellitus and initiated a program of long-term follow up of patients, confirming that a considerable proportion would go on to develop diabetes in later life. He also promoted lifestyle interventions and ran a trial of oral hypoglycaemic to prevent the onset of type 2 diabetes.

Having established the obstetric credentials of the hospital, Norman turned his attention to expanding the gynaecological services, coinciding with a name change of the institution to Mercy Hospital for Women. Realising the need for specialised expertise in the management of gynaecological malignancies, he set up the Gynaecological Oncology Unit and appointed Robert Planner in charge of the unit. Robert aggressively undertook radical surgical and debulking procedures in patients with advanced ovarian malignancies, obtaining superior results at a time when chemotherapy was limited by the paucity of effective drugs. He set up the Urodynamics Clinic appointing Peter Dwyer as clinician in charge, allowing him to further develop his interest in urogynaecology. Norman recognised the rapidly advancing area of laparoscopic surgery in gynaecology and supported Peter Maher in setting up the Minimally Invasive Surgery Unit and funding the fellowship position through the Mercy Maternity Hospital Research Fund. Norman acknowledged the need for other specialist clinics and appointed Graeme Dennerstein to establish the first multidisciplinary Vulvar Diseases Clinic, which provided a unique and essential service within a difficult area of gynaecology. These specialist clinics and the obstetric units under his direct supervision enabled the Mercy Hospital for Women to grow into a first-class facility caring for the women of Victoria and training medical students, future obstetricians, gynaecologists, and subspecialists.

Norman took over from Eric Mackay as Editor of the *Australian and New Zealand Journal of Obstetrics and Gynaecology* in 1983 and remained in this role until his retirement in 2000. Under his direction, the Journal flourished largely by allowing the publication of many clinical articles often preceded by an Editor's comment that allowed him to add relevance to even obscure articles and point out the take-home message of the author.

Norman was an excellent clinician who was always supportive of the junior staff. He never felt the need to justify the indication for a caesarean section and stated that the caesarean section rate was always a reflection that at all times the best decision had been made for the care of mothers and babies. Notably, Norman was asked to give his expert opinion at the hearings of William McBride in Sydney where he reviewed many cases of alleged mismanagement and found no cause to substantiate these claims.

Following his retirement from the University Department at the Mercy Hospital for Women, Norman remained active as Chair of the Medical Research Foundation for Women and Babies, founded by him in 1981 as the Mercy Maternity Hospital Research Foundation. The Foundation was renamed the Norman Beischer Medical Research Foundation after his death in 2015, in recognition of his significant contribution to the Foundation and to medical research.

Norman was honoured with the Order of Australia in 2000 with the citation, 'For service in the field of obstetrics and gynaecology and for clinical research into the causes and prevention of maternal and perinatal deaths'. In 2013, Norman was awarded an Honorary Doctorate of Medical Science from the University of Melbourne in recognition of his contribution to medical research and to the improvement of maternity care which in turn transformed the lives of countless women and their families across the world. He devoted his life to advancing our knowledge of obstetrics and gynaecology and improving the health of mothers and babies. His contribution to our discipline and the influence he had on his colleagues will be enduring and the breadth of his achievements would position him as the last true Professor of O&G, the likes of which will never be seen again.

Dr Salvatore Sfameni
FRANZCOG

Dr Peter Wein
FRANZCOG

Dr Philip Edward Norman Suter 1932–2019

Philip Suter was born in the UK in 1932, graduated there in 1957 and then acquired Fellowship of the RCOG and, later, RANZCOG. Before migrating to Australia in 1976, he worked in London, Germany and Kenya. We met as fellow obstetricians at Essendon and District Memorial Hospital where we managed both public and private patients until its regrettable closure in 1992. Philip was the senior obstetrician at the time. He also had appointments at the Royal Women's Hospital and the Dermogynaecology Clinic at the Mercy Hospital for Women (one of Prof Beischer's very successful innovations). After retiring from private practice, he continued at the Royal Women's Hospital and assisted with private surgery. In addition to being a particularly competent specialist, he was an accomplished musician, having been a church organist in his youth. He was a keen golfer with the Royal Women's Hospital golf club, which he kept up until his heart surgery this year. He is survived by his partner Erika and Martin, Kate and Helen, the children of his former marriage, along with four grandchildren. A thorough British gentleman, he will be well remembered for his ability in so many areas and his kindness and altruism.

Dr Graeme Dennerstein
FRANZCOG

Dr Eva Irene Popper.

Dr Eva Irene Popper 1934–2019

Dr Eva Popper was born in Vienna in 1934, the only child of Erna and Felix Popper. Eva was the first female Queensland medical graduate to train and graduate in the specialty of O&G and to become a consultant at the Royal Women's Hospital in Brisbane.

She and her parents escaped from the escalating tragedy in Europe in 1938, arriving in Australia in February 1939. Her father had been sponsored by a Queensland senator who arranged for him to get a job at a local cardboard factory. The family lived under the factory manager's house.

In 1952, Eva commenced the medical course at the University of Queensland with the intention of becoming a paediatrician; however, in fifth year she was introduced to the labour ward and her lifelong love for obstetrics was born.

Eva graduated MBBS in 1957 from the University of Queensland and began two years of rotating internship at the Royal Brisbane Hospital. She applied for a registrarship in O&G at the Royal Brisbane and Royal Women's Hospitals and, in 1961, became the first woman in Queensland to be granted a position in the specialty.

Although there had been some initial opposition to her appointment by some of the senior consultants, they eventually became accustomed to a female registrar and even admitted that brute force was not a prerequisite for successful training! She had excellent teaching that she passed on to her junior resident staff and medical students with plenty of hands-on experience.

In 1962, Eva travelled to the UK and obtained her MRCOG (London), returning to Brisbane in 1963 where she commenced private practice in O&G, continuing until 1994. At first, referrals from general practitioners were slow as they had no experience of a female specialist consultant, but gradually she overcame this male prejudice and she thoroughly enjoyed her working career.

Eva estimated that she had delivered about 5000 babies, (affectionately referred to as Proper Popper Products) and many of these families became her lifelong friends.

In 1963, Eva was appointed to the Moorooka Antenatal Clinic in Brisbane, followed by appointments as visiting consultant obstetrician to Royal Women's Hospital (1964–1990) and visiting gynaecologist to Royal Brisbane Hospital (1972–1991). Eva enjoyed teaching and contributed manipulative skills and experience rather than just pure theoretical knowledge. In 1967, she was involved in the formation of a consultative clinic at the Royal Women's Hospital for the management of Rhesus sensitisation.

Judaism was central to Eva's life and her contribution to the Jewish community in Brisbane was enormous. In 2009, Eva was awarded the Queensland State Zionist Council's Rabin Award for her services to the Jewish Community and, in 2010, the Union for Progressive Judaism's Vatik Award for her services as President and for her long commitment to Progressive Judaism.

Eva had a wide range of interests that included a love of music, the fine arts and literature. She enjoyed bushwalking and birdwatching and was well travelled both overseas as well as within Australia. It was following a trip to Israel in 2015 to see relatives that she was diagnosed with lung cancer (one of the one-in-three women who develop this disease that never smoked). Eva courageously accepted the challenge, but finally succumbed on 2 March 2019. On the plaque mounted over the niche where her ashes are interred are the following words: Loved and missed by her family, friends and the community she served.

Dr Edward John Vesey
FRANZCOG, FRCOG

Dr Paul William Robinson 1966–2019

Dr Paul William Robinson was farewelled and his life celebrated by a large gathering of family, friends and colleagues at Auckland's Holy Trinity Cathedral.

Paul was the eldest of three boys, born into a farming family and raised in the Waikato. Following a very active rural childhood, he attended St Paul's Collegiate in Hamilton as a boarder and was head prefect there in his final year. On leaving school, Paul went on to Waikato University and completed a Masters degree in Technical Science. It was while at Waikato that Paul met and married his wife, Michelle.

When Michelle had an opportunity to complete postgraduate study at UCLA in California, Paul travelled as her house husband, before finding some part-time work in a diabetes research laboratory. This stimulated his interest in medicine, and with Michelle's encouragement, Paul gained entry into the University of Auckland School of Medicine on their return to New Zealand. Life was busy for Paul and Michelle as medical studies were fitted around family life, with the birth of their son Zach, later followed by daughters Meg and Kate.

An interest and aptitude in O&G as a student led to Paul pursuing a career in the specialty. He completed RANZCOG specialist training at National Women's, Middlemore and Tauranga hospitals before starting work as a specialist at Auckland City Hospital in 2007. Paul was a very able general O&G, with interests in both colposcopy and infertility. He combined his public work with a successful private obstetric practice, working energetically in both capacities.

Ever since boarding school, Paul had been keen on road cycling, a passion that remained throughout his life. He competed in many events, including the nationally renowned Tour of Southland, and had the opportunity to travel overseas to follow both the Tour de France and the Giro d'Italia.

Paul and Michelle were keen supporters of the NZ Gynae Club, attending several enjoyable meetings throughout the Pacific. They were involved at an organisational level and formed strong friendships with colleagues from all around New Zealand.

On being diagnosed with cancer in late 2014, Paul ceased his private practice, but remained a valued part-time member of the senior medical staff at Auckland City Hospital's O&G department. His preference to remain involved in his work was part of what Paul termed his work-life-treatment balance; alongside a rekindled interest in choral singing and his enthusiastic ownership of both an e-bike and an electric car. To all who knew him, his relentlessly positive attitude was an inspiration.

With a sudden decline in his health, Paul finished work just a few weeks before he died on 30 May 2019.

Paul is survived by his wife Michelle, children Zach, Meg and Kate, and his beloved dog, Cairo.

Dr Tim Dawson
FRANZCOG

Remembering Our Fellows

Our College acknowledges the life and career of Fellows that have passed away:

- Dr Phillip Edward Norman Suter, Vic, 17 August 2019
- Dr Michael David Kaye, NSW, 19 September 2019

WA/SA/NT

2020 Regional Scientific Meeting
Mirror, Mirror, on the Wall

6–8 MARCH 2020
THE VINES RESORT, SWAN VALLEY, WA

Visit the beautiful Swan Valley, WA's oldest wine region, located only 30 minutes from Perth. The meeting will feature guest speakers, workshops and opportunities to present research. Stay tuned for further details or email wa@ranzcog.edu.au

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists
Excellence in Women's Health

A RANZCOG event

RANZCOG congratulates our new Fellows

Dr Diana Ackerman
Dr Fergus Adams
Dr Sonia Anwar
Dr Sally Aubrey
Dr Kristi Bateman
Dr Sophia Berkemeier
Dr Jacqueline Brown
Dr Alison Bryant-Smith
Dr Aaron Budden
Dr Emma Chesterman
Dr Anna Clare
Dr Jesse Clifford
Dr Catherine Coffey
Dr Dean Conrad
Dr Giselle Crawford
Dr Angela Cross
Dr Catherine Dash
Dr Philippa Davey
Dr Georgina Davis
Dr Natalie De Cure
Dr Ausha De Silva
Dr Melissa Delgado
Dr Nonni Dimoska
Dr Richard Foon
Dr Julia Francis
Dr Arpita Ghosh
Dr Kate Gowling
Dr Stephanie Green
Dr Eliza Griffiths
Dr Erik Gunderson
Dr Tristan Hardy
Dr Tamara Harris
Dr Georgina Hawkins
Dr Frances Hills
Dr Sonia Hossain
Dr Arshad Hussain
Dr Amy Jamieson
Dr Cherynne Johansson
Dr Karen Joseph
Dr Albert Jung
Dr Deb Karmakar
Dr Shamitha Kathurusinghe
Samina Kausar
Dr Jodi Keane
Dr Anisha Kellogg
Dr Amber Kennedy
Dr Krishna Lalloo
Dr Fiona Langdon
Dr Wei How Lim
Dr Kent Lin
Dr Belinda Lowe
Dr Tane Luna Ramirez
Dr Jerome Mayers
Dr Rose McDonnell
Dr Andrew McIntyre
Dr Jessie McMicking
Dr Kirstin Millard
Dr Rebecca Mitchell
Dr Ali Mohamed
Dr Sarah Moore
Dr Silipa Naiqiso
Dr Jonathan Nettle
Dr Sam Newbury
Dr Tran Nguyen
Dr Brooke O'Brien
Dr Chris Overton
Dr Alexander Owen
Dr Charlotte Oyston
Dr Anupam Parange
Dr Sneha Parghi
Dr Charlotte Paull
Dr Hayley Peckston
Dr Yasmin Pilgrim
Dr Sathana Ponnampalam
Dr Amanda Poprzeczny
Dr Michelle Proud
Dr Ujvala Rao
Dr Charlotte Reddington
Dr Oybek Rustamov
Dr Amelia Ryan
Dr Maha Sabir
Dr Sumi Saha
Dr Meenu Sharma
Dr Vasi Sivagnanam
Dr Kasia Siwicki
Dr Victoria Snowball
Dr Priya Sokhal
Dr Judith Spicer
Dr Meghan Stafford
Dr Nicole Stamatopoulos
Dr Kate Strawson
Dr Anusha Sudhahar
Dr Amy Swanson
Dr Naz Syed Noh
Dr Soong Ern Grace Tan
Dr Keisuke Tanaka
Dr Emma Tetstall
Dr Elizabeth Todd
Dr Alenna Vallely
Dr Cornelis van der Wal
Dr Alia Vemuri
Dr Gian Ventresca
Dr Jorien Vercruyssen
Dr Pip Walker
Dr Amanda Ward
Dr Jason Waugh
Dr Lilantha Wedisinghe
Dr Jennifer Weishaupt
Dr Daisy Wildash
Dr Sara Yeoh
Dr Vicki Yin
Dr Monica Zen

Recognition of Outstanding Achievement in RANZCOG Examinations

Training Program	Type	Name	State
CWH	Written	Tanja Baltus	NSW
CWH	Written	Sophia Hill	NSW
DRANZCOG	Written	Jayna-Lee Garratt	WA
DRANZCOG	Written	Jessica Lawford	NSW
DRANZCOG Advanced	Oral	Danielle Crosby	SA
DRANZCOG Advanced	Oral	Stephen Tucker	QLD
DRANZCOG Advanced	Oral	Ranjita Bains	WA
DRANZCOG Advanced	Oral	Daina Waugh	QLD
FRANZCOG	Written	Sebastian Leathersich	WA
FRANZCOG	Written	Jordon Wimsett	NZ
FRANZCOG	Oral	Sarah Te Whaiti	NZ
FRANZCOG	Oral	Jennifer Rose Lyon	NZ

RANZCOG congratulates our 35-Year Fellows

Dr Bella Ajayoglu
Dr John Allan
Dr Bill Antonas
Dr Alexander Astill
Dr Michael Baird
Mr Geoff Baker
Dr John Barcham
Dr Malcolm Barnett
Dr Grahame Bates
Dr Richard Bellingham
A/Prof Pete Benny
Dr Christine Bessell
Dr Neelam Bhardwaj
Dr Tom Boogert
Dr Colin Bova
Dr Bernie Brenner
Dr Claude Calandra
Dr Ed Caldwell
Dr John Campbell
Dr Peter Caska
A/Prof Deryck Charters
Prof Christopher Chen
Dr Robert Child
Dr Howard Clentworth
Dr Maxwell Cole
Dr Tom Cottee
Dr Denys Court
Prof Alex Crandon
A/Prof John Currie
A/Prof Marg Davy
Dr Warren De Ambrosis
Prof Caroline de Costa
Dr Graeme Dennerstein
Dr Celia Devenish
Dr Paul Devenish-Meares
Dr Deepali Dhillon
Dr Al Donoghue
Prof Peter Dwyer
Dr Tom Eggers
Dr Elizabeth Farrell
Dr George Finikiotis
Dr Susan Fleming
Dr David Freidin
Dr Roald Fullerton
Dr Peter Fung
Dr Robert Garland
Dr Kenneth Geier
Dr Bruno Giorgio
Dr Michael Gordon
Dr Frederick Graham
Dr John Grey
Prof Jurgis Grudzinskas
Dr Claude Hakim
Dr Philip Hall
Dr Peter Hammill
Dr Keith Hartman
Dr Maxwell Haverfield
Dr Peter Henderson
Dr Greg Hicks
Dr Max Holsman
Dr Oscar Horky
Dr John Howland
Dr Graeme Hughes
Dr Peter Hugo
Prof Michael Humphrey
A/Prof Louis Izzo
Dr Mark Jalland
Dr Chris James
Dr Tim Jeffery
Dr Rosie Jones
Mr Max Jotkowitz
Dr George Kaladelfos
Dr Criton Kasby
Dr Joseph Keeping
Dr Geoff Kelsey
Prof Andrew Korda
Dr Irving Korman
Prof Gab Kovacs
Dr Tony Krins
Dr James Kustin
Dr Peter Kwok
Dr Eric Lai
Dr Lew Lander
Mr Michael Laney
Dr David Laurie
Dr Robert Law
Dr Mark Lawrence
Dr Gerald Lawson
Dr Leo Leader
Dr Peter Lee
Dr Chee Mun Leong
Dr Maurice Lichter
Dr Peter Lo
Dr Nick Lolatgis
Dr Andrew Mackintosh
Prof Peter Maher
A/Prof John McBain
Dr Greg McGrath
Dr Robert McKimm
A/Prof Harry Merkur
Prof Con Michael
Dr Geoffrey Moss
Dr Anthony Murphy
Dr John Mutton
Dr John Neil
Prof John Newnham
Prof Jeremy Oats
Prof Mike O'Connor
Dr Vivienne O'Connor
Prof Colm O'Herlihy
Dr George Olesnicky
Dr Kar Ooi
Dr Robert O'Shea
Dr Ross Pagano
Dr John Palmer
Dr Isidor Papapetros
Prof Roger Pepperell
A/Prof Ossie Petrucco
A/Prof Ian Pettigrew
Dr Gordon Pullin
Dr Sujon Purkayastha
Dr Jay Rao
Dr Rajann Rasiah
A/Prof Leslie Reti
Dr Ian Roberts
A/Prof Robert Rome
Dr Solomon Sahhar
Dr John Salmon
Dr John Schmidt
Dr Paul Shekleton
Dr Jock Shumack
Dr Stephen Steigrad
A/Prof John Svigos
Dr Gary Sykes
Dr Richard Tai
Dr John Taylor
Dr Derrick Thompson
Dr Michael Tomaszewski
Prof Brian Trudinger
Dr Paul Truscott
Dr Ian Tucker
Dr Malcolm Tucker
Dr Simon Turner
Dr Diana Wellby
Dr John Wilson
Prof Don Wilson
Dr Thomas Wright
Dr Len Yared
Dr John Yovich

College Statements update July 2019

Revised College Statements

The following statements were approved by RANZCOG Council and Board in July 2019:

Use of Rh Isoimmunisation (C-Obs 6)
Revisions include:
- Updated references

Categorisation of urgency for caesarean section (C-Obs 14)
Revisions include:
- Updated references
- Inclusion of new section 3.2 relating to clinical capability framework and hospital infrastructure
- Inclusion of new section 3.3 providing guidance on intrauterine resuscitation while waiting for theatre
- Inclusion of new section on communication

Maternal Group B Streptococcus in pregnancy: screening and management (C-Obs 19)
Revisions include:
- Updated references
- Removal of paragraph that discussed vaginal seeding at elective LUSCS
- Inclusion of new section 5.7 relating to water birth and water immersion, aligned to College statement C-Obs 24
- Inclusion of new section 5.8 relating to high-risk women declining intrapartum antibiotic prophylaxis
- Inclusion of new section 5.9 relating to women with previous carriage of GBS.

Prenatal screening for fetal genetic and structural conditions (C-Obs 35)
Revisions include:
- Updated references
- Inclusion of carrier screening counselling

Pre-pregnancy and pregnancy related vaccinations (C-Obs 44)
Revisions include:
- Updated references
- New recommendation on healthcare worker vaccination.

Tamoxifen and the endometrium (C-Gyn 12)
This statement has undergone a rewrite due to the new evidence and number of suggested changes.

Guidelines for performing gynaecological endoscopic procedures (C-Trg 2)
Revisions include:
- Additional sentence relating to credentialing due to correspondence and feedback from Fellows

Consent and provision of information NZ (C-Gen2B)
Revisions include:
- Updated references

Clinical Handover (WPI 19)
Greater emphasis on the New Zealand setting

A full list of College statements can be viewed at www.ranzcog.edu.au/Statements-Guidelines.

RANZCOG Patient Information

There are 39 RANZCOG patient information pamphlets, including the Pregnancy and Childbirth pack of 18 pamphlets, now available. All of these products can be viewed and ordered from: www.ranzcog.edu.au/Womens-Health/Patient-Information-Guides/Patient-Information-Pamphlets.

The following titles were approved for publication and are now available:
- Genetic Carrier Screening
- Gestational Diabetes

Prof Yee Leung
Chair
RANZCOG Women's Health Committee