Vol. 24 No. 1 | Autumn 2022

a **RANZCOG** publication

O&G MAGAZINE

Vol. 24 No. 1 Autumn 2022

Editorial Communications
O&G Magazine Advisory Group
RANZCOG
1 Bowen Crescent
Melbourne, VIC 3004 Australia
(t) +61 3 9417 1699
(e) OGmag@ranzcog.edu.au

Advertising Sales
Minnis Journals
(t) +61 3 9836 2808
(e) minnis@minnisjournals.com.au

Printer
SouthernImpact
(t) +61 3 8796 7000

O&G Magazine authorised by Ms Vase Jovanoska

For further information about contributing to *O&G Magazine* visit: ogmagazine.org.au.

ISSN 1442-5319

The College

Blood

RANZCOG acknowledges and pays respect to the Traditional Custodians of the lands, waters and communities across Australia, on which our members live and work, and to their Elders, past, present and future.

Women's health

The College

RANZCOG recognises the special status of Māori as tangata whenua in Aotearoa New Zealand and is committed to meeting its obligations as Te Tiriti o Waitangi partners.

From the President

Dr Benjamin Bopp
President

This issue of *O&G Magazine* takes the theme of Blood and covers, amongst others, such diverse topics as postpartum haemorrhage and its management, thromboembolism, thalassaemia, and cord blood collection.

In a display of excellent timing, there will also be an article detailing periods after covid vaccination!

We also welcome the first article submitted by the RANZCOG Consumer Network Working Group. I am sure clinicians will appreciate the perspective of postpartum haemorrhage as elaborated by consumers from their real-life experience.

And so, it seems 2022 has started pretty much the same way as 2021 – under the shadow of a worldwide pandemic, now with another new, faster spreading variant that requires booster vaccinations to tackle effectively.

Locally, Australia has spent a festive season under the pressure of Omicron. Over a few weeks, single-digit, daily case and fatality numbers escalated to tens of thousands, leaving medical and other resources under severe strain.

At the two-year mark, there has been over 350 million confirmed COVID-19 cases worldwide and 5.5 million deaths. Our colleagues in New Zealand, much like Queensland and Western Australia in late 2021, have prepared for the coming wave.

One of our new reality's tools, the Zoom meeting, has come to the fore with a binational link up of New Zealand and Australian based members held to assist with pandemic planning.

Again, the College acknowledges the great work and leadership undertaken by members, particularly in New South Wales and Victoria. These teams not only dealt with the extensive challenges of the pandemic locally but also shared their experiences, expertise, advice and management knowledge with colleagues in more sheltered jurisdictions.

When we look back at this challenge, we realise necessity truly is the mother of invention and how willingly the RANZCOG family supports its members.

Iron deficiency and infusion is another interesting topic covered in this issue.

It's noteworthy how our routine approach to certain issues changes over time. Ten years ago, standard practice was only oral iron supplementation for those felt to have a low haemoglobin in pregnancy, but we did not religiously pursue iron status.

For some, much like vitamin D before it, iron deficiency in pregnancy may come across as a bit 'flavour of the month'.

Has our attention been focused on a seemingly peripheral matter, or does this have real merit?

Ironically, the pregnant population appear extremely keen, accepting, and responsive to advice regarding iron infusion in pregnancy whilst at the same time show an ongoing resistance or hesitancy to be vaccinated against Covid!

This conclusion seems not to reflect an informed assessment of the relative risks of Covid infection versus iron deficiency in pregnancy or the complication profiles of vaccination versus iron infusion.

February will have seen orientation of our new Australian FRANZCOG trainees, their colleagues in New Zealand having commenced late last year. Welcome all!

We will also have officially opened our new College Place – 1 Bowen Crescent Melbourne.

College Place is a modern, open plan, fit-for-purpose building representing a strong investment in our future.

Thanks to the members and staff who have worked tirelessly under difficult circumstances over the last two years to realise this significant new chapter in the history of RANZCOG.

A pandemic, by definition, does not last forever and hopefully this year will see us all have the opportunity to gather at our new College home.

As always, thank you to the team at *O&G Magazine* and please, enjoy this issue and keep safe and well.

From the CEO

Vase Jovanoska
Chief Executive Officer

It is a pleasure to welcome everyone to the first issue of *O&G Magazine* for 2022.

I would firstly like to extend my appreciation and acknowledgment to our members and trainees who have continued to work in a healthcare system that is under immense pressure with the current covid outbreak. Your commitment to our community does not go unnoticed and the College is here to continue to provide you with the support that you need.

We continue to work with the Australian Technical Advisory Group on Immunisation (ATAGI) and New Zealand Aotearoa Ministry of Health, in advocating vaccination for pregnant women. We also welcomed the temporary extension of telehealth in Australia, and we are advocating for this support to be made permanent.

In 2022, we look forward to launching our 2022–2024 Strategic Plan which will set the College's focus and objectives for the next three years. At the time of writing this article, the draft plan is out for wide consultation and feedback from our RANZCOG members, trainees, staff, and external stakeholders. This follows a very successful consultation period with the College's newly formed 12th RANZCOG Board and Council who spent much time workshopping and then reviewing the draft plan.

We recently welcomed our new trainees in Aotearoa New Zealand and in Australia who have recently taken part in their orientation sessions; we wish them every success with their training. The College is here to support our trainees and we encourage you to contact us with any queries you may have.

We are currently working on the Australian Medical Council (AMC) and Medical Council of New Zealand (MCNZ) Accreditation Progress Report with multiple stakeholders and committees across the College. The report is due in March. This report is part of our yearly reporting to regulatory bodies the AMC and MCNZ before we have our full reaccreditation submission the following year.

In 2022, the College will continue to run our exams and try to accommodate individual trainees' requirements as much as possible while we continue to navigate new challenges presented by the recent covid outbreak. At the same time, our exams and IT team are working on improving our systems and processes and creating efficiencies. We encourage and appreciate all your feedback on service delivery and look forward to continuing to engage with you this year.

The RANZCOG Symposium 2022: New Perspectives, is scheduled for 28 February to 1 March. It will be delivered in a hybrid model and will showcase many key informative and topical sessions including on Wellbeing, Pelvic Pain and Endometriosis, Indigenous Australian and Māori Health, Obstetric Trauma to name a few. You will hear from an impressive line-up of experts in O&G, and see excellent Free Communication and ePoster presentations.

The Symposium is set to coincide with the Fellowship ceremony, and the long-anticipated official opening of 1 Bowen Crescent Melbourne. Over the last two years we haven't had the opportunity to hold these special ceremonies and it will be great to be able to hold them this year, to celebrate your achievements. Our Diplomates will be presented at their own special ceremony in October.

I would like to congratulate all our new Fellows and Diplomates and wish them a successful career in O&G. The opening of Bowen Crescent will be marked with a Welcome to Country and smoking ceremony, prior to the unveiling of the official new name of the building. We look forward to welcoming you to your new College home, taking you on a tour and enjoying connecting with each other.

I would like to thank the 12th Council and all 12th Council Committee members for their hard work and dedication to the College; we aare grateful for your contribution, your time and commitment. Finally, I would like to acknowledge our College Board and RANZCOG President Dr Ben Bopp, for their exemplary leadership and support.

The start of 2022 may not have been what we expected, but we will get through it, and have hope for a bright and promising year.

LEADERS IN FOCUS

Dr Nisha Khot
MBBS, MD, FRCOG, AFRACMA, FRANZCOG

This feature sees Dr Nisha Khot in conversation with women's health leaders in a broad range of leadership positions. We hope you find this an interesting and inspiring read.

Join the conversation on Twitter
#CelebratingLeadership @RANZCOG @Nishaobgyn

Dr Neelam Bhardwaj FRANZCOG

I first heard of Dr Neelam Bhardwaj when I moved to Melbourne in 2010. In casual conversation with my next-door neighbour, a lady of Sri Lankan origin, she realised that I was an O&G and shared the story of her mother who had arrived in Australia in the 1970s, having completed a degree in pharmacy in Sri Lanka. Finding herself pregnant soon after arrival, she had tried very hard to find a doctor who would provide culturally appropriate care. At the time, Dr Bhardwaj was one of only two female obstetricians of subcontinental origin in Melbourne and had been a comfortable choice. Years later when my neighbour was pregnant, she didn't think twice about choosing Dr Bhardwaj for pregnancy care. I was fascinated by this story of an O&G who came from my part of the world and had helped bring two generations of the same family into this world. When I eventually met Neelam, she was a soft-spoken, gentle and kind person willing to take a newly arrived doctor like me under her wing.

This column has over the last three years featured many specialist leaders in O&G, but this is the first time we are featuring a woman IMG of Indian origin. The White Australia policy meant that non-white IMGs only arrived in Australia in the 60s and 70s. Many of them faced (and continue to do so) racism, discrimination and bullying. They rarely brought up these issues, choosing instead to focus on their work and their family. Their contribution to the Australian healthcare system cannot be overstated.

IMGs like Dr Bhardwaj were in truth, the embodiment of Donald McGannon's famous quote, 'Leadership is action, not a position.' They may not have held the traditional leaderships positions of Clinical Director, Executive Director etc but, by their actions, they laid the foundations for future generations of IMGs (myself included) to embrace leadership in all its forms. They gave us the confidence to speak up against discrimination and racism.

Australian healthcare has a long way to go to achieve true equity, diversity and inclusion. If you feel otherwise, I gently suggest that you do a back-of-envelope exercise: count the number of women of colour in leadership positions in your department and divide this number by the total number of women of colour in the department. Do the same with other groups for comparison. Any department that has a large non-white staff with predominantly white leaders has a problem. Any department that has a large female staff with predominantly male leaders also has a problem. Add the two problems together and a very uncomfortable picture emerges. We should not shy away from this. Instead, we should call it out and address it. The time for lip-service is past, it is now time for action.

I want to know about your early years. Where did you grow up? Where did you do your basic medical training?

I was born in India. My father was a WWII fighter pilot and, in his civilian life, in-charge of the airports in India and frequently required to move to different cities. This meant that as a young girl, I travelled all over India and got to experience the rich diversity of the country. We ultimately settled down in India's capital city, New Delhi and this is where I did my senior school years and basic medical training. I am very fortunate to be an alumnus of the prestigious Maulana Azad Medical College in New Delhi, lovingly referred to as MAMC (M'aam C). The foundation stone for MAMC was laid in 1959 at the site of the old Delhi Central Jail which had seen its share of political prisoners, arrested for their role in India's freedom struggle. The College bears the name of India's first education minister, Maulana Abul Kalam Azad. It was officially opened in 1961 and its first batch of graduates had 60 students. I belong to one of the batches in the first decade of its existence to complete MBBS from this institution.

(Author's note: I digress with a nugget of information for readers about another medical college located in Delhi called the Lady Hardinge Medical College. Established in 1916 and named after Lady Hardinge, the wife of the then Viceroy of India, Baron Hardinge, this was and still is a medical college just for women. Lady Hardinge recognised the challenges that women in India in the 1900s faced with access to higher education and raised funds to set up a medical college exclusively for women. Sadly, she

passed away in 1914 and did not live to see the college inaugurated. The first batch consisted of 16 women students and the college has maintained its reputation as a premier medical institution).

What was your journey as an IMG and why did you choose to specialise in O&G?

I completed my internship in 1972 in India and immediately after, moved to Melbourne. I had arrived too late in the year to be able to apply for a training position. The resident jobs in O&G for the year had already been allocated. So, initially I did a stint in psychiatry and haematology. It turned out to be a great experience because I learned how the Australian health system worked and also got to make some friends. I joined the Queen Victoria Hospital in Melbourne in 1975 as a trainee in O&G. I was one of only five women trainees in O&G in Victoria and the only IMG.

As an undergraduate in India, I had seen firsthand the lack of good medical care for women during my O&G rotation. We had a whole ward dedicated to women with puerperal sepsis. Women would come in bullock carts from the villages in obstructed labour and it would take them two days to get to the hospital. Women would have evacuations for incomplete miscarriages performed with no anaesthetic because it was not considered worthy of the time and effort of going to theatre for an evacuation. These experiences made a huge impact that stayed with me even after I left India. I was inspired to follow in the footsteps of two inspiring women Professors of O&G in India during my undergraduate years who were expert clinicians and empathetic communicators. And yes, India had world-renowned women Professors of O&G before Australia!

What was your experience of training in O&G in Melbourne in the mid-70s?

It was not easy competing with local graduates for a training position in O&G. I was an outsider, I had no local connections, no one knew me. I had to start at the beginning and prove myself. Initially, it was slow, time consuming and repetitive. As I gained more confidence, I was able to apply for a training position. Along the way, I made lifelong friends and mentors. My training was a little fragmented with rotations to the old PANCH hospital in Preston and Western General Hospital in Footscray, rather than concentrated at a single tertiary hospital. This was the only option available to me at the time and I embraced all my rotations happily because each provided a unique learning opportunity.

As a woman and an IMG, did you experience discrimination and how did you deal with it?

I had an advantage in that although I was an IMG, my postgraduate training was in Australia. This helped a lot because it was recognised as being local experience. I suppose if I had come to Australia as a fully qualified specialist, I may have faced questions and suspicions about the validity of my training. I did not experience blatant racism or discrimination but there was certainly an undercurrent of it. When I applied for registrar positions, I was asked about my plans to have a family. This was considered a very valid question to ask at an interview! When I first arrived in Melbourne, I didn't have any formal Western clothes, so I wore one of my nicest sarees for an interview. I was asked, 'How on earth do you deliver babies in that?'

Some perceptions were very entrenched. I remember a time when I was called to assist a colleague at caesarean section at the old St Andrews Hospital. We were in scrubs and had just made a cup of coffee while discussing the case we were about to start. A senior male obstetrician walked in and asked us to make him a cup of tea. He was very polite, of course, just like he would have been with the tea ladies, which he presumed we were because of our ethnicity. I think these perceptions and biases have changed over time.

There were instances when you would be overlooked for senior leadership positions although you were better qualified and had more experience than the person who eventually got appointed to the position. At the time it was disappointing but there were very few avenues for formal complaints. In the 70s, it was pretty much take-it-or-leave-it. Over the years, we all faced racism and gender discrimination to a lesser or greater extent and now, as we mature, we face ageism. So, I can say that I have now faced the full triad of the 'isms'.

But despite these challenges, migrant doctors have made massive contributions to the Australian health system, both in public healthcare and private healthcare. The presence of migrant doctors has contributed greatly to the understanding of the health needs of migrant communities and develop a greater empathy for women who are vulnerable, who don't have family supports, who don't speak English, who depend on family members for financial security. Migrant doctors have been a success story and have raised the profile of the entire migrant community. Australian trainees have benefitted from

the wealth of experience that migrant doctors bring with them and are able to impart to trainees who will probably never encounter those rare conditions and complications in their clinical practice in Australia.

How did you cope with being far away from your own family?

In the 70s, my weekend on-call shift started on a Saturday morning and finished on Monday afternoon. They were long, tiring hours but we didn't know any different then. These long hours didn't leave much time to brood over things that you were missing. In those days, keeping in touch with family in India was not easy. If you wanted to make a phone call, you had to be connected by an operator and the phone calls were very expensive. You could only afford to make phone calls once a month. But the excitement of learning surgical procedures and acquiring new skills kept me going.

When I finished training and was just setting up a private practice, my marriage ended. I found myself in the unenviable position of being a single medical mum with no family support and an obstetric private practice. At that point, I was seriously considering giving up my practice. Fortunately, my parents took it in turns to come to Melbourne and live with me for the next decade, helping me bring up my two boys while still maintaining my practice so I had an income. I also had really supportive colleagues who became my Australian family and helped me not just with the practicalities but also on an emotional level. I would not have been able to manage on my own and I owe my parents not just my success but also the success of my sons. My boys grew up knowing that there was always a grandparent at home when they came back from school, and it made all the difference to them.

What has given you the greatest joy?

My work has always been my source of joy. Even after a tiring night on-call, I always leapt out of bed in the morning with a sense of excitement about what the day would bring. Having the confidence that you were really making a difference in the lives of those who trusted you with the most precious time in their life, when they were having a baby, was a very special feeling. And when they referred their sisters, friends, aunties, cousins, daughters and even granddaughters to you because of this trust and the belief that you would be able to help, that gave me the greatest joy of all. I had a solo O&G practice for 33 years and have looked after two and sometimes, three generations women from the same family. I feel very privileged to have had these wonderful experiences.

What has been your involvement with RANZCOG or other organisations?

I have contributed locally on city councils, health committees and boards. I am a founding member of a charity called Disha (www.disha.org.au) that raises funds for worthwhile causes like vital equipment for hospitals in Melbourne including The Royal Children's Hospital and The Royal Women's Hospital.

I have enjoyed training and mentoring a new generation of specialists in O&G. I have been an examiner for undergraduate medical exams as well as fellowship exams for RANZCOG. I have presented at meetings and conferences. The highlight for me was a trip to Mongolia, meeting the doctors there and helping establish a colposcopy facility at a women's hospital in their capital city, Ulaan Baatar.

Dr Neelam Bharadwaj.

Raising my family as a single mother while maintaining a busy obstetric practice left very little time to get involved in major roles within RANZCOG or in other organisations. So, I didn't put my hand up for these roles. It is heartening for me to see young consultants participate in RANZCOG leadership and help shape the future of O&G training in Australia. I know we have come a long way in addressing some of the barriers that existed when I was a newbie but there is more to be done.

What advice do you have for junior doctors or medical students considering a career in O&G?

This discipline is one that is full of opportunities and the different subspecialties mean that there is so much choice available for each trainee to go down a unique path. Trainees often worry about quality of life and work-life balance given the long hours. But I think the future is one of group practice rather than solo practice. Patients are embracing this model as well. I would encourage medical students and junior doctors to not be put off by the thought of long hours.

My other bit of advice is to never underestimate the importance of lived experience. Simulation and reading are a very important addition, but they can't replace real patient interactions. Hands-on experience is the most valuable and will teach you lessons that will stay with you for a lifetime. If you are

interested in O&G, spend as much time as you can during your rotations speaking to patients, assisting in theatre, caring for women in labour and postnatally. I acknowledge that the pandemic has severely affected the ability to get hands-on experience and I hope we will find ways to make up for lost time.

If you could go back in time, is there anything you would do differently and why?

I never appreciated the potential of this new (at the time) discipline called IVF. It was being born in front of my eyes, but I didn't realise how important it would become. Looking back, I am amazed at the speed with which the science has progressed. I wish I had had foresight and not been so involved with obstetrics at the time. I would have loved to explore fertility treatment options and study reproductive technology.

Your career has spanned a time of significant change in O&G. Could you describe your experience of managing these changes?

Yes, there have been many, many changes in the 35+ years that I have been practicing as a specialist O&G. If I describe some of the things that were the norm in the 70s, you will find it difficult to believe that I am talking about Melbourne and not some medieval town. The 70s and 80s were a time when our thinking about women's health and practice of O&G grew by leaps and bounds. I had the great pleasure and privilege of learning with the great pioneers in our specialty. Indulge me here while I reminisce...

The first CTG machines (from memory) were installed in the Queen Victoria Hospital in the mid-70s. Prof Carl Wood had learned about this new method of monitoring the fetus in labour and he was the one who introduced CTG monitoring to Victoria. At the time, we could only capture the fetal heart activity by attaching a little screw in the baby's scalp. It would often fall off when the patients were writhing in labour and had to be put back on. We used guarded surgical blades to get fetal blood from the scalp for testing of pH. Labour analgesia for primigravidas was heroin! Multis got morphine but can you imagine using heroin as routine analgesia?! We used black silk sutures for episiotomies and one of my jobs as a Year 1 resident was to go from bed to bed with my trolley removing these sutures. These wards were the old Nightingale wards with beds separated by curtains so there was very little privacy for women. Ultrasounds hadn't been introduced to Melbourne hospitals, so we diagnosed placenta previa by X-ray after placing a metal grid on the woman's abdomen and using a complicated way of measuring where the fetal presenting part was in relation to the grid and trying to work out where the placental edge was. Amniocentesis was done on the ward by the resident, without ultrasound guidance. We palpated the mother's abdomen and used our hands to work out a 'safe' place to put the needle in! We were doing amniocentesis for L:S ratio (Lecithin:Sphingomyelin) to decide timing of delivery by calculating lung maturity. Laparoscopic surgeries were the new thing and we used unipolar diathermy for tubal sterilisation. This gave way to the use of the Fallope ring for the same procedure. This was also the time when IVF was just starting to take shape as a real option for management of fertility.

Another welcome change was that menopause became a real thing! There had never been any menopause clinics anywhere in the country and women were usually expected to put up with symptoms. The only help they had was the various traditional medicines, potions and creams sold over the counter, most of which didn't work. I first heard of a dedicated menopause clinic at Prince Henry's Hospital. As an aside, the fact that most of the hospitals I have mentioned no longer exist is also symbolic of the changes that have occurred in the last 50 years.

Leboyer births were all the rage in the 70s. Dr Frédérick Leboyer, a French physician, had published *Birth Without Violence* in 1974 in which he argued that babies felt pain, anxiety and suffering and that the manner in which they came into the world shaped the adults they would become. His method involved keeping the birth room dimly lit and quiet, to reduce sensory overload on the baby, not holding the baby upside down and spanking its bottom or whisking it away to be examined immediately after birth (these were all the norm at the time). Dr Leboyer drew a lot of scorn from the medical fraternity at the time, but practice did change.

Trends came and went, and we had to evolve with these changes. In my time, we all started as generalist O&Gs. Subspeciality training was not an option. Usually, with time and experience, some of us developed special interests, but the majority stayed in a generalist role. All the technology and knowledge that we now have available to us was in its infancy at the time. It was a very exciting time. You really didn't know what would come next. To cope with the rapidly changing scenario, you had to be open: to learn new things, to trial new technology, to accept that there could be a better way to do a particular procedure. You could not have a closed mind. You had to keep up with new information and remember, at the time, information was either in the form of a journal or presented at a conference. If you came across a rare condition, you had to go back to your trusted texts and read up about it. Access to information was not easy but you tried your best to keep up and stay abreast of all the emerging research.

What are your future plans as you approach retirement?

I am currently working part-time doing office gynaecology and dermo-gynaecology. I am looking forward to spending more time playing tennis, learning to bake, catching up on reading, going to galleries and live theatre. Most of all, I am looking forward to not missing out on all the milestones achieved by my grandchildren. Looking back, I missed some of my sons' milestones because I was at work. I have made up my mind that I don't want to repeat that with my grandchildren. I have six gorgeous grandchildren and I am really looking forward to being part of their childhood and growing years.

He Hono Wāhine

He Tāngata (The People)

Dr Leigh Duncan (Ngā Mahanga, Taranaki Tūturu)
MBChB (Otago), Dip. Obs (Auckland), MRCOG, FRANZCOG
Chair of He Hono Wāhine

Bailey Parata (Ngāi Tahu, Te Atiawa)
Kaitohutohu Hauora Wāhine Māori
Māori Women's Health Advisor

Whakapapa is not just about past ancestors and blood relatives, it is also a person presently, and their future. Whakapapa literally means 'to make layers' but is translated as genealogy. Whakapapa explains the many layers of a person, their tinana (body), wairua (spirit), consciousness (hinengaro) and whānau.

History of the physical whakapapa

Predominantly, Māori narratives point to the creation of Hineahuone as the origin of the human body. Hineahuone was formed from clay by Tāne.[1] Hineahuone derives from the words 'Hine' (woman), 'ahu' (to originate) and 'one' (clay).[2] Hineahuone therefore means 'woman originating from the soil'. Tāne blew his mauri (life force), into the mouth and nose of Hineahuone, this mauri gave life to her organs and initiated the beating of her heart.[3] Often at the end of Karakia (prayer, ritual) you will hear 'Tīhei Mauri Ora' (the sneeze/breath of life).

The sacrality of the body, especially a woman's body, is due to its ability to bring new life into the world. In times of a higher risk of injury, the level of tapu (sacred, restricted) would increase to keep that person safe. For instance, at the time of sickness, a woman's menstruation, pregnancy, and death. Different times of life can bring different levels of tapu, this same idea is evident with different parts of the body. This also relates to the removal of body parts, and the importance of checking whether patients would like to receive these back, or what they are comfortable with in regard to disposal.

The placenta after birth is a common example of the importance of returning body parts. The te reo Māori word for placenta is whenua. This also translates to land. As all life is born from Papatūānuku (Earth Mother), the whenua is often returned to Papatūānuku by the whanau and buried in a significant place as a reciprocal relationship of the new-born pēpi (baby), and the whenua in which they come from. This is again a very important conversation to have with whānau in regard to their personal wishes regarding placenta and other body parts. Whānau may also have wishes regarding their body parts or fluids not leaving the whenua (land, Aotearoa New Zealand) for testing. For example, the NIPT testing. Communicating the consent process and testing process with whānau is important at every step.

Te Awa Atua is the study of menstruation in pre-colonial Māori society, available for those who may be interested. This book examines stories about menstruation located in iwi histories, oral literatures, ceremonies, and rites. The author, Ngāhuia Murphy, suggests menstruation as a medium of whakapapa (genealogy) that connected Māori women to atua (gods).[4]

Tapu cannot be discussed without the connection to noa (unrestricted). Tapu and noa are often seen as the opposite of one another; however, these are more concepts that are complimentary of each other. Whakanoa (remove tapu) is needed when something is out of balance, or to tapu for it to be safely handled. Therefore, whakanoa acts to restore the tapu/noa harmony.[5] Certain elements can be used in the action of whakanoa, including water, food, karakia. Such processes of whakanoa can be seen where water is left at the exits of urupā (cemetery) to 'neutralise' a person from the tapu of death upon exiting.[6] Tapu, noa and whakanoa have important roles within Māori thought processes and often guide action and behaviours.

Whakanoa is also very important in clearing environments of tapu. Many hospitals and care facilities will use the process of whakanoa to clear an environment after someone has died as this is a very meaningful practice for some whanau. This process can be done by almost anyone, however it is important to involve whanau in decision making on who and how to complete whakanoa. Most hospitals in Aotearoa New Zealand will have a team or person you can contact to learn more about this process, and who can support whanau during this, and other, te Ao Māori tikanga (custom).

Whakapapa and whānau

One of the foundations of whānau is whakapapa, which has great importance in te Ao Māori. Whakapapa places people 'in the whole context of relationships and therefore how we relate to each other and how we should work with each other, argue with each other, live with each other'.[7]

Whakapapa allows relationships to be established and maintained. This can be done with close or distant whanaunga (relatives), as well as physical places of significance to hapū, whanau, and iwi, for example mountains, rivers, and oceans.

Meihana model and whānau in clinical settings

The Meihana Model is a clinical assessment tool that can be utilised by medical practitioners. The Meihana Model places whānau at the heart of the assessment and intervention processes. The patient is not an individual but a part of a collective. The model discusses the importance of engaging with the wider family as parts of the assessment and treatment processes. Whānau should also be involved in time to identify what level of integration of cultural input they want in their care.

RANZCOG are fortunate enough to work alongside MIHI (Māori/Indigenous Health Institute) of the University of Otago, who offer all RANZCOG trainees and Fellows a cultural competence course. This course discusses the Meihana Model in depth and connects the use of the model in clinical O&G settings.

Sign up information can be found here: www.otago.ac.nz/continuingeducation/otago731565.html

References

1. Keane B. Traditional Māori religion – ngā karakia a te Māori - Ngā atua – the gods. Te Ara - the Encyclopaedia of New Zealand. Available from: www.TeAra.govt.nz/en/traditional-maori-religion-nga-karakia-a-te-maori/page-1
2. Te Ahukaramū Charles Royal. Papatūānuku – the land - Papatūānuku – the earth mother. Te Ara - the Encyclopaedia of New Zealand. Available from: www.TeAra.govt.nz/en/artwork/11431/hineahuone-and-tane
3. Rāwiri Taonui. Ranginui – the sky - Ranginui as knowledge and life. Te Ara - the Encyclopaedia of New Zealand. Available from: www.TeAra.govt.nz/en/artwork/5173/tane-breathes-life-into-hineahuone
4. Murphy N. Te Awa Atua, Te Awa Tapu, Te Awa Wahine: An examination of stories, ceremonies and practices regarding menstruation in the pre-colonial Māori world. (Thesis, Master of Arts (MA)). University of Waikato, Hamilton, New Zealand. 2011. Available from: https://hdl.handle.net/10289/5532
5. Barlow C. Tikanga whakaaro – Key concepts in Māori culture. Auckland: Oxford University Press. 1991. Cited in: Courtney Sullivan (2017). Hauiti Hakopa, Internship report, University of Otago, Te Koronga www.maramatanga.co.nz/sites/default/files/project-reports/Sullivan%2C%20Courtney%20-%2017INT02%20-%202017%20-%20PDF%20Report.pdf
6. Sullivan CLT. Te okiokinga mutungakore – The eternal rest: Investigating Māori attitudes towards death. MA Thesis. University of Otago. 2012. Cited in: Courtney Sullivan (2017). Hauiti Hakopa, Internship report, University of Otago, Te Koronga www.maramatanga.co.nz/sites/default/files/project-reports/Sullivan%2C%20Courtney%20-%2017INT02%20-%202017%20-%20PDF%20Report.pdf
7. Quoted in Joan Metge, New growth from old. Wellington: Victoria University Press, 1995. Cited in: Tai Walker. Whānau – Māori and family - Whānau, whakapapa and tribal structure. Te Ara - the Encyclopaedia of New Zealand. Available from: www.TeAra.govt.nz/en/whanau-maori-and-family/page-4

Subspecialty Committees Election Results

Gynaecological Oncology (CGO) Subspecialty Committee — Early Career CGO Subspecialist Representative	Dr Shih-Ern Yao
Gynaecological Oncology (CGO) Subspecialty Committee — Subspecialist CGO Representatives	Dr Vivek Arora Dr Russel Hogg
Obstetric and Gynaecological Ultrasound (COGU) Subspecialty Committee — Early Career COGU Subspecialist Representative	Dr Edward O'Mahony
Obstetric and Gynaecological Ultrasound (COGU) Subspecialty Committee — Subspecialist COGU Representatives	Dr Sashi Siva Dr Jacqueline Chua Dr Stanley Ng
Reproductive Endocrinology and Infertility (CREI) Subspecialty Committee — Early Career CREI Subspecialist Representative	Dr Unmandani Gupta
Reproductive Endocrinology and Infertility (CREI) Subspecialty Committee — Subspecialist CREI Representatives	Dr Michele Kwik Dr Marcin Stankiewicz Dr Gregory Phillipson
Maternal Fetal Medicine (CMFM) Subspecialty Committee — Early Career CMFM Subspecialist Representative	Dr Lindsay Edwards
Maternal Fetal Medicine (CMFM) Subspecialty Committee — Subspecialist CMFM Representative	Dr Phillipa Kyle Dr Emily Olive Dr Carol Portmann
Urogynaecology (CU) Subspecialty Committee — Early Career CMFM Subspecialist Representative	Dr Bernadette Brown
Urogynaecology (CU) Subspecialty Committee — Subspecialist CMFM Representative	Dr Peta Higgs Dr Fay Lin Chao Dr Salwan Ali-Salihi

Editorial

Dr Sue Belgrave
MBChB, MRCOG, FRANZCOG, DDU

When I thought about writing an editorial for this issue of *O&G Magazine,* I was reminded of all the scary times over my career when bleeding was catastrophic and life threatening. I am also aware of the progress we have made in managing these clinical situations resulting in better outcomes for women.

Blood is vital to life, and for centuries we have known that if we lose too much of it, we die. Blood has its strict medical definition, but in literature and in day-to-day use it has a much wider meaning to include such things as lineage and passion. Examples we hear commonly: makes my blood boil, her blood ran cold, you can't get blood out of a stone, they have blood on their hands, we need new blood, he is my blood brother and blood is thicker than water.

Early in my career, I had exposure to several incidents of massive haemorrhage. Most O&Gs spend their careers preventing blood loss, whether it be from menstruation, early pregnancy complications, during and after childbirth or related to surgery. We rely on the ability to transfuse blood and other blood products such as platelets and cryoprecipitate to get us out of trouble and save the day.

Whatever branch of medicine we consider, it is interesting to review the history and development, leading up to what we take for granted today. In 1628, an English physician discovered how blood circulated through the body. The earliest blood transfusions occurred in 1665 and the first human blood transfusion was performed in 1795.The first successful blood transfusion was recorded in 1818 by James Blundell, a British obstetrician who transfused a mother with postpartum haemorrhage using her husband's blood.

In later transfusions, two main problems were identified: collected blood clotted and half the patients had severe reactions.

In 1900, Karl Landsteiner discovered three human blood groups and was awarded the Nobel Prize for medicine for this in 1930. AB was discovered by two of his students in 1902. Soon after, Reuban Ottenberg used blood typing and cross match for the first time.

Transfusions in surgery began in 1903. In 1916, Rous and Turner introduced a citrate-glucose solution that, when added to collected blood, allowed it to be stored and refrigerated for several days before being transfused. In 1926, the British Red Cross instituted the first human blood transfusion service in the world. The first blood bank was established in Leningrad in 1932. The rhesus system was identified in 1939 and named in 1940. By 1950, plastic bags replaced bottles and there have been many advances since. Whole blood fractionation techniques provided the means for efficient use of the various components. Blood is now routinely tested for hepatitis and HIV.

As a trainee intern working in the UK, I met a young woman in hypovolaemic shock from intra-abdominal bleeding secondary to a ruptured ectopic pregnancy. She was Jehovah's Witness and her family refused blood transfusion for religious reasons and reminded us of this, as we ran down the corridor on our way to theatre. I was shocked and did not understand how a family could allow a young woman to die rather than giving her a blood transfusion. We now have much better understanding of Jehovah Witness belief, patient autonomy, the use of advance directives, ways to minimise blood loss, cell saver use, multidisciplinary management protocols and ways to improve oxygenation.

Blood seen outside the body is a clear red flag, visible to everyone including the patient and her family and almost certainly leads to action. Hidden blood loss is harder to recognise but just as important. I looked after a woman who lost more than twice her blood volume into her retroperitoneal space after a vaginal

birth at home. There was no visible bleeding. My previous clinical experience enabled me to recognise what was happening, make the diagnosis and resuscitate her successfully. Her predominant early symptom was severe pain which occurred well before the tachycardia and hypotension. Healthy women with normal haemoglobin and iron stores can lose a vast amount of blood before they decompensate. I learnt this as a student seeing two litres of measured postpartum haemorrhage immediately after delivery without the woman showing any obvious signs or symptoms of blood loss.

The life-threatening bleeds I have been aware of in more recent years have occurred at caesarean section with unrecognised placenta accreta spectrum. This is highly preventable with antenatal diagnosis, referral to an appropriate team and a planned multidisciplinary approach to delivery.

Prevention, recognition and management of postpartum haemorrhage is an important part of our specialty. Improved outcomes for women have occurred with the development of training and guidelines and protocols to manage this complication. We have early warning scores for maternity and also for postoperative care. We have massive transfusion protocols and emergency skills training. It is necessary for us to develop the skills but also involve the multidisciplinary team within our own units.

This issue of *O&G Magazine* has some surprising articles such as menstruation in COVID and some gaps such as Rhesus disease and anti D prophylaxis. New Zealand's Anti-D guidelines were updated in 2020 and guidelines for both our College jurisdictions can be found on the RANZCOG website. My early obstetrics was at National Women's hospital in Auckland New Zealand where I met and learned under Prof William Lilely famous for his early research into the management of rhesus disease in pregnancy. He developed the Liley curve to obtain an indirect measure of amniotic fluid bilirubin. I should have written this article.

There are articles on improving menstrual health, thalassaemia and haemoglobinopathy screening, iron deficiency anaemia, thrombocytopaenia, thromboembolism and umbilical cord banking. I thank the authors for their time and contribution to this issue.

A period in the time of Covid

Dr Kara Thompson
MBBS, BmedSci, FRANZCOG
Department of O&G,
Joan Kirner Women's and Children's Hospital,
University Hospital Geelong

The importance of clear and honest health communication has been highlighted during the pandemic as we are faced with increasing online misinformation and a growing distrust of medical experts.

This article explores how a possible effect of the covid vaccine on menstrual bleeding has intersected with the spread of online conspiracies and false information. It looks at women's health research in an historical context, and how a combination of lack of data and a missed communication opportunity has resulted in an important lesson for women's healthcare.

Misinformation regarding the covid vaccine and women's health began in 2020. False claims arose that the head of research at Pfizer believed the vaccines caused female sterilisation and that clinical trials should be stopped. The claim was thoroughly debunked. But for some, the damage had been done. Where previous surveys had not identified a gender difference, a large survey in the UK following the spread of this misinformation found the demographic most likely to refuse the vaccine were 18–34-year-old women, with many citing fertility as a primary concern.[1]

Online commentators began incorporating false claims of infertility into larger conspiracy theories centred around a corporate plot to sterilise and depopulate the earth and the ability of vaccines to act as a software platform to receive uploads.[2]

Whilst these increasingly bizarre theories spread online, there was a real phenomenon playing out in homes around the world. Thousands and thousands of women and menstruating people had noted a change in their next menstrual cycle after receiving the covid vaccine.

Some reported a heavier period, some a delay in menstruation, and others noted new or breakthrough bleeding. Whilst people had been informed to expect possible fatigue, myalgia, fever or a sore arm following vaccination, no official sources had warned them to expect period changes.

What was going on? Whilst the anecdotes grew, official sources remained silent. It emerged that changes to menstruation following the vaccine had not been researched.[1] Whilst trial participants had been questioned for myriad side effects, menstrual cycles changes were not included.

Predictably, the lack of official data on menstruation created a vacuum of knowledge that became a breeding ground for misinformation and conspiracy theories.

In April 2021, prominent author and anti-vaccine campaigner Naomi Wolf began sharing these stories on social media platforms, and linked the reports back to previously debunked associations with infertility, miscarriages and pregnancy complications. This narrative was picked up by other influencers, and fake or misleading news stories began to appear on clickbait type websites.[2]

Given reassuring fertility and pregnancy data did exist, there was a need for expert bodies to confidently dismiss these false claims. Concurrently, there was a need to balance reassurance with a frank recognition that any association with menstrual irregularity had not been studied. Perhaps there were concerns that nuanced communication and acknowledging a knowledge gap may be 'playing into the hands' of those seeking to discredit the vaccine.

RCOG's initial statement in May of 2021 appeared, to many, to be sceptical of a possible association between period changes and the vaccine. Rather than querying a possible biological plausibility, and acknowledging the lack of any relevant data, the statement instead focused on other factors that may affect menstruation and noted that 'the degree to which changing hormone levels will affect someone is often informed by her psychological wellbeing at that time. We know that life events can make PMS symptoms feel worse and something as all-consuming and life-changing as a global pandemic could result in women experiencing their periods differently'.[3]

In Australia, a physician and immunisation specialist told the ABC's Corona Check in April that he was sceptical of anecdotes that were spreading via social media because individual experiences could be shaped by stress, anxiety and other factors.[4]

The initial response of experts; to attribute reported menstrual changes to psychology and stress, despite the fact that researchers had failed to collect relevant data, were interpreted by some as dismissive and condescending,[5] with some commentators feeling that the response was an example of gaslighting of women's experience of their bodies.[6]

It is timely to pause here to reflect on the historical context of women's health research. Medicine has, until very recently, been practiced exclusively by men. The illnesses or processes that relate to female bodies – female genitals, menstruation, pregnancy, and the menopause – have historically been viewed as unimportant at best, or suspicious and inherently inferior at worst.

History is full of examples in the way in which women's health has been considered 'other' or viewed as simply reproductive bodies with hysterical tendencies.[7] Failing to include women at all in many older research trials means the effect of many common treatments and medications on the menstrual cycle and the female body remain unknown. When female predominant symptoms such as pelvic pain or menstrual abnormalities are recognised, explanations are often cloaked in emotional and psychological language, in a way that is not commonly applied to male bodies.[8]

Fast forwarding now to the second half of 2021, a few months into the vaccine roll out, and the trickle of individual reports had morphed into something much larger and harder to dismiss. By August 2021, two researchers in the US had collected over 140 000 self-reports from women who had noticed a change in their periods following vaccination.[9] By September, the UK medicines regulation agency's 'yellow card surveillance' program, the equivalent of the Therapeutic Goods Administration for adverse drug events reporting in Australia, had received over 30 000 self-reported notifications for menstrual changes following the vaccine.[10]

Whilst these reports were not evidence of a definitive link, and occurred in the setting of millions of doses of vaccine administered, it was nonetheless significant enough for the BMJ to issue an editorial in September stating that the link was plausible and should be investigated.[11]

The BMJ editorial noted that biologically plausible mechanisms existed that could explain a possible association. These included an immune response to the hormones that regulate menstruation, or an effect occurring in the immune cells in the endometrium itself, a theory supported by recent research out of Yale in the US that immune cells play a role in both building up and breaking down the uterine lining during a cycle.[12] Menstrual changes have been reported after both types of covid vaccines suggesting that, if there is a connection, it is likely to be a result of the immune response, rather than a specific vaccine component itself.[11] Furthermore, precedent existed. Menstrual changes following vaccination have been demonstrated following large scale studies of the HPV vaccine.[13]

Alongside the BMJ editorial, RCOG also released an updated statement.[10] This time there was less emphasis on pandemic stress and emotional wellbeing and more on the possible biological mechanisms of any possible link and the need to determine any possible association. The tone had shifted.

In the setting of millions of worldwide deaths from the global pandemic, both speed and safety in vaccine development were essential. A large number of vaccine side effects were investigated and tracked, and the general public was notified and prepared for these possible risks. There is no doubt that vaccine development has been overwhelmingly successful, with incredibly safe and effective vaccines developed.

It is nonetheless unfortunate that the effect on menstruation was not included in this initial information gathering. The resulting absence of data to address any menstrual concerns as they arose, and an initial willingness to dismiss an association, was fertile ground for breeding misinformation and distrust. The result likely contributed to the reluctance on the part of some to participate in this crucial public health initiative.

Time and research will determine whether a link between the covid vaccine and menstrual irregularity does exist. There are currently several research projects under way and some early findings from retrospective data published in Obstetrics and Gynaecology in January of 2022 have demonstrated an association with transiently altered cycle length.[14]

If an association does exist, it is not likely that this information would have altered the decision for many women regarding vaccine uptake. Short-term menstrual irregularity, whilst important, is not life-threatening and, if any link is proven, appears to be short lived, self resolving, and has reassuringly not resulted in any changes in fertility or pregnancy outcomes. It is much more likely that this information would have been used simply to prepare and to reassure.

Unfortunately, the lack of any useful data has elevated this possible association from one of a dot point in a list of possible side effects, to a conduit for misinformation and a sense of condescension and dismissal for some women.

And so, whilst it is tempting to lay the blame completely on the toxic nature of social media and internet discourse, and the algorithms that allow false information to propagate, we must also acknowledge the contribution of our willingness to dismiss the lived experience of women as relating predominantly to emotion or perception, whilst concurrently failing to adequately investigate any association or biological mechanism.

As in all scientific research, the information that we find will only relate to the questions that we ask, and to the concerns that we take seriously.

We must acknowledge this important lesson and ensure that the effects of any medication or medical interventions on menstruation are not merely an afterthought in future research.

References

1. Speed B. Coronovirus latest: Young women are the unlikely new face of vaccine resistance. 2021. Available from: https://inews.co.uk/news/health/coronavirus-latest-experts-debunk-vaccine-fertility-myths-women-819783
2. Brumfiel G. The life cycle of a Covid-19 Vaccine lie. 2021. Available from: www.npr.org/sections/health-shots/2021/07/20/1016912079/the-life-cycle-of-a-covid-19-vaccine-lie
3. Ward S. Royal College of Obstetrics and Gynaecology statement. 2021. Available from: www.rcog.org.uk/en/news/rcog-responds-to-reports-that-covid-19-vaccine-affects-periods/
4. Wood N. Corona-Check ABC News Article. 2021. Available from: www.abc.net.au/news/2021-04-30/coronacheck-menstruation-periods-vaccines-misinformation-facts/100099778
5. Mahdawi A. Who says it's no big deal if the Covid vaccine temporarily disrupts menstrual cycles? 2021. Available from: www.theguardian.com/commentisfree/2021/sep/18/covid-vaccine-changes-menstrual-cycles
6. Griffin A. Maybe it's Moderna, Maybe It's Menopause. The Cut. 2021. Available from: www.google.com/amp/s/www.thecut.com/amp/2021/09/covid-19-vaccine-affect-menstruation-periods.html

Full Reference list available online

More than providing pads

Dr Dani Barrington
PhD, BE (Hons), BSc, FHEA
School of Population and Global Health,
University of Western Australia

It's likely that at least once a week, you see an online story about menstrual health – recently defined as 'a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity, in relation to the menstrual cycle'.[1] While menstruation is having its moment in the spotlight, most of the light shines on pieces about 'Period Poverty,' loosely defined as the condition in which someone cannot afford the menstrual materials they would like to use during their period. Period Poverty, it is widely assumed, prevents school attendance, workforce participation and illness despite a dearth of data to substantiative these causalities. In fact, there is limited evidence that programs that provide menstrual materials in low- and middle-income countries work to improve school attendance and psychosocial outcomes[2] and essentially no robust evidence that they do so in high-income countries.

Although there are certainly people around the globe who cannot access menstrual materials, often the stories we see in the media use shocking anecdotes to tug at heartstrings; these accounts do not necessarily represent the experiences of most menstruators.[3] In addition, when speaking about low- and middle-income countries, these representations often 'lapse into sensationalized or patronizing accounts of menstrual beliefs and practices that disregard and, in some cases, even ridicule cultural and religious traditions... largely fail(ing) to understand the complex and diverse meanings of menstrual beliefs and practices'.[4] Nevertheless, these accounts motivate well-meaning individuals and organisations to rush to provide the products they believe women, girls and others who menstruate (for example, those who identify as non-gender binary or trans-men) need to manage their periods. Many such initiatives elevate menstrual care practices in high-income countries as aspirational, an articulation of 'West is Best' attitudes.

Menstruation is an incredibly complex topic, a physiological reality shaped by its sociocultural context. Globally, it is considered a taboo topic of conversation, and as a result menstrual literacy is woefully inadequate. Much of the recent research documenting menstrual inequities has focused on menstruators in low- and middle-income countries, with a review of these studies published in 2019.[5] To enable a truly global view, we recently completed a review of menstrual experiences in high-income countries.[6] Together these reviews investigated the lived experiences of almost 10 000 people from 51 countries. We summarised all the data on menstrual experiences that has ever been collected during interviews, focus groups and written narratives, and developed models that identify several pathways through which menstrual experiences take shape. Together, the reviews highlight that around the world menstruation is overwhelmingly considered a negative occurrence that produces a range of adverse personal impacts.

Across diverse sites, the sociocultural environment, essentially a mandate of shame, silence and secrecy around menstruation, leads to strict behavioural expectations to hide menstruation (particularly menstrual fluid), and limits access to knowledge about the menstrual cycle. Menstrual stigma also constrains access to suitable menstrual materials and a clean and private place to change, wash and dispose of them. People who menstruate are often unhappy with their own practices, sometimes feeling disgusted and distressed, and often lack the confidence to manage their period or engage in their usual activities during menstruation. They may live with negative emotions, from frustration to strong distress and shame. In high-income countries, when seeking medical assistance for discomforts including pain related to menstruation, many are dismissed by health professionals. Where healthcare workers do acknowledge the experience of pain and/or heavy bleeding they often express that menstrual symptoms are just a normal part of being a woman, or that the patient must have 'a very low pain threshold'.[7]

The models demonstrate that poor menstrual experiences everywhere lead to detrimental impacts on physical health, psychological health, personal relationships and participation in society, including in school and employment. What is clear is that negative menstrual experiences are the consequence of more than Period Poverty. Indeed, pervasive and entrenched menstrual stigma trivialises menstruation to the point where resources are limited, painful experiences are ignored and the burden to conceal menstrual status is so great that many would prefer to avoid public life than risk the embarrassment of a leak.

We need programs that focus on menstrual health more broadly than most of those in operation today. A more holistic approach ensures that not only do those who menstruate have access to menstrual materials (which they choose for themselves, not those others assume are most appropriate) and suitable facilities to change, wash and dispose of them, but also promotes access to knowledge about the menstrual cycle, timely medical diagnosis and treatment, a positive and respectful environment (including when seeking medical care), and the choice of whether and how those who menstruate participate in all spheres of life.[1] Furthermore, such programs need to consider the cultural context within which they exist; they must not assume that menstrual practices common in high-income countries are always preferred or 'the best'.

It is laudable that discussions of menstruation are now so mainstream, but if we are going to sustainably achieve good menstrual health for everyone, we must do more than throw free pads at the problem.

References available online

Menstruation: society and environment

Dr Mounika Penmethsa
FRANZCOG Trainee
Eastern Health, Victoria

Dr Nisha Khot
FRANZCOG
Western Health, Victoria

More than 800 million girls and women menstruate every day.[1] Albeit a physiological process, experience of menstruation is strongly influenced by sociocultural and religious beliefs, which may also affect how women view menstrual disorders and seek help. We acknowledge that although we have used the terms 'girl' and 'woman', not everyone who menstruates identifies as a girl or woman. This article focuses on menstruation experiences of women and girls. We do not have the expertise to address the specific challenges faced by non-binary people who menstruate.

Menstrual health is defined as a 'state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity, in relation to the menstrual cycle'.[2,3] It is also being increasingly recognised as integral to improving global health, achieving the Sustainable Development Goals, realising gender equity and human rights.[4] In this article we aim to review science, sociocultural and environmental issues pertaining to menstruation.

Menstruation and society

Pliny the Elder, writing in his work *Naturalis Historia* in the 1st century AD said of contact with menstrual blood, 'The wine is sour, flowers wilt, seeds dry out, bee colonies die, even the mirror becomes dull and ivory loses its gloss'. Most of the world's major religions including Islam, Christianity, Judaism and Hinduism, refer to menstruating women as unclean. A significant proportion of menstruating girls and women go through a miserable cycle of pain, discomfort, shame, anxiety and isolation during their periods.

In many Asian cultures, women are restricted from participating in daily lives, not allowed to offer prayers, touch holy books, enter kitchens, take baths, and have to bury their clothes used during menstruation due their association with evil spirits.[5] For example, in Western Nepal, many communities follow 'Chaupadi' a harmful religious practice where women and girls are isolated and sent to menstruation 'Chhau' huts, which are livestock sheds, to live and sleep.[6] Menstruation is considered private 'women's business' in many Aboriginal and Torres Strait Islander cultures, making it a particularly sensitive topic to discuss.[7]

Because of deep-rooted stigma and taboos in most cultures, menstruation is rarely discussed in families and for many girls health information comes either too late or never. According to a UNICEF study, one-in-three girls in South Asia had no knowledge of menstruation before their first period, 48% of girls in Iran thought it was a disease,[8] and 48% of girls in the UK were embarrassed by their periods.[9] For most young women and girls, a major concern of menstruation is concealment, and the worst form of menstrual shame is blood being seen. In 2015, Kiran Gandhi decided to 'free bleed' while running the London Marathon. Her decision garnered international attention and was considered a radical move. Ms Gandhi received praise for combating stigma as well as criticism for being 'disgusting' 'unladylike' 'unsanitary' and 'attention-seeking' showing that period stigma runs deep and that a lot of work is still needed to build a world that is inclusive of menstruation as a normal, physiological process.

In contrast, many cultures around the world celebrate menarche and the 'coming of age' with special ceremonies. In south India, for example, a girl's first period is welcomed through a ceremony called Ritushuddhi where the girl receives gifts and clothes. In Japan, when a girl gets her first period, the family celebrates by eating a traditional dish called sekihan, made of sticky rice and adzuki beans, the red colour symbolising happiness. In Iceland, girls are treated to a red and white cake when they get their first period. Some of these traditions can be traced back to pre-mainstream-religious societies where women's bodies were thought to be spiritually powerful, with this power increasing during menstruation. These ceremonies may have helped foster positive associations with menstruation and bodily functions.

Period poverty and scope of problem

WHO defines period poverty 'as lack of knowledge of menstruation and an inability to access necessary sanitary materials'.[10]

Limited access to pads, tampons and cups pushes women to use proxy materials such as toilet paper, socks, leaves, mud, animal skins etc to absorb menstrual flow.

Period poverty is a global issue, not just for low- and middle-income countries. According to a survey conducted by an Australian based NGO, Share the Dignity, more than one-in-five Australians are using toilet paper or socks to manage their periods.[11] One in 12 in New Zealand cannot afford menstrual products. Only 12% of 355 million menstruating women in India use sanitary products during menstruation.[8]

UNICEF recommends access to WASH (water, sanitation and hygiene) facilities during menstruation as crucial for menstrual health and hygiene; this includes private space, safe disposal of sanitary products, running water and soap to wash hands.[12] Limited access to menstrual products compounded with lack of appropriate and hygienic infrastructure at schools forces girls absenteeism due to lack of privacy, dignity and fear of exposing menstrual flow, significantly affecting their performance at school, which has far reaching implications in the communities. Around 500 million girls and women lack access to adequate facilities to manage their periods worldwide. Almost 40% of girls and women surveyed in the Pacific reported lack of access to facilities to manage their periods hygienically. In Ethiopia, around 50% of girls miss school every month during their periods.[8] UNESCO reports 10% of African girls quit school because of menstruation-related issues.[9]

Ending period poverty

Peak bodies advocating for women's health, including RANZCOG, are calling for action from governments to remove the cost of menstruation as a step forward towards gender equality. In Australia, from January 2019 Goods and Service Tax (GST) was removed on menstrual products known as 'tampon tax '.[13] Scotland became the first country in the world to make period products free for all in November 2020. New Zealand has made period products available for free to all students in schools from June 2021. Some jurisdictions in Australia now have menstrual products available for free in government schools for students.

Strategies to end menstruation stigma

Breaking the deep-rooted attitudes of secrecy and stigma around menstruation needs a holistic approach. Age appropriate, gender and culturally sensitive menstrual education in schools, along with creating supportive and positive environments where girls and women can freely talk about their concerns, confidently manage their periods and access healthcare early to address problems related to periods such as endometriosis, menstrual migraine and premenstrual dysphoric disorder. It is also important for men and boys to understand menstruation so they can support their partners, daughters, mothers, students, employees and peers.[5] #periodemoji, a 'drop of blood' emoji to signify menstruation, was accepted by the Unicode Consortium in 2019 and is considered a step forward in normalising conversations around menstruation.

Menstrual health interventions

Hennegan et al conducted a systematic review and qualitative meta synthesis of women and girls' experience of menstrual health interventions in low- and middle-income countries.[3] Included studies captured experiences from six countries and over 900 participants from India, Uganda, Kenya, Ethiopia, Zimbabwe and South Africa. They concluded that menstrual health interventions provoked changes to women's and girls' expectations and may mediate desired impacts on outcomes such as school attendance.

In an intervention-based study in rural India conducted from 2018–2019 in 202 remote areas, including educating frontline health workers and teachers, and provision of free menstrual products to girls in schools and community centres, outcomes were assessed in 27 randomly selected villages. Of 550 girls assessed, use of safe menstrual products increased from 69% to 90.5%. Their knowledge of the uterus as the origin of menstrual blood increased from 6.3% to 66% with significant reduction in school absenteeism during menstruation from 24% to 14%.[14]

Sustainable menstruation

Menstrual products can have a huge impact on the environment, with the average woman using 10 000–12 000 single-use menstrual products in their lifetime. Pads take up to 500 years to biodegrade. In Australia alone, around 300 million tampons and 500 million pads end up in landfill each year.[15]

Biodegradable pads and tampons, period pants, cloth pads and menstrual cups are some of the modern sustainable alternatives, which are also more economical long term (eg. a tampon cost 50 cents while a menstrual cup costs 0.09cents per use).[15,16]

A 2019 study from the Lancet[17] showed that menstrual cups are a safe option for menstrual management with no adverse effects on vaginal flora. However, there were incidences of severe pain, vaginal wounds, allergies and toxic shock syndrome. Further research into cost effectiveness and environmental impacts of different menstrual products is needed.

References.

1. www.globalwaters.org/events/menstrual-hygiene-day-2021
2. Barrington DJ, et al. Experience of menstruation in high income countries: A systematic review, qualitative evidence synthesis and comparison to low and middle income countries. *PLoS Med*. 2021;16(7); e0255001.
3. Hennegan J, et al. Women's and girl's experiences of menstruation in low- and middle-income countries: A systematic review and qualitative metasynthesis. *PLoS Med*. 2019;16(5):e1002803.
4. Hennegan J, et al. Menstrual health: a definition for policy, practice, and research. *Sex Reprod Health Matters*. 2021;29(1):1911618.
5. Garg S, Anand T, Menstruation related myths in India: Strategies for combating it. *J Family Med Prim Care*. 2015;4(2):184-6.
6. Thakuri DS, et al. A harmful religio-cultural practice (Chhaupadi) during menstruation among adolescent girls in Nepal: Prevalence and policies for eradication. *PLoS One*. 2021;16(9):e0256968.
7. Krusz E, et al. Menstrual health and hygiene among Indigenous Australian girls and women: barriers and opportunities. *BMC Women's Health*. 2019;19:146.
8. https://plan-international.org/sexual-health/menstruation
9. Normalising menstruation and empowering girls. *Lancer Child Adolesc Health*. 2018;2(6):379.
10. https://pmnch.who.int/news-and-events/news/item/28-05-2020-menstrual-hygiene-and-health-a-call-for-dignity-rights-and-empowerment

Full Reference list available online

Umbilical cord blood banking in New Zealand

Dr Aimee Humphries
PGDipObstMedGyn, MBChB, BMedSc (Hons)
Department of Obstetrics and Gynaecology,
Auckland Hospital, New Zealand

Dr Megan Overdevest
DRANZCOG trainee
Department of Obstetrics and Gynaecology,
North Shore Hospital, New Zealand

Dr Rory Bennett
MBChB
Department of Haematology,
Auckland Hospital, New Zealand

Dr Prathima Chowdary
MBChB, MEngSt, FRANZCOG, AGES Fellowship
Department of Obstetrics and Gynaecology,
North Shore Hospital, New Zealand and
University of Auckland, New Zealand

The blood obtained from the umbilical cord and placenta after delivery is a rich source of multipotent stem cells. These cells have the capacity to reconstitute the various cell lineages of the haematopoietic system and can be utilised in stem cell transplantation. This procedure is used to treat various acquired and inherited adult and childhood conditions including malignancies, immune deficiencies, metabolic and autoimmune disease. Additionally, there has been growing interest in stem cell utilisation in regenerative medicine to treat traumatic brain injuries, cerebrovascular disease, Parkinson's and myocardial infarction. In light of their potential use, there is considerable interest worldwide in the practice of umbilical cord blood banking.[1,2]

Umbilical cord blood can be collected from the umbilical vein whilst still attached to the placenta, before or after placental delivery at either vaginal or Caesarean delivery. In pursuit of an adequate collection, delayed cord clamping is not able to be performed. Umbilical cord blood units are expertly produced with assessment of stem cell enumeration and, if properly cryopreserved, can be stored for at least 20 years for future use. Umbilical cord blood banks now exist worldwide. The more numerous private cord blood banks provide preparation, testing, and storage of cord blood units for potential future autologous return, at a cost to new parents. Public cord blood banks rely on altruistic donation of umbilical cord blood for the use in allogeneic transplants, at no cost to the recipient, rather to the healthcare provider. The number of stored units in private banks exceeds those in public banks globally, at approximately 5:1. All umbilical cord blood banks should be accredited to relevant international standards of processing, testing and storage.[3]

Clinical Relevance

Umbilical cord blood transplants have been performed for several decades and provide an alternative, less invasive source of stem cells to bone marrow and peripheral blood. An estimated 40 000 or more umbilical cord stem cell transplants have been performed worldwide, both in children and adults. Simplistically, stem cells can be infused intravenously following conditioning chemotherapy which then migrate to the bone marrow, proliferate, and, with engraftment, demonstrate differentiation into mature cells.[1,2]

Table 1. Pros and cons of private umbilical cord blood banking for autologous return in New Zealand.

Pros	Cons
• Easily obtainable and minimally invasive • Robust storage potentially up to 20 years for autologous use • Potential use for research • Potential for regenerative medicine and future novel therapies	• Unable to perform delayed cord clamping at delivery • Upfront and annual costs for private storage • Low likelihood of utilisation due to low lifetime incidence of diseases treated • Redundancy in that stem cells can be readily collected at diagnosis • Often insufficient stem cell yields for one or multiple oncological transplants • Potential manipulation of new parents by private cord banks

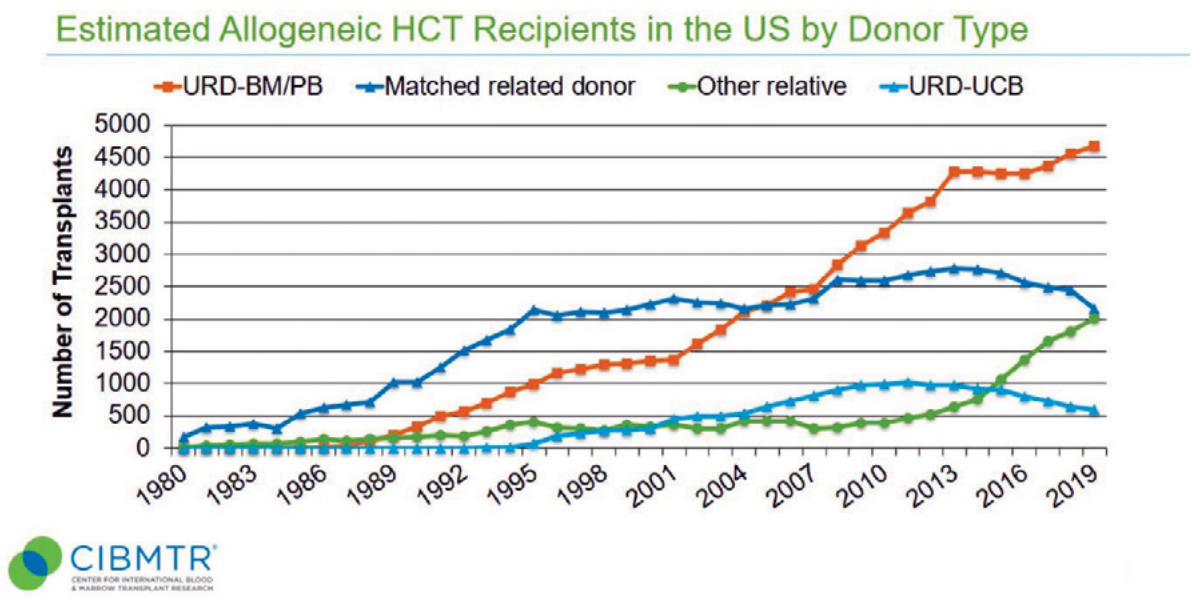


Figure 1. Rates of allogeneic stem cell transplants per year in the US.
URD-BM/PB = unrelated donor - bone marrow/peripheral blood, other relative - haploidentical donors, URD-UCB = unrelated donor - umbilical cord blood.[5]

Allogeneic stem cell transplants involve infusion of stem cells from donors who are HLA matched (traditionally from full siblings) or matched unrelated donors from registries or cord banks. Recently, haploidentical donor stem cells (half matched donor, usually a family member) have shown success in allogeneic transplants.[4] When treating haematological malignancies, allogeneic stem cell transplants harness both myeloablative conditioning chemotherapy used, and a potential graft versus disease effect from the donor stem cells. Allogeneic stem cell transplants may be used in the treatment of leukaemia, lymphoma, inheritable bone marrow failure syndromes, severe haemoglobinopathies, severe immune deficiencies, and inherited metabolic conditions. With comparison to bone marrow or blood-derived stem cells, immunologically naïve umbilical cord blood-derived allogeneic stem cell transplants have greater flexibility in HLA matching. They are associated with low rates of graft versus host disease and reduced risk of viral pathogen transmission. Cord blood derived allogeneic stem cells are, however, associated with slower haematopoietic engraftment. The pros and cons in clinical use are listed in Table 1 and 2. Due to the nature of their source, absolute numbers of stem cells may be insufficient for successful engraftment, especially in adults, hence at least two units may be required per transplant.[1-3] With the success of haploidentical stem cell transplants which increase the breadth of feasible donor options, numbers of unrelated cord blood allogeneic transplants performed are declining worldwide (Figure 1).[5]

Autologous stem cell transplantation describes return of one's own stem cells to facilitate use of therapeutic high-intensity chemotherapy. Unlike allogeneic transplants, the potential immunological benefits of introducing foreign stem cells do not exist, hence no graft versus disease effect is achieved. As the immune system is not replaced by donor-derived cells, inheritable blood conditions are not eradicated. Although there is considerable interest in autoimmune conditions and genetic manipulation of autologous stem cells, the vast majority of autologous transplants performed are for a limited set of haematological and non-haematological cancers only. In adults, this largely comprises high risk or refractory lymphoma and myeloma. For children and young adults, autologous transplants may also have a role in the treatment of brain tumours, germ cell tumours, and neuroblastoma. Importantly, unlike with allogeneic stem cell transplants, certain cancers such as acute leukaemias cannot be treated successfully with autologous stem cell transplants.[1-2]

The diseases for which autologous stem cell transplant may have a treatment role are generally uncommon or rare. Autologous transplants are also generally reserved for high risk or refractory cases of the disease in which less intense treatment is unlikely to be, or has not been, successful. For many of the paediatric cancers listed, treatment protocols often include tandem or even triple autologous transplants. In these cases, the absolute number of stem cells required to perform such transplants is likely to exceed those available from autologous cord blood banking alone. It is important to also note that autologous stem cells can be readily harvested from patients at the time of diagnosis in the vast majority of cases, and treatment options do not depend upon availability of prior banked umbilical cord blood units. What is unclear and cannot be easily predicted is the potential role for autologous cord blood cells in research and in future novel therapies.[6]

Commercialisation of umbilical cord blood banking

New Zealand does not have any public cord banking options available, although a small number of private cord blood banks currently operate. The cost to collect and bank umbilical cord blood is in the realm of $3000 NZD with an annual storage fee of $200–300 NZD. It is important to underline that private

Table 2. Pros and cons of public umbilical cord blood banking for allogeneic usage worldwide.

Pros	Cons
• Easily obtainable, minimally invasive, robust storage • Allows altruistic donation • Greater flexibility in HLA matching • Reduced risk of viral transmission • Lower rates of graft versus host disease • Facilitates research	• Unable to perform delayed cord clamping at delivery • Existence of easily obtained alternative stem cell sources and increasing donor options • Slower haematopoietic engraftment • Commonly insufficient stem cell yields often necessitating two units per transplant

banks provide cord blood units for autologous return only. They have been criticised for directly publicising their services to expectant parents using data based on the successful use of cord blood from unrelated donors in allogeneic stem cell transplantation, often omitting the crucial distinction between allogeneic and autologous stem cell transplantation. This may result in exploitation of vulnerable parents who may not have enough information to make an informed decision. Private banks may also withhold commercially sensitive information regarding the adequacy of their products.[6]

Umbilical cord blood is a potentially valuable resource and a rich source of stem cells that can be used in treating a host of adult and childhood cancers. Private cord blood banking remains a controversial topic and an ethical dilemma for NZ clinicians, encompassing commercial interests, health inequities and the desire to do all that we can for our patients. It is important for clinicians to be cognisant of umbilical cord blood banking marketing to new parents and be able to provide evidence-based information for informed decision making (Tables 1 and 2).

Discussion

Ultimately, the decision to store umbilical cord blood is a very personal one for expectant parents, reflecting their own beliefs, values and priorities. Lead maternity carers play an important role in accurately counselling parents and providing evidence-based, unbiased information about their options. Expectant parents frequently identify healthcare professionals as their key source of information regarding cord banking options. However, healthcare professionals identify that they are poorly equipped to counsel those parents and were found to obtain their information from private cord banks, creating a conflict of interest.[7] It is important for clinicians to have access to unbiased information about the pros and cons of cord blood banking. Discussions with patients should ideally define the restricted use of autologous cord blood units, the availability of other sources of stem cells including bone marrow and peripheral blood, as well as balance the benefits of delayed cord clamping.

The authors would like to acknowledge Dr Richard Charlewood (Transfusion Medicine Specialist) at New Zealand Blood Service for his expertise on the topic.

References

1. Butler MG, Menitove JE. Umbilical cord blood banking: an update. *Journal of Assisted Reproduction and Genetics*. 2011;28(8):669-76.
2. Narayanan DL, Phadke SR. Concepts, Utility and Limitations of Cord Blood Banking: What Clinicians Need to Know. *The Indian Journal of Pediatrics*. 2019;86(1):44-8.
3. Mayani H, Wagner JE, Broxmeyer HE. Cord blood research, banking, and transplantation: achievements, challenges, and perspectives. *Bone Marrow Transplantation*. 2020;55(1):48-61.
4. Zheng X, Tian Z. Which is better, HLA-matched sibling or haploidentical transplantation?. *Cellular & Molecular Immunology*. 2021;18(5):1347.
5. Phelan R, Arora M, Chen M. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR US summary slides. Center for International Blood and Marrow Transplant Research. 2020.
6. Sullivan M, Browett P, Patton N. Private umbilical cord blood banking: a biological insurance of dubious future benefit! *New Zealand Medical Journal*. 2005;118(1208).
7. Peberdy L, Young J, Kearney L. Health care professionals' knowledge, attitudes and practices relating to umbilical cord blood banking and donation: an integrative review. *BMC Pregnancy and Childbirth*. 2016;16(1):1-9.

Consumer Network

Consumer experience: improving PPH care

Ms Laura Simpson
CNWG Consumer Representative

Welcome to the first article from the RANZCOG Consumer Network Working Group (CNWG) for 2022. The CNWG has had many discussions around topics across obstetrics and gynaecology since the group was created in late 2020.

Recently I had the joy of talking with Dr Kara Thompson (obstetrician at Western Health and Barwon Health) about the importance of consumer engagement and how her practice as an obstetrician has changed after listening to many consumer stories with Dr Alex Umbers (GP obstetric trainee) on their podcast, 'Pregnancy Uncut'. Dr Thompson explained that 'I thought I had a solid understanding of obstetrics and all its joyful, tragic and unpredictable permutations. I had read all the textbooks and sat all the exams and worked in the field for a decade. But as doctors we only have a true understanding of what the experience is like from a professional perspective, and perhaps one or two personal experiences of our own. Over the last year I have sat down over a cup of tea with birthing families who have experienced various complications in their pregnancies and listened. I mean really listened. Not ticking all the boxes of a postpartum review or a standardised debrief.'

'It's incredible how much you can learn from women telling their stories. There are so many insights that are not taught in textbooks. Interviewing women about their births and understanding the huge power of obstetricians and midwives in helping to shape these profound life experiences, has changed almost every aspect of the way I practice'. This is the kind of impact, as consumer representatives, we hope to have while working with RANZCOG and its members.

With the focus on postpartum haemorrhage (PPH) for this issue, I had a discussion with 63 consumers who had endured a PPH. PPH is one of the most common birth complications and leader worldwide for morbidity and mortality, but what does it mean for the consumer, the birthing partner and families? How does it really feel for them and how can obstetricians, midwives and other health professionals use this consumer experience to better their practice and improve health outcomes? Amy Dawes, co-founder of Australasian Birth Trauma Association (ABTA Birthtrauma.org) works with many birthing consumers and their families and believes that PPH is a 'huge trigger for birth trauma for the many families that we support (both the birthing and non-birthing parents).'

After having four babies myself and having multiple PPHs, one over three litres and then the last being over eight litres requiring an emergency transfer and subsequent hysterectomy to preserve life, I have learnt that my experience and the feelings that arose were similar to other women who experienced mild to catastrophic PPHs. They often report common short- and long-term effects.

The birth of your children, either vaginally or via caesarean section, is a significant moment in your life: something that comes with great anticipation and sometimes a little trepidation. We all hope and wish that things go perfectly well, even though we understand the risks that come with childbirth.

During the discussion, 92% of consumers reported that their PPH occurred during or after the third stage of labour, as did my own. The shock and relief of having their baby was shortly followed with what many described as a fear for their life. It was commonly noted that patients felt like there was something majorly wrong with them before anyone else in the room realised, yet they felt unable to advocate those feeling due to the shock setting in. At this point, they talked about the moment they wanted to 'fight' for life against the strong urge to drift to sleep because the pain and weakness was too much, a feeling that all never forgot.

A PPH comes with a sense of emergency, the button being pushed, the rush of staff into the room, the look of concerned faces and sometimes the shock of seeing the amount of blood in the room. It is in these moments that the consumers notice the little things, the body is hypervigilant. The sounds, the smells, what people are wearing, the numbers from the blood pressure or heart rate and the words being spoken often stay with them for years to come. If the consumer develops symptoms of post-traumatic stress disorder (PTSD) in the future, these are often the source of triggers for them. Dr Thompson also learnt that 'everything you say to a woman in their pregnancy may be that comment they remember forever. Almost every woman has

several quotes they can directly recall from their births, including who said it and most importantly, how it made them feel. What may be a throwaway comment on a busy night running between birthing rooms may be the words that run through their minds, often during those lonely 3am feeds, for months and years to come'.

The women expressed that once settled in their rooms and the emergency had subsided, they were overcome with great fatigue and weakness, feelings of dizziness and were scared to move. Many felt robbed of their time with their little ones due to these affects. The shock of what had just happened and the feeling of failure as a birthing person crept in. In some cases, the separation from their little ones hurt even more, yet that gratitude for still being alive was strong, even though they were angry at the situation that had unfolded. The women in this discussion ranged from six weeks to five years postpartum and all had different stories to share long term. For myself, it wasn't until later that I realised the true effects of what my body had endured. I was so focused on surviving, getting better and back to my baby that the psychological aspect of the experience didn't hit until eight weeks postpartum. The psychological aspect of the birth often surprised many other consumers and as they felt like they 'didn't come out from under the cloud' for months. That extreme fatigue and shortness of breath continued when doing small tasks and it consumed them.

Over half the consumers reported that they had PTSD-like symptoms, anxiety, and problems within their families from a lack of understanding, which led to a feeling of loneliness. Birthing partners often experienced their own form of trauma in relation to the birth, and this at times made it difficult for them to connect as a family. The women felt like they needed extra care during this time but also felt reluctant to speak to a health professional about this due to stigma. The inclusion of their partners and birthing partners during discussion was appreciated and gave them a feeling of acknowledgement. The women needed to be seen, heard, and reassured by their health team that they had indeed suffered something difficult. Amy Dawes added that 'to help ward off potential traumatic stress, communication was key, through the process, never underestimate the kind words, gentle touch, letting them know that you are there (and if you can't, making sure there is someone that is explaining what is happening).'

Debriefing was the most valued form of aftercare that made a distinct difference to their health outcomes; however, there were definite characteristics that defined successful debriefing. Consumers suggested that the most effective debriefing was provided immediately, again in the following days and then over the coming weeks and months. 35% of the consumers noted that they couldn't process the debriefing until two years later when they were diagnosed with PTSD or had worked with a psychologist. They found that often their body was still in 'protection' mode and their ability to understand and accept what had happened was low. Another defining characteristic was who the debrief came from. 96% of the consumers insisted that they needed to debrief with the obstetrician and midwife involved with their birth rather than a GP or hospital management. They felt they had developed the relationship with these people and needed to discuss it with who was there. This was more important for people who experienced life-threatening PPH. Dr Thompson agreed with 'the importance of timely and ongoing debrief after every birth, not just for those who we might consider having had a traumatic experience. Almost every woman we have spoken to has some degree of confusion about why something was done during their labour or pregnancy. Part of addressing this, in addition to routine birth debriefing, is improving women's access to comprehensive antenatal education to empower them with knowledge about the birth process and possible complications, before they arise'.

Amy Dawes felt that 'providing adequate aftercare and opportunity to ask questions' was essential. She agreed that this could be 'weeks or months after as it often takes people some time to process the experience and recognise that they need to talk and understand'. Her Peer2Peer support structure has been heavily welcomed by birthing families as they have been able to connect with others who have experienced similar complications.

With the added difficulty of COVID-19, where consumers have had less support in the birthing room and during the hospital stay, many felt that it was more important than ever to have trauma informed care and that the health professionals in the room had an added responsibility for awareness to help the birthing person feel safe and supported to reduce PTSD, postnatal depression and postnatal anxiety. In the immediate moments of the PPH, the women valued the health professionals who spoke to them in a way they understood, and someone who took them seriously when they explained concerns such as feeling dizzy, weak, heavy in the chest or in pain. One woman expressed that due to a language barrier and no support during COVID-19 restrictions, she was unable to communicate her concern to the attending doctors and nurses. She felt that the importance of a translator being available in an emergency when her birthing partner was unable to attend would have been highly valued.

100% of the women recalled that their experience really scared them and their family, that they were afraid of having future children even though they desired a larger family. They felt the need for reassurance from their obstetrician and a higher level of informed care. The consumers that proceeded to have another child felt safer when their healthcare team explained how they could prevent another PPH and how they would be treated in the event of another PPH. This also included explaining the risks and providing options. Continued reassurance and understanding also contributed to feeling at ease. Many women also noted that EMDR (eye movement desensitization and reprocessing) helped with extreme cases.

In conclusion, the CNWG looks forward to working with RANZCOG over the coming years to strengthen the collaboration between consumers and clinicians, to plan, evaluate and improve their clinical practices for better public health outcomes.

References

1. Pregnancy Uncut, Dr Alex Umbers and Dr Kara Thompson. 2021. Available at: www.pregnancyuncut.com
2. Amy Dawes (Co-founder, CEO and Director of Australasian Birth Trauma Association (ABTA). www.birthtrauma.org.au

PPH: numbers, bloody numbers

Dr Lucy Brodnik
MBBS
Obstetrics and Gynaecology Registrar

Dr Meg Willis
MD
Obstetrics and Gynaecology Registrar

Blood loss in the immediate postpartum period is associated with significant morbidity and mortality.[1] As 40% of postpartum haemorrhage (PPH) occurs in low-risk women, every woman giving birth is at risk.[2] The amount of loss that constitutes an excessive blood loss is one of continued debate. The World Health Organization (WHO) definition is frequently cited: >500mL post vaginal birth and >1000mL post caesarean section.[1] Consensus for this definition arose in the 1960s; however, there is little enduring evidence supporting 500mL as a threshold for PPH-related morbidity.[3,4]

The American College of Obstetricians and Gynaecologists (ACOG) rationalised their definition of PPH to be 'blood loss greater than or equal to 1000mL or blood loss accompanied by signs or symptoms of hypovolemia'.[4] Despite a lack of evidence, Australian guidelines (including RANZCOG) continue to use the 500mL definition.

Statewide Guidelines – a comparison

There is comparatively little randomised control trial (RCT) evidence to guide the management of PPH. Hence most interventions are guided by best practice rather than high-quality evidence.[6] This may partially account for variation in management guidelines between states.

Third stage prophylaxis - to carbetocin or not to carbetocin?

There is, however, good evidence for active management of the third stage of labour including use of a prophylactic uterotonic. The WHO recommends that all women giving birth should receive a prophylactic uterotonic agent for the prevention of PPH and specifies oxytocin 10IU IM as the drug of choice.[1] This recommendation is echoed in the 2014 RANZCOG and 2016 Green Top Guidelines, which also recommend oxytocin 10IU IM for prophylaxis in the third stage of labour for women without risk factors for PPH who deliver vaginally.[5,6] The Greentop Guideline goes on to state that Syntometrine® (oxytocin 5IU + ergometrine 500µg IM) may be used in the absence of hypertension, in women at increased risk of haemorrhage, as it reduces the risk of minor PPH.[6]

A 2018 Cochrane Systematic Review (meta-analysis of 196 RCTs, >135 000 participants) showed the use of oxytocin plus misoprostol, oxytocin plus ergometrine, or carbetocin alone, reduced the use of additional uterotonic drugs and blood transfusion compared with oxytocin alone, but not necessarily overall rate of PPH. Subgroup analyses did not reveal important subgroup differences for patients undergoing vaginal versus caesarean birth or for patients at high versus low risk for PPH.[7]

Queensland Guidelines recommend routine use of oxytocin in preference to Syntometrine® or carbetocin for low-risk births. In women at risk for PPH who have a vaginal birth, carbetocin may be considered first line. In women at risk for PPH who have an elective or emergency caesarean section, carbetocin may be considered under epidural or spinal anaesthesia but is not recommended in women having a general anaesthetic.[15]

Victorian guidelines also refer to carbetocin, recommending its use for all births (not just caesarean sections) in contexts where its cost is comparable to other effective uterotonics. Oxytocin is still recommended for the prevention of PPH for all births. Syntometrine® may be used but should be avoided for women with hypertension.[9]

New South Wales and South Australia both recommend routine use of prophylactic oxytocin for management of third stage, regardless of risk factors;[10] though South Australia's guideline considers alternate prophylaxis with Syntometrine®.[11] Western Australia also recommends routine oxytocin for women who birth vaginally without risk factors, and to consider Syntometrine® in women who are high risk without contraindications.[12] Neither NSW, SA nor WA reference carbetocin in their guidelines.[9,11,12]

Oxytocin: is 30 the new 40?

Even the most ubiquitous oxytocic doses still vary state to state. The RANZCOG guideline suggests PR misoprostol administration with dosage up to 1000µg.[5] State guidelines for misoprostol prescribing ranges from 400–1000µg and include buccal/sublingual and rectal routes.

An oxytocin infusion is also used to maintain uterine tone once bleeding is controlled, commonly prescribed as oxytocin 40IU in 1L crystalloid infused over 4 hours (10IU/hr). This contrasts with the lower dose oxytocin infusion used for induction of labour, a 10IU in 1L crystalloid titrated infusion used by most states.

Queensland, however, recommends an oxytocin 30IU in 500mL infusion for both induction of labour and management of PPH. Having previously used the standard 40U infusion for PPH management, this change was in response to the state's updated guideline for induction of labour. An oxytocin infusion of 30IU in 500mL crystalloid is titrated for induction of labour and the same concentration is infused at 167mL/hr (10IU/hr) for management of PPH. This change aimed to simplify pharmacological management and prevent errors.[8] In these authors' Queensland clinical experience, simplified prescribing has certainly streamlined emergency management.

TXA – will it save the day?

In response to evidence from the WOMAN trial, the WHO now strongly recommends the addition of IV tranexamic acid (within three hours of birth) to management for women where vaginal birth or caesarean section is complicated by PPH, regardless of cause.[1,13] The majority of the state guidelines include this recommendation.

Is measuring EBL a worthy task?

The WHO PPH Guidelines contains thirty-three recommendations for the prevention and management of PPH, but only one recommendation for accurate diagnosis.[1] Delay in diagnosis is thought to have a direct correlation to the severity of bleeding and is a common finding in cases of severe morbidity and mortality. A major cause for delay in diagnosis is inaccurate clinician estimation of blood loss.[13] Evaluation for clinical signs and symptoms of hypovolaemia are important in the assessment of PPH; however, due to the physiological adaptations of pregnancy, these become far less sensitive and therefore other clinical practices for estimating loss are required.[22]

Visual estimation – your guess is as good as mine

Visual estimation remains the primary method of determining blood loss, particularly following vaginal birth. It is well established that visual estimation is both inaccurate and subjective.[13] Visual tools for comparison of volume have been developed to improve estimation; however, these have not been shown to correlate with consistent clinical improvement.[16] Interestingly, visual estimation accuracy does not appear to improve with the speciality of the health care provider or their clinical experience.[17]

Quantitative measures – should the scales weigh in?

Quantitative measurement techniques are consistently shown to improve accuracy of blood loss assessment and include:

- Gravimetric assessment – measurement of total weight of bloody materials, subtracting the known dry weight of same materials to achieve total blood loss in mL
- Volumetric assessment – the use of calibrated measurement containers/V-drapes with calibrated pockets

A prospective cohort study of 150 women compared visual estimation to gravimetric assessment and found that visual estimation is associated with an error of 30%.[18] Calibrated bags have also demonstrated accurate assessment of blood loss in clinical practice and simulations.[16,19] The largest randomised trial to compare calibrated bags to visual assessment included 25 381 vaginal deliveries in 13 European countries.[20] Severe PPH occurred in 1.71% of births in the intervention group and 2.06% in the control group and the difference was not statistically significant. The authors explained this by suggesting that a more accurate assessment of postpartum blood loss is not itself sufficient to change behaviours of caregivers and improve the management of PPH.[20]

Correlation with clinical outcomes – do the ends justify the means?

Quantitative measurement is more accurate than visual estimation, but whether this correlates with improved maternal outcomes has not been demonstrated. A 2018 Cochrane Review found no differences when comparing subjective and objective quantification of blood loss and clinical outcomes such as use of uterotonics and need for blood transfusion.[21] Most studies aiming to improve recognition and response to PPH have focussed on improving volume estimates. Qualitative data in this area has found that the numerical quantification of blood loss is often retrospective and that factors that affect initial decision making in PPH include the nature and rate of blood loss and the clinical condition of the patient.[22,23] This may explain why improved accuracy of measurement alone is not clearly associated with improved clinical outcomes.

Areas for improvement – surely there's a bundle for that?

The US has initiated several bundles to attempt to improve PPH prevention, diagnosis and management at several levels. The largest of these is the California Maternal Quality Care Collaborative state-wide haemorrhage quality improvement initiative that compares outcomes before and after the implementation of an obstetric haemorrhage bundle (n=99) versus comparison hospitals (n=48).[1,22] There was a 20.8% reduction in severe maternal morbidity in the collaborative hospitals compared to a 1.2% reduction in the comparison hospitals. These results have been replicated in two studies from single institutions, demonstrating a significant reduction in adverse outcomes relating to PPH following implementation of an obstetric haemorrhage bundle.[25,26]

Standardised evidence-based clinical guidelines across states may not be practical, but similarities are stronger than the differences. Accurate quantification of blood loss remains a worthy task in minimising adverse maternal outcomes from PPH. Bundled healthcare strategies include the use of quantitative measures over visual estimation for improved accuracy. There continues to be ample room for improvement, even in our most common obstetric emergency.

Full Reference list available online

Management of severe postpartum haemorrhage and use of blood products

Dr Patrick CF Tan
MBBS, BMedSc, FANZCA
Department of Anaesthesia,
Royal Women's Hospital, Melbourne

Postpartum haemorrhage (PPH) is common. It is a source of significant morbidity and mortality for pregnant women, especially in low-income countries.[1] However, probably most pertinent of all, the disease burden of PPH is largely preventable. The local incidence of PPH as a cause of maternal death has been on the rise. This is contrary to the overall rate of maternal mortality which has been on the decline in Australia and New Zealand.[2]

RANZCOG defines PPH as the loss of 500ml or more of blood from the genital tract within 24 hours of the birth of a baby. A PPH is considered major if the blood loss exceeds 1000ml and severe if it exceeds 2000ml.[3]

This article addresses some interesting literature on severe PPH and obstetric blood management and provides insight into an obstetric anaesthetist's management perspective.

Massive obstetric haemorrhage: what the data shows

Understanding contributing predictors for severe complications is a logical step towards improving outcomes. This can help clinicians lead these at-risk women onto the appropriate clinical pathways and escalation of level of care.

In 2020, Lasica et al published one of the largest reported studies on massive obstetric haemorrhage (MOH) and transfusion management.[4] It was a bi-national (Australia and New Zealand) cohort study which included 19 hospitals and 249 cases of MOH. The definition used for MOH was bleeding requiring ≥5 units of red blood cells (RBC) within four hours. Data from the registry (2008–2015) showed that two-thirds of MOH occurred in the out of hours period. Another major finding was that a significant percentage (52%) of MOH cases in this study recorded a low fibrinogen level (<2 g/l) in the first 24 hours after commencement of massive transfusion. It also demonstrated independent risk factors for emergency hysterectomy (see Table 1).

Other relevant findings were:

- Predominant causes of MOH were uterine atony (22%), placenta praevia (20%) and obstetric trauma (19%)
- 44% of cases required intensive care unit admission
- 29% of cases required hysterectomy
- Three cases died

This data highlights key issues when assessing risk of complications associated with MOH. It also demonstrates the level of associated morbidity and mortality in our local (high income) setting and emphasises the important role of timely, adequate replacement of fibrinogen within the resuscitative management.

Table 1. Risk factors for emergency hysterectomy with MOH. Values expressed as odd ratios and 95% confidence intervals.

Risk Factor	Odds Ratio	95% confidence interval
Emergency caesarean section	4.9	2.0–11.7
Placenta praevia	7.2	2.0–26.4
Transfusion of ≥ 6 units of RBC prior to first unit of cryoprecipitate	3.5	1.7–7.2

Blood transfusion targets

There is no longer debate on the adverse effects of anaemia on the pregnant woman and her baby. The exhaustive list of these includes (but is not limited to):

- Neonatal: low birth weight, preterm birth, perinatal mortality[5,6]
- Maternal: peripartum infection, PPH and transfusion, preeclampsia, mental health issues, fatigue and maternal mortality[5,7-9]

The most common definition of anaemia is from the World Health Organization (WHO), which defines anaemia as a haemoglobin level of <120 g/l for women and <110 g/l for pregnant women. Severe anaemia during pregnancy is further defined as a haemoglobin level < 70 g/l.[10] However, more recently, Ferguson and Dennis have challenged these definitions which were established in 1968. These authors point to more contemporary data which suggests that haemoglobin levels in iron-replete pregnant women are higher than previously perceived.[11] Even mild anaemia can give rise to adverse outcomes in pregnant women and thus a definition of anaemia which may underestimate the 'normal' haemoglobin level of a pregnant woman is clearly undesirable. This is the importance of re-examining the target and threshold of optimal haemoglobin in pregnant women. The Australian National Blood Authority suggest that a reasonable range for normal pregnancy haemoglobin levels is between 103–146 g/l.[12] This range also takes into consideration the potential complications of blood and blood products transfusion and the independent adverse effects of a high Hb in pregnant women.[13]

Anecdotally, the majority of anaesthetists in our institution would decide to transfuse blood at a haemoglobin level < 70 g/l or additionally at a haemoglobin level < 90 g/l if bleeding is ongoing or the woman shows signs of haemodynamic instability and adequate crystalloid volume has already been administered. The latter step is a subjective assessment by the treating clinician so as to avoid excessive dilution of circulating clotting factors which would contribute to a dilutional coagulopathy.

Key management principles

The National Blood Authority (Australia) has published guidelines specifically addressing patient blood management in the obstetrics and maternity setting. This is a comprehensive document created through multi-disciplinary collaboration of all key stakeholders. The current version is under review. On the topic of critical obstetric bleeding, these guidelines strongly recommend a structured and planned approach to escalate procedures, administer blood (and blood products) and manage obstetric haemorrhage when it develops rapidly. Frequent clinical assessment is key and should be supplemented with measurements of temperature, acid-base status, ionised calcium, haemoglobin, platelet count and coagulation profile. The key aim being the avoidance of the lethal combination of hypothermia, hypocalcaemia, acidosis and coagulopathy whilst achieving adequate resuscitation of the bleeding patient.[12]

It is worth noting that a large proportion of major PPH occurs post vaginal delivery with or without instrumental assistance.[4] This subgroup may or may not require anaesthetic involvement. However, the practicalities and fundamentals of management overlap significantly whether in an operating theatre or in the labour ward.

Resuscitation and management of a woman having a severe PPH is a complex scenario. The cognitive load is high and the interplay with human factors is significant. At our institution, there are dedicated policies, guidelines and cognitive aids.[14] All team member roles are clearly delineated. This includes obstetrics, anaesthetics, haematology, midwifery, nursing, laboratory, theatre technician and a team leader. As with all critical medical scenarios, good leadership and followship is crucial, with concise and frequent closed loop communication allowing smooth and efficient care whilst minimising errors. Cognitive aids provide mental assistance to staff (especially those in training) in stressful conditions in order to facilitate timely stepwise escalation in medical and surgical interventions. That being said, early senior clinician involvement is recommended in these cases.

Conclusion

Severe PPH has associated morbidity and mortality even in high income health systems. A clinician's understanding of the factors that contribute to associated complications are pivotal to triggering appropriate care responses. The main ones are emergency after-hours cases, abnormal placentation and low fibrinogen levels that have not been replaced despite massive blood transfusion occurring. Management of a severe PPH is a team game and best practice includes having a pre-planned systematic approach which encompasses modern day transfusion targets.

References

1. Kassebaum NJ, Bertozzi-Villa A, Coggeshall MS, et al. Global, regional, and national levels and causes of maternal mortality during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2014;384(9947):980-1004.
2. Australian Institute of Health and Welfare. Australia's mothers and babies web report 2021. Available from: www.aihw.gov.au/getmedia/bba093ef-a623-4cfd-818b-1bb5af9f0d20/Australia-s-mothers-and-babies.pdf.aspx?inline=true.
3. Mavrides E, Allard S, Chandraharan E, et al on behalf of the Royal College of Obstetricians and Gynaecologists. Prevention and management of postpartum haemorrhage. *BJOG*. 2016;124:e106–e149.
4. Lasica M, Sparrow RL, Tacey M, et al. Haematological features, transfusion management and outcomes of massive obstetric haemorrhage: findings from the Australian and New Zealand Massive Transfusion Registry. *Br J Haematol*. 2020;190(4):618-28.
5. Nair M, Choudhury MK, Choudhury SS, et al. Association between maternal anaemia and pregnancy outcomes: a cohort study in Assam, India. *BMJ Glob Health*. 2016;1(1):e000026.
6. Rahman MM, Abe SK, Rahman MS, et al. Maternal anemia and risk of adverse birth and health outcomes in low- and middle-income countries: systematic review and meta-analysis. *Am J Clin Nutr*. 2016;103(2):495-504.
7. Rukuni R, Bhattacharya S, Murphy MF, et al. Maternal and neonatal outcomes of antenatal anemia in a Scottish population: a retrospective cohort study. *Acta Obstet Gynecol Scand*. 2016;95(5):555-64.
8. Ali AA, Rayis DA, Abdallah TM, et al. Severe anaemia is associated with a higher risk for preeclampsia and poor perinatal outcomes in Kassala hospital, eastern Sudan. *BMC Res Notes*. 2011;4:311.
9. Brabin BJ, Hakimi M, Pelletier D. An analysis of anemia and pregnancy-related maternal mortality. *J Nutr*. 2001;131(2S-2):604S-14S; discussion 14S-15S.
10. WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System. Geneva, World Health Organization, 2011 (WHO/NMH/NHD/MNM/11.1) Available from: www.who.int/vmnis/indicators/haemoglobin.pdf
11. Ferguson MT, Dennis AT. Defining peri-operative anaemia in pregnant women - challenging the status quo. *Anaesthesia*. 2019;74(2):237-45.
12. National Blood Authority Australia. Patient Blood Management Guidelines: Module 5 Obstetrics and Maternity 2015. Available from: www.blood.gov.au/system/files/documents/20180426-Module5-WEB.pdf
13. Stephansson O, Dickman PW, Johansson A, Cnattingius S. Maternal hemoglobin concentration during pregnancy and risk of stillbirth. *Journal of the American Medical Association*. 2000;284(20):2611–7.
14. Royal Women's Hospital (VIC). Postpartum Haemorrhage Guideline. 2021.

Thromboembolism in pregnancy

Dr Eileen Merriman
MBChB, BMLSc, FRACP, FRCPA, PhD
Clinical Director Haematology
and Lead Thrombosis Clinician
Dept of Haematology, Waitemata DHB

Pulmonary embolism (PE) is the leading cause of maternal mortality in the developed world,[1] and deep vein thrombosis (DVT) can lead to post-thrombotic syndrome, which is associated with a reduced quality of life. The incidence of VTE (venous thromboembolism, mainly comprising DVT and PE) in pregnancy is approximately 1–2 in 1000 pregnancies,[4,5] with a risk that is static across the three trimesters; however, the daily absolute risk is highest in the postpartum period.5 Approximately two-thirds of lower-limb DVT occur in the antepartum period,[5] with left-sided involvement in over 95% of cases;[1] however, the majority of pregnancy-related PE occur in the postpartum period.[5]

Pregnancy is a hypercoagulable state, which is necessary to prepare the woman for the haemostatic challenge of delivery. Levels of fibrinogen and factors V, IX, X and VIII are increased, leading to enhanced thrombin generation, along with von Willebrand factor. Levels of the anticoagulant protein S is reduced, and pregnancy leads to a state of acquired protein C resistance.[5] Venous stasis begins in the first trimester and peaks at 36 weeks gestation, due to a combination of oestrogen-mediated reduction in venous smooth muscle tone (leading to venous distension), pelvic venous compression by the gravid uterus and endothelial injury at the point of crossing/compression of the left iliac vein by the right iliac artery.[5,6] The latter likely explains the striking propensity for involvement of the left leg veins by DVT. Endothelial damage occurring at the time of delivery likely accounts for the higher daily risk of VTE postpartum.[6]

Risk factors for pregnancy-related VTE include hereditary or acquired thrombophilia, personal or family history of VTE, superficial venous thrombosis, obesity, postpartum haemorrhage, caesarean delivery and assisted reproduction (Table 1).

Diagnosis

The threshold of suspicion for VTE in pregnancy is low, due to high maternal morbidity and mortality, and due to many symptoms of normal pregnancy mimicking those of VTE. The D-dimer rises steadily throughout pregnancy and often above the diagnostic cut-off threshold of 500mcg/L,[1] and only a few studies have addressed clinical decision rules combined with D-dimer in pregnancy.

One such study evaluated 498 pregnant women with clinically suspected PE using three criteria from the YEARS algorithm (clinical signs of DVT, haemoptysis and PE as the most likely diagnosis).[2] PE was ruled out if none of the three criteria were met and the D-dimer level was <1000ng/mL, or if one or more of the three criteria were met and the D-dimer level

Table 1. Risk Factors for pregnancy associated VTE.

Risk Factor	Odds ratio (95% CI)
Factor V Leiden (heterozygous)	8.3 (5.4–12.7)
Factor V Leiden (homozygous)	34.4 (9.9–120.1)
Antithrombin deficiency	4.7 (1.3–16.9)
Protein C deficiency	4.8 (2.2–10.6)
Protein S deficiency	3.2 (1.5–6.9)
Antiphospholipid antibodies	15.8 (10.9–22.8)
Previous VTE	24.8 (17.1–36.0)
Family history of VTE	3.9*
BMI >30mg/m2	5.3 (2.1–13.5)
Assisted reproduction	4.3 (2.0–9.4)
Blood transfusion	7.6 (6.2–9.4)
Antepartum haemorrhage	2.3 (1.8–2.8)
Postpartum haemorrhage	4.1 (2.3–7.3)
Pre-eclampsia	3.1 (1.8–5.3)
IUGR	3.8 (1.4–10.2)
Pre-eclampsia and IUGR	5.8 (2.1–16.0)
Emergency caesarean delivery	2.7 (1.8–4.1)

*95% CI not reported
Data from Bourjeily et al,[5] Chunilal & Bates,[6] Greer[7]

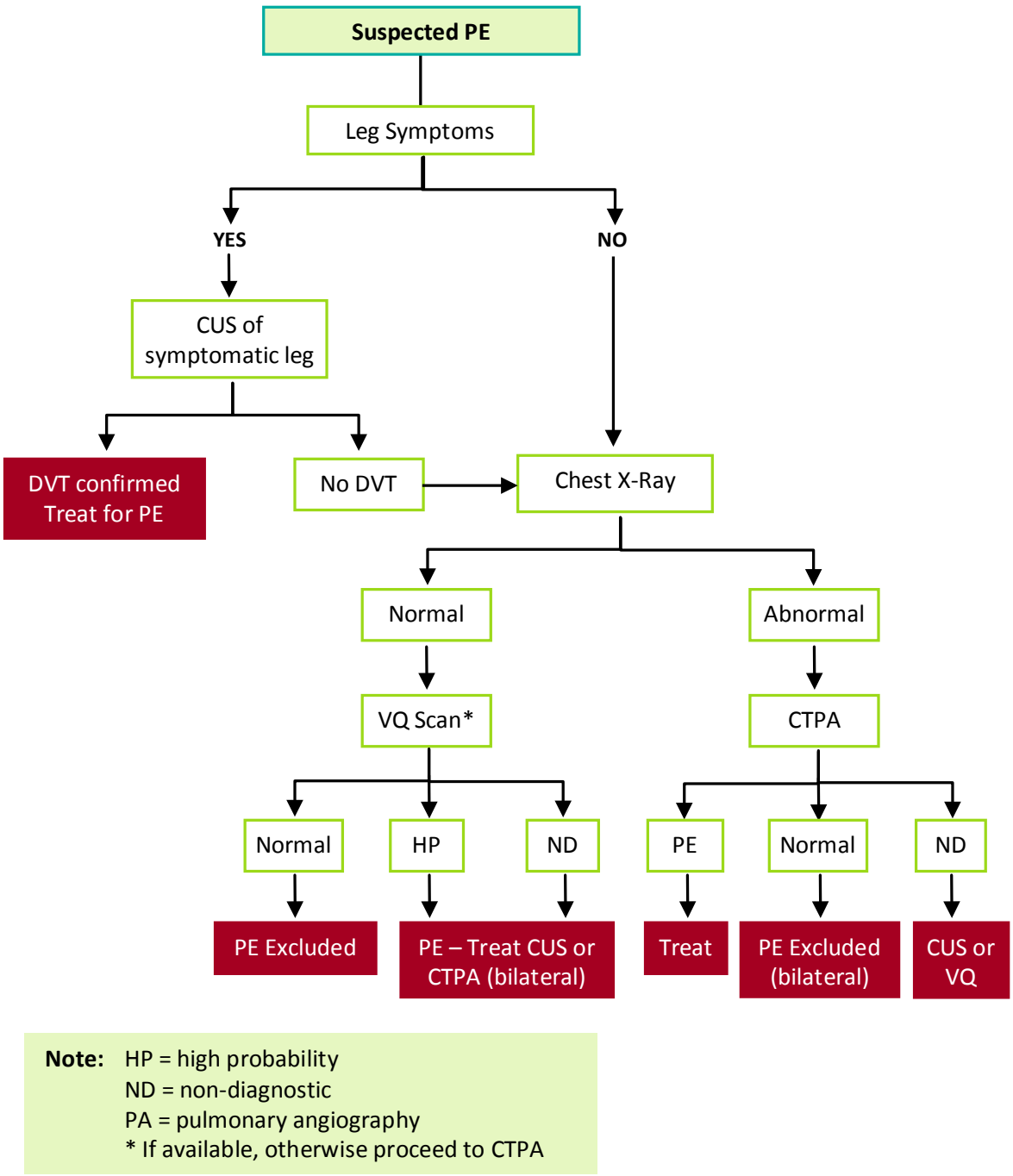


Figure 1. Diagnostic algorithm for PE in pregnancy.

was <500ng/mL; amounting to a PE rule-out in 65% of patients in the first trimester and 32% in the third trimester. The VTE rate at three-month follow up was low at 0.21% (95% CI 0.04-1.2). However, this relies on the experience of the clinician when evaluating whether or not PE is the most likely diagnosis.

A recent meta-analysis of four studies showed that a negative D-dimer was highly sensitive to rule out VTE in pregnant women with suspected VTE and a disease prevalence consistent with a low/intermediate or unlikely pretest probability, with a high negative predictive value.[3] However, the numbers included in the studies are small and further trials are needed to derive and validate specific clinical decision rules, and to determine the optimal D-dimer cut off during pregnancy.

The gold standard investigation for diagnosis of lower-limb DVT during pregnancy is complete compression ultrasound with visualisation of the iliac vein. If clinical suspicion remains despite a negative CUS, then MRI of the pelvic veins may be considered, although this technique is not validated for DVT.[4,5]

Figure 1 shows a suggested algorithm for diagnosis of PE in pregnancy. Imaging of the lungs for PE using CTPA or VQ scanning expose both the pregnant woman and her fetus to radiation. The radiation exposure to the fetus is lower for CTPA compared with VQ scanning, but negligible via both methods. However, exposure to the proliferating breast tissue of the woman is lower with a VQ scan.[1,4-7] For this reason, many guidelines recommend VQ scanning as

the preferred test in pregnant women with suspected PE. However, VQ scanning is not widely available, and breast shielding reduces breast radiation exposure from CTPA by >50%.[5,6] If a woman is suspected of having PE but also has symptoms suggestive of DVT (unilateral leg pain and/or swelling), then a leg ultrasound should be performed and if a DVT is diagnosed, this obviates the need for lung scanning as the treatment is identical.

Treatment

Low molecular weight heparin (LMWH) is the anticoagulant of choice for pregnant women, as LMWH does not cross the placenta and does not affect the developing fetus. Warfarin is teratogenic during pregnancy, but safe to use during breastfeeding. Direct oral anticoagulants (DOACs) are contraindicated in pregnancy and during breastfeeding due to limited human safety data and possible animal toxicity.[5]

For initial VTE treatment, there is no advantage in using a twice-daily LWMH regimen over once-daily, except in cases of extensive PE or DVT where a twice-daily regimen may be preferred for the first two weeks. It is usual to dose based on total body weight rather than pre-pregnancy weight. Monitoring with anti-Xa levels is not necessary except for women at extremes of body weight (<50kg or >90kg) or those with renal impairment (Cre Cl <30 ml/min) or recurrent VTE.[7] In such cases, an anti-Xa peak level of 0.5-1.0 U/mL four hours post-injection is recommended.[4]

The anticoagulation should be continued throughout pregnancy and for at least six weeks postpartum, with a minimum of six months anticoagulation for acute proximal DVT/PE.[3] A shorter total duration of therapy (6–8 weeks) may be appropriate in women with isolated distal (calf vein) DVT, with a possible reduction to prophylactic LMWH for the remainder of pregnancy and six-week postpartum period.[3] A reduced intensity of anticoagulation after a period of full-dose treatment during pregnancy could be considered and has been safe in other patient populations;[9] however, data from large-scale prospective studies in pregnant women is not available.

Thrombolysis should not be withheld in pregnant women who have life-threatening haemodynamic instability.[9] A literature review on 23 cases of pregnant women receiving systemic thrombolysis for massive PE reported no maternal deaths, with bleeding complications in 39% of cases (major bleeding in 22%), with 9% of fetuses dying.[10]

Management of anticoagulants around time of delivery

For pregnant women receiving prophylactic doses of LMWH around the time of delivery, the ASH 2018 guideline[9] suggests against scheduled delivery with discontinuation of prophylactic anticoagulation compared with allowing spontaneous labour. Women should be advised to stop LMWH at the first sign of contractions. For pregnant women that received therapeutic doses of LMWH around the time of delivery, the same guideline suggests scheduled delivery with prior discontinuation of anticoagulant therapy.

For women with VTE occurring more than three months prior to delivery, the last dose of 1mg/kg enoxaparin can be given 24 hours prior to a planned induction/caesarean section. For women with VTE occurring 1–3 months prior to delivery, the last dose of 1mg/kg enoxaparin can be given on the evening prior to induction; the patient can then be admitted the next morning and commenced on IV unfractionated heparin (IVUH) without a bolus. The heparin should be discontinued once the woman is in established labour (delivery anticipated within next 4–6 hours). The IVUH can be restarted 6–12 hours after delivery without a bolus (start at a low dose eg. 500 IU/hour) if haemostasis is adequate.

For VTE diagnosed within 1–3 weeks of delivery, a planned induction or caesarean section should be used as above with the use of IV heparin to allow the shortest time off anticoagulant. Placement of a retrievable IVC filter can be considered, especially within the first two weeks; however, the evidence base for these in pregnancy are limited and complications are potentially higher in this group.[11]

Conclusion

PE is the leading cause of maternal mortality in the developed world. Further trials are needed to derive/validate clinical decision rules, and to determine the optimal D-dimer cut-off in pregnancy. LMWH is the anticoagulant of choice for VTE prophylaxis and treatment during pregnancy; warfarin can safely be used postpartum. Delivery should be according to obstetric indications, with planned stopping and starting of anticoagulation in those on therapeutic anticoagulation.

References

1. Bourjeily, et al. Pulmonary embolism in pregnancy. *Lancet*. 2010;375:500-12.
2. Van der Pol L, et al. Pregnancy-adapted YEARS algorithm for diagnosis of suspected pulmonary embolism. *NEJM*. 2019;380:1139-49.
3. Bellesini M, et al. D-dimer to rule out venous thromboembolism during pregnancy: A systematic review and meta-analysis. *Thromb Haemost*. 2021;19:2454-67.
4. McLintock C, et al. Recommendations for the prevention of pregnancy-associated venous thromboembolism. *ANZJOG*. 2012;52(1):3-13.
5. Middeldorp S, Ganzevoort W. How I treat venous thromboembolism in pregnancy. *Blood*. 2020;136(19):2133-42.
6. Chunilal S, Bates S. Venous thromboembolism in pregnancy: diagnosis, management and prevention. *Thromb Haemost*. 2009;101:428-38.
7. Thrombosis in pregnancy: updates in diagnosis and management. Hematology *Am Soc Hematol Edu Program*. 2012:203-7.
8. Lee, et al. Low-Molecular-Weight-Heparin versus a Coumarin for the Prevention of Recurrent Venous Thromboembolism in Patients with Cancer. *NEJM*. 2003;349:146-53.
9. Bates SM, et al. American Society of Haematology 2018 guidelines for management of venous thromboembolism: venous thromboembolism in the context of pregnancy. *Blood Adv*. 2018;2(22):3317-59.
10. Heavner MS, et al. Thrombolysis for Massive Pulmonary Embolism in Pregnancy. *Pharmacotherapy*. 2007;37(11);1449-57.
11. Crosby D, et al. Retrievable inferior vena cava filters in pregnancy: Risk versus benefit? *Eur J Obstet Gynecol Reprod Biol*. 2018;222:25-30.

Thrombocytopenia in pregnancy

Dr Simon Kavanagh
MBBS, FRACP, FRCPA
Clinical Haematologist,
St John of God Health Care
Laboratory Haematologist,
PathWest Laboratory Medicine

Thrombocytopenia (defined by a circulating platelet count <150 x 10^9/L) is a common finding in pregnancy, affecting 5–10% of all pregnancies. The platelet count rarely falls below 100, with approximately 1% of pregnant women having a platelet count below this threshold.[1]

Pregnancy-associated thrombocytopenia may not require treatment but almost always requires additional surveillance and, if more severe, may have implications for delivery.

Aetiology

Common or clinically relevant causes of thrombocytopenia in pregnancy are shown in Table 1. This paper focuses primarily on causes of thrombocytopenia that are common (or of particular significance) in pregnancy.

Gestational thrombocytopenia

Gestation thrombocytopenia (GT) accounts for ~75% of all thrombocytopenia in pregnancy.[2,3] It usually presents with mild and isolated thrombocytopenia developing during the second or third trimester. The platelet count tends to fall with advancing gestation. The pathogenesis of GT is incompletely understood but may reflect a combination of haemodilution (due to plasma volume expansion) and increased platelet clearance.[4]

Though GT is usually mild, platelet counts as low as 50–70 have been reported. A platelet count <50 is unlikely to be gestational and alternative causes should be pursued.

Thrombocytopenia associated with systemic disorders

Disorders in this group differ widely in aetiology and pathogenesis but share a number of clinical features. Thrombocytopenia, hypertension, red blood cell (RBC) fragmentation, elevated liver enzymes, renal failure, abdominal and neurological symptoms may all be seen.[4] These conditions often follow an aggressive clinical course and require urgent investigation and treatment. A multi-disciplinary approach is essential to improve maternal and fetal outcomes.

Immune thrombocytopenia

While not unique to pregnancy, immune thrombocytopenia (ITP) is the most common cause for a platelet count <50 in the first and second trimesters.[4] It occurs due to IgG antibody binding to the platelet surface, accelerating clearance of the platelet-antibody complex by splenic/hepatic macrophages.[5] ITP may be detected in isolation but may also be seen in viral (hepatitis C, HIV) infection and in some autoimmune disease.

Investigation

A detailed clinical history, particularly relating to medication therapy, personal/family history

Table 1. Common/important causes of thrombocytopenia in pregnancy.

	Pregnancy-specific	Not specific to pregnancy
Isolated thrombocytopenia	• Gestational thrombocytopenia	• Artefactual thrombocytopenia • Immune thrombocytopenia (ITP) • Medication therapy/drugs • Type 2B von Willebrand disease • Inherited thrombocytopenia
Thrombocytopenia associated with systemic disorders	• Pre-eclampsia • HELLP* syndrome • Acute fatty liver of pregnancy	• TTP/HUS† • Autoimmune disease (SLE, APS‡) • Infection (especially viral) • Bone marrow disorders • Nutritional deficiency • Liver disease/splenic sequestration

* Haemolysis, Elevated Liver enzymes, Low Platelets

† Thrombotic Thrombocytopenic Purpura/Haemolytic Uraemic Syndrome

‡ Systemic Lupus Erythematosus, Antiphospholipid Syndrome

of thrombocytopenia, diet and the presence of other illness (eg. infection, skin rash, arthritis) is essential. The gestational age at onset and severity of thrombocytopenia must be established. Pre-pregnancy blood counts, if available, should be reviewed.

In vitro platelet aggregation, most often seen in EDTA-anticoagulated samples, warrants special mention. This is a common cause of artefactual thrombocytopenia. When platelet aggregation is identified on blood film review, or if there is onset of unexpected thrombocytopenia, repeat counts – including one collected into citrate anticoagulant – are recommended. Discussion with the haematology laboratory is often useful.

Not all women who develop thrombocytopenia during pregnancy need extensive investigation. One study demonstrated that, of 621 women with platelet counts between 116–149, none had obstetric complications related to thrombocytopenia.[3] Some authors have suggested that a count of 115 be considered the lower bound for the reference interval at term.[6]

Mild and late-onset thrombocytopenia in a well woman suggests GT and surveillance alone may be appropriate. Thrombocytopenia should generally be further investigated if it develops before or during the first trimester, is associated with systemic illness or the platelet count is <80. Initial investigation is context dependent but common initial investigations are shown in Table 2.

Detection of an autoantibody (eg. positive ANA) supports, though does not prove, an immune cause. Negative results do not exclude ITP. Antiphospholipid antibodies are particularly important to detect given their association with thrombotic risk. *Helicobacter pylori* serology (or urease breath test) is of use in confirmed ITP. Haemolytic markers (eg. direct antiglobulin test, haptoglobins) and ADAMTS13 assay should be performed where there is significant RBC fragmentation.

Management considerations

In general, a platelet count >100 does not require intervention, though ongoing surveillance blood is warranted. The frequency of testing depends on the platelet count and gestational age. A full blood count (FBC) every four weeks is often adequate in early pregnancy. Fortnightly testing is generally performed from 32–34 weeks gestation; weekly counts are advised when thrombocytopenia is more severe or if the clinical situation is unstable.

Delivery

Patients with a platelet count <100 should generally deliver in a hospital with obstetric experience and 24-hour access to laboratory testing and blood bank support. Significant bleeding is unlikely with either C-section or vaginal delivery with a stable platelet count of >50.[7] The decision between these modes of delivery should be based on obstetric factors. Rapidly progressive thrombocytopenia, or milder thrombocytopenia with platelet dysfunction, may be associated with higher risk of bleeding and caution used in these scenarios. Use of a ROTEM-guided critical bleeding protocol is recommended if significant bleeding is observed. Platelet transfusion may be needed.

Table 2. Initial investigation of thrombocytopenia in pregnancy.

FBC + blood film	Lupus anticoagulant
Reticulocyte count	Antiphospholipid antibodies
Coagulation studies	Autoantibodies (eg. anti-nuclear antibody +/- others)
Biochemistry (renal + liver function)	Viral serology (HIV, hepatitis B/C)
Lactate dehydrogenase (LDH)	Vitamin B12/folate
Thyroid function tests	Iron studies

Anaesthesia

Thrombocytopenia increases the risk of bleeding in neuraxial anaesthesia, particularly when epidural catheters are placed. The 'safe' platelet count depends on multiple factors including anaesthetist experience, procedure (spinal vs. epidural), use of medication/s that may impair platelet function, tempo of onset of thrombocytopenia and the presence of other medical issues. A recent position paper suggests that a neuraxial anaesthesia be considered in women with a platelet count >70, a normal coagulation profile and absence of other risk factors for bleeding.[8]

Venous thromboembolism

Thrombocytopenia does not provide adequate protection against venous thrombosis. The risk of thrombosis should be considered ante- and postpartum and weighed against the perceived risk of bleeding. Pharmacological thromboprophylaxis is generally safe when the platelet count is >50. Antiphospholipid syndrome, which may result in thrombocytopenia and heightened thrombotic risk, is a particularly challenging scenario requiring specialist input.

Neonatal management

Implications for the neonate depend on the cause of maternal thrombocytopenia. True gestational thrombocytopenia does not impact the newborn and measurement of the neonatal platelet count is not required if this diagnosis is secure.

In contrast, ITP may affect the newborn when antibodies of IgG isotype cross the placenta. Reported severity varies. Platelet counts <50 have been reported in ~10% of newborns of mothers with ITP while platelet counts <20 are reported in ~1% of neonates.[4,9] The maternal platelet count does not correlate with neonatal thrombocytopenia and only a history of a previously affected sibling is predictive. Unlike neonatal allo-immune thrombocytopenia (NAIT), which is not associated with maternal thrombocytopenia, intracranial haemorrhage due to maternal ITP is rare (<1%).[8] A platelet count should be performed at delivery. If thrombocytopenic, repeat counts in the first few days of life are recommended. As exposure to maternal antibody stops at delivery, serial testing of the neonate is not required if the initial platelet count is normal.

Treatment

Treatment is dependent on the cause and severity of thrombocytopenia. Availability of pharmacological and blood products – particularly intravenous immunoglobulin (IVIg) and platelets – should be considered in advance of delivery.

A trial of corticosteroids is often considered as the platelet count falls, especially if neuraxial anaesthesia is desired and ITP cannot be excluded. A significant increment in platelet count supports a diagnosis of ITP. Prednisolone at doses between 10–40mg is often used. In the absence of high-quality data on the optimal schedule, dosing depends on clinical urgency and other factors (eg. gestational diabetes). Following response, the dose should be tapered to the lowest effective dose. Non-response to steroids does not exclude ITP with at least one study suggesting that response rates to steroids are lower in pregnant (vs. non-pregnant) women.[10]

IVIg is often administered as second-line therapy in ITP. Response rates are in the order of 40%, somewhat lower than seen in non-pregnant populations.[10] While generally well-tolerated, responses to IVIg are often transient and repeat dosing may be required. ITP refractory to steroids and IVIg is a challenging scenario. Splenectomy, preferably in the second trimester, may be considered. Immunosuppression or thrombopoietin mimetics are uncommonly used in pregnancy. Platelet transfusion is typically reserved for when delivery or neuraxial anaesthesia are required and there has been refractoriness to (or insufficient time to trial) alternate therapies.

Treatment of thrombocytopenia associated with systemic disorders differs. In selected cases of pre-eclampsia expectant management may be appropriate. Delivery must be expedited if there is worsening thrombocytopenia, HELLP or other deterioration in maternal/fetal condition. Other disorders (eg. TTP/HUS, HELLP) typically require urgent delivery and additional specific therapy depending on the diagnosis. TTP is generally treated with plasma exchange (+/- other agents) while atypical haemolytic uraemic syndrome (aHUS) often requires renal support and use of inhibitors of complement activation. These conditions must be managed in a tertiary hospital environment.

Conclusion

Thrombocytopenia is a common finding in pregnancy. Establishing a diagnosis hinges on the time of onset, severity of thrombocytopenia and presence of other abnormalities. While surveillance is often sufficient, clinicians must remain alert to the possibility of other systemic disturbance that might indicate a more serious disease process. Treatment must be individualised and take into consideration preferences regarding neuraxial anaesthesia and availability of blood products.

References

1. Reese JA, Peck JD, Deschamps DR, et al. Platelet Counts during Pregnancy. *New England Journal of Medicine*. 2018;379(1):32–43.
2. Burrows RF, Kelton JG. Thrombocytopenia at delivery: a prospective survey of 6715 deliveries. *Am J Obstet Gynecol.* 1990;162(3):731–4.
3. Boehlen F, Hohlfeld P, Extermann P, et al. Platelet count at term pregnancy: a reappraisal of the threshold. *Obstet Gynecol.* 2000;95(1):29–33.
4. Cines DB, Levine LD. Thrombocytopenia in pregnancy. *Blood.* 2017;130(21):2271–7.
5. Cines DB, Blanchette VS. Immune Thrombocytopenic Purpura. *New England Journal of Medicine.* 2002;346(13):995–1008.
6. Pavord S, Hunt B. The Obstetric Haematology Manual. Cambridge University Press; 2018.
7. Xu X, Zhang Y, Yu X, Huang Y. Preoperative moderate thrombocytopenia is not associated with increased blood loss for low-risk cesarean section: a retrospective cohort study. *BMC Pregnancy and Childbirth.* 2019;19(1):269.
8. Eslick R, Cutts B, Merriman E, et al. HOW Collaborative position paper on the management of thrombocytopenia in pregnancy. *ANZJOG.* 2021;61(2):195–204.
9. Webert KE, Mittal R, Sigouin C, et al. A retrospective 11-year analysis of obstetric patients with idiopathic thrombocytopenic purpura. *Blood.* 2003;102(13):4306–11.
10. Sun D, Shehata N, Ye XY, et al. Corticosteroids compared with intravenous immunoglobulin for the treatment of immune thrombocytopenia in pregnancy. *Blood.* 2016;128(10):1329–35.

Porphyria: often misunderstood and rarely diagnosed

Jessica Betterridge
President
Porphyria Association Inc. (Australia)

Dr Gayle Ross
MBBS (Hons) FACD
Royal Melbourne Hospital, Victoria

The porphyrias are a group of rare genetic metabolic diseases that are often misunderstood and rarely diagnosed. They are characterised by changes to the heme biosynthesis pathway. The different subtypes of porphyria are often confused by medical professionals and patients alike. There are eight types of porphyria, and they are broken down into acute and cutaneous subcategories.

The Acute Hepatic Porphyrias (AHP); Acute Intermittent Porphyria, Variegate Porphyria, and Hereditary Coproporphyria are most typically associated with abdominal pain and other symptom clusters that patients might report to a GP, gastroenterologist or O&G. This article will be focusing on the experiences of people who have been diagnosed with AHP rather than Cutaneous Porphyria.

The acute porphyrias present as acute attacks that are triggered by a variety of environmental and pathological factors. Symptoms tend to be worse in women than men and attacks can be life-threatening if not promptly identified and treated. In women, attacks may be associated with the luteal phase of menstruation. The word acute refers to the presentation of this type of porphyria which comes on in acute attacks, typically lasting days to weeks; however, some patients can develop chronic pain postulated to be related to nerve damage from repeated acute attacks.

I represent the Australian Porphyria Association; I have been the President of the Association since 2015. The Association is in the process of lobbying for access to GIVLAARI® (givosiran), Normosang® (human hemin) and SCENESSE® (afamelanotide). Increased access to treatments has been a key objective for the association for a number of years. Doctors have been key in this process, running clinical trials and partnering with consumer groups to improve patient health outcomes. During my time at the association, I have heard the stories of many men and women who have AHP. It is always quite interesting to hear their stories, they often sound like they are reading from the same script. For this article I will focus on the stories of the women that contact us.

Usually, people experiencing AHP for the first time will present between ages 18 and 35. People with AHP typically experience considerable non-localised abdominal pain, nausea, neurological changes, light sensitivity, and reddish-brown urine (that contains no blood). The most typical time to have an onset of AHP is after puberty, trauma, or pregnancy.

The story of women with AHP is common. The first thing patients tell me is that they saw their GP for their unexplained abdominal pain and other seemingly random symptoms. Their GP will usually refer them to a gynaecologist who will then often perform an explorative laparoscopy to look for endometriosis. If nothing is found, it is common for them to have their appendix and/or gallbladder removed. Unfortunately, during this surgical exploration process, they typically become more unwell despite having no specific findings on usual tests, further confusing the clinical picture. This can be due to the use of contraindicated medications or fasting from surgery. Once usual surgical and diagnostic imaging options have been explored and nothing has been found, they are discharged without a diagnosis or management plan. Those that are persistent will then go back to their GP who then refer them onto a psychiatrist for assessment. This can be incredibly distressing for the patients who are then told that the symptoms they are experiencing are 'all in their head', but treatable peripheral drivers have not been excluded. Patients are typically misdiagnosed with an array of conditions before the correct diagnosis is established.

Dr Gayle Ross, the head clinician at the Royal Melbourne Hospital Porphyria Clinic recently came across a new case of hereditary coproporphyria (HCP). A 28-year-old woman presented to the porphyria clinic at Royal Melbourne hospital with a 4-year history of recurrent episodes of generalised, severe abdominal pain. It flared premenstrually and was associated with nausea and vomiting. She had a rash on her face consisting of sores with scabs. She had been extensively investigated for both gastrointestinal and gynaecological causes of abdominal pain and was being considered for a total colectomy. Porphyrin studies were ordered and were consistent with HCP. Given her ongoing episodes that caused incapacitation premenstrually, she was

treated with prophylactic haem arginate, monthly via a portacath for several years, with suboptimal control. She had recurrent symptoms that included poor coordination and falls. She became more complicated when she attempted IVF conception with resulting flares due to the hormones, and this was ultimately unsuccessful. Gonadotropin releasing hormone (GnRH) Analogues were not tolerated. At the age of 44, she underwent a hysterectomy and bilateral oophorectomy to induce menopause in order to stop her episodes of abdominal pain. She is now on low-dose hormone replacement therapy and her porphyria symptoms have almost completely resolved. She is being managed for osteoporosis.

Without the correct diagnostic testing, this can be the end of the journey to diagnosis for patients. Many women can have a delay of up to ten years until the correct diagnosis is confirmed. Those who are lucky enough to have a doctor who is knowledgeable about porphyria have a shorter diagnosis period and can avoid many years of permanent physical damage and emotional distress.

The good news is that testing for porphyria is straightforward and inexpensive. The testing for porphyria involves a simple blood, urine, and faecal test: write on the pathology request 'porphyrin studies, porphyrin screen'. See pathology form on the next page for an example.

All samples need to be protected from light by covering the specimen jar/tube with aluminium foil and can be collected at any hospital or pathology clinic. Porphyria can only be confirmed by positive biochemical testing, not by symptoms alone.
The Medical Advisory Board of the Australian Porphyria Association recommends that all types of porphyria should be tested for in the screening test but recommend that any family history and symptoms are recorded on the pathology form. There is currently a lack of testing for AHP with only approximately 400 pathology tests for undiagnosed patients requested in Victoria annually. Given the very minimal cost, it is hard to imagine why someone might have expensive repeated CT imaging, recurrent emergency presentations and not a once-off inexpensive test.

If AHP was regularly tested for in people presenting to their GP or gynaecologist with persistent, unexplained abdominal pain, we would see the numbers of patients diagnosed increase. Experts in Australia have long expressed how underdiagnosed AHP is. It is estimated that there are over 500 patients that are currently undiagnosed in Australia and New Zealand.

Porphyria is underdiagnosed, and while there are some major centres that have clinics, we need more research into the disease. One of the questions that have perplexed doctors is the prevalence of HCP as the dominant subtype of AHP in Australia and New Zealand.

Porphyria patients can often struggle with being heard and listened to by medical professionals. Many patients tell me that they were labelled as 'drug seekers' or 'attention seekers' during and/or after their diagnosis. This could partly be due to the confusing and complicated way that they might present. They also may not have many changes to their pathology until the attack progresses to a life-threatening stage. In addition, AHP can affect people neurologically which might change their typical behaviour and they could be experiencing anxiety

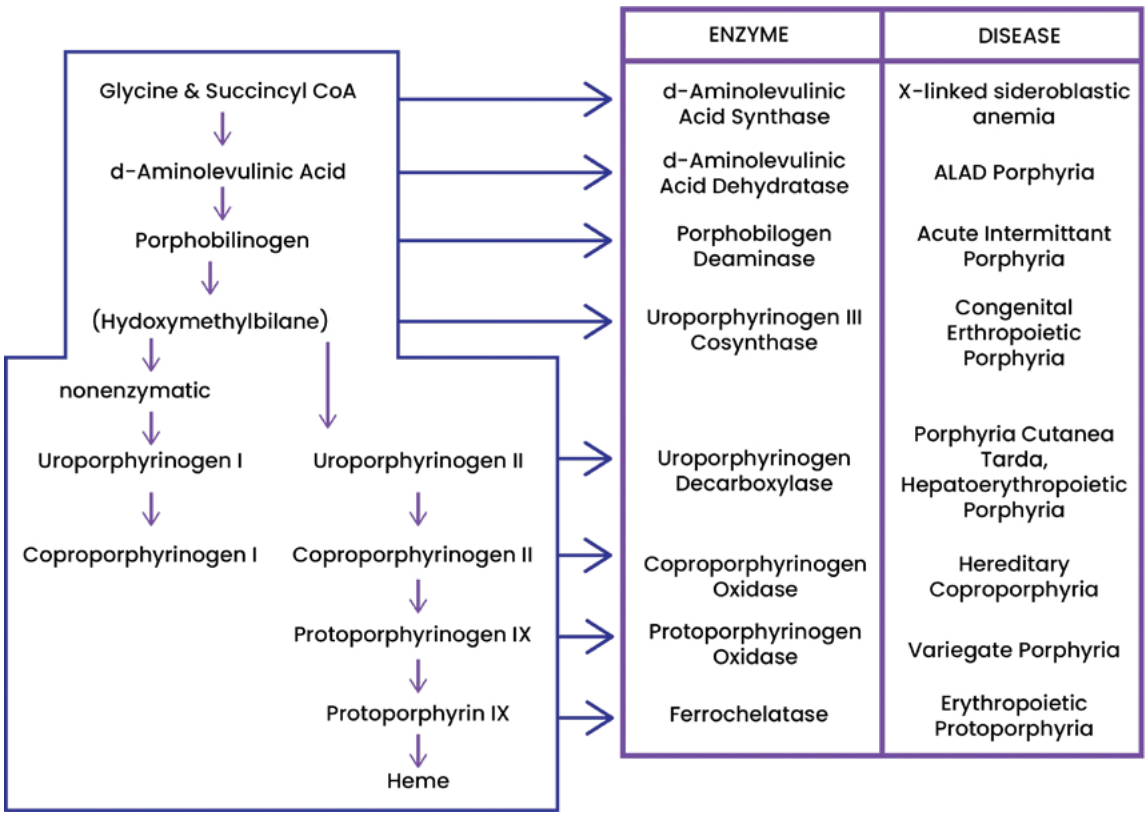
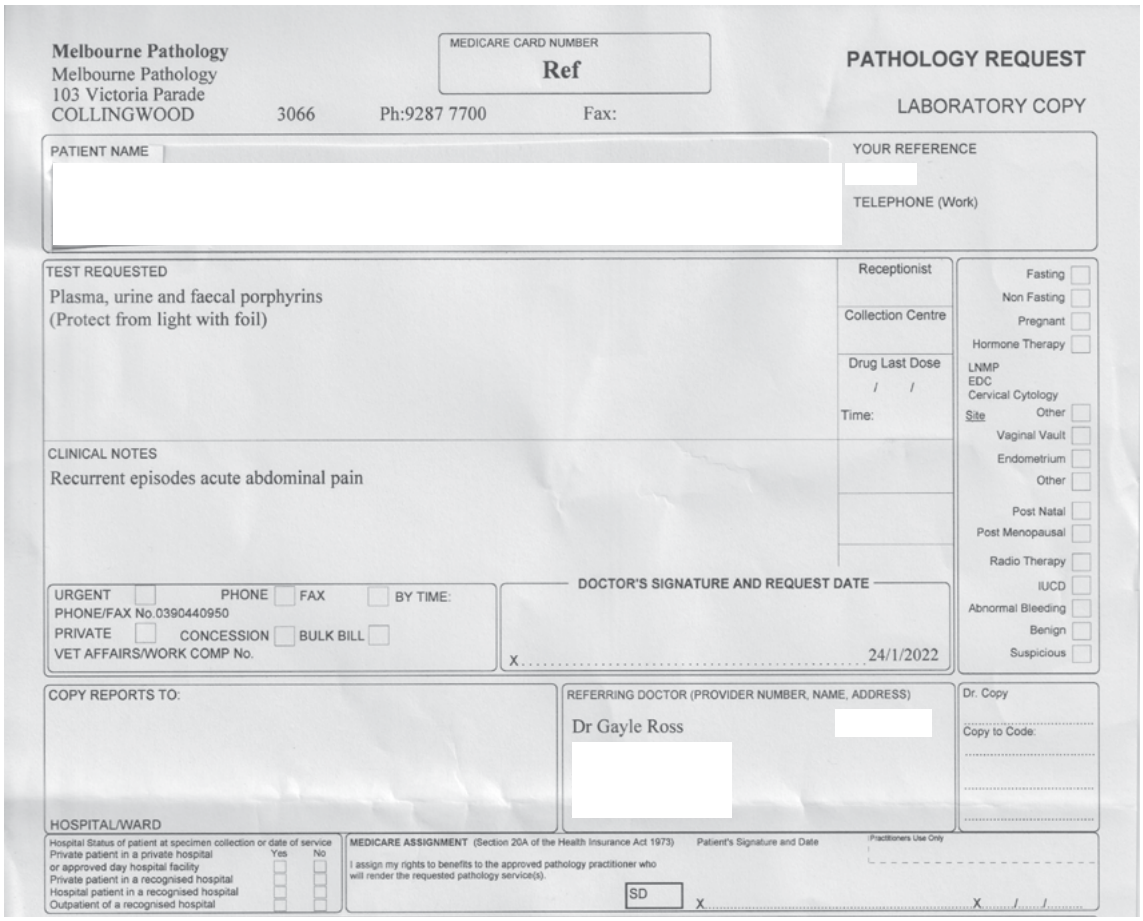


Figure 1. Heme Biosynthesis Pathway.



Melbourne Pathology
Melbourne Pathology
103 Victoria Parade
COLLINGWOOD 3066 Ph:9287 7700 Fax:

MEDICARE CARD NUMBER
Ref

PATHOLOGY REQUEST
LABORATORY COPY

PATIENT NAME

YOUR REFERENCE

TELEPHONE (Work)

TEST REQUESTED
Plasma, urine and faecal porphyrins
(Protect from light with foil)

Receptionist
Collection Centre
Drug Last Dose / /
Time:

Fasting
Non Fasting
Pregnant
Hormone Therapy
LNMP
EDC
Cervical Cytology
Site Other
Vaginal Vault
Endometrium
Other
Post Natal
Post Menopausal
Radio Therapy
IUCD
Abnormal Bleeding
Benign
Suspicious

CLINICAL NOTES
Recurrent episodes acute abdominal pain

URGENT PHONE FAX BY TIME:
PHONE/FAX No.0390440950
PRIVATE CONCESSION BULK BILL
VET AFFAIRS/WORK COMP No.

DOCTOR'S SIGNATURE AND REQUEST DATE
X 24/1/2022

COPY REPORTS TO:

HOSPITAL/WARD

REFERRING DOCTOR (PROVIDER NUMBER, NAME, ADDRESS)
Dr Gayle Ross

Dr. Copy
Copy to Code:

Hospital Status of patient at specimen collection or date of service
Private patient in a private hospital or approved day hospital facility
Private patient in a recognised hospital
Hospital patient in a recognised hospital
Outpatient of a recognised hospital
Yes No

MEDICARE ASSIGNMENT (Section 20A of the Health Insurance Act 1973)
I assign my rights to benefits to the approved pathology practitioner who will render the requested pathology service(s).
SD

Patient's Signature and Date
X

Practitioners Use Only
X / /

Figure 2. Example pathology form.

and brain fog due to the acute attack. Understanding and awareness of the disease are key drivers to help improve the care that these women receive. It is very important to listen to the patients and to be aware that they have probably had some negative and distressing experiences with health professionals before they walked into your room. Women will tell me how excited they were when either their GP or specialist understood their disease and were relieved they didn't feel the need to explain it to them.

In O&G, consider porphyria in your patient who has unexplained abdominal pain, and perhaps multiple sensitivities to medicines or intolerance of the pill and other hormones. Know there are specific treatments available but that most of our knowledge comes from case series from specialised units. Depending on the genetics, women may choose IVF and PGD prior to pregnancy and consider contacting us to source the genetic counsellor and doctor with most experience in your area. Testing, listening and knowledge is key for the better treatment of women with AHP. If you were considering research in this area, there are many investigated areas that you could conduct research in. Some of these topics are:

1. What proportion of women presenting to emergency departments have porphyria?
2. What is the incidence of porphyria in patients with undiagnosed abdominal pain?
3. How should a woman with AHP requiring contraception be counselled?
4. Pregnancy outcomes in patients with AHP. How many have porphyria flares? Any implications for delivery?
5. Can patients accurately tell whether their abdominal pain is porphyria versus alternative gynaecological diagnoses?

For more information, please go to the Australian Porphyria Association's Website www.porphyria-australia.org or to watch the new educational video series that has been developed by leading Australian and New Zealand specialists and scientists in the field, see the Australian Porphyria Associations Facebook page www.facebook.com/porphyriaaustralia/videos/?ref=page_internal.

Special thanks to Dr Marilla Druitt for assistance with this article.

References

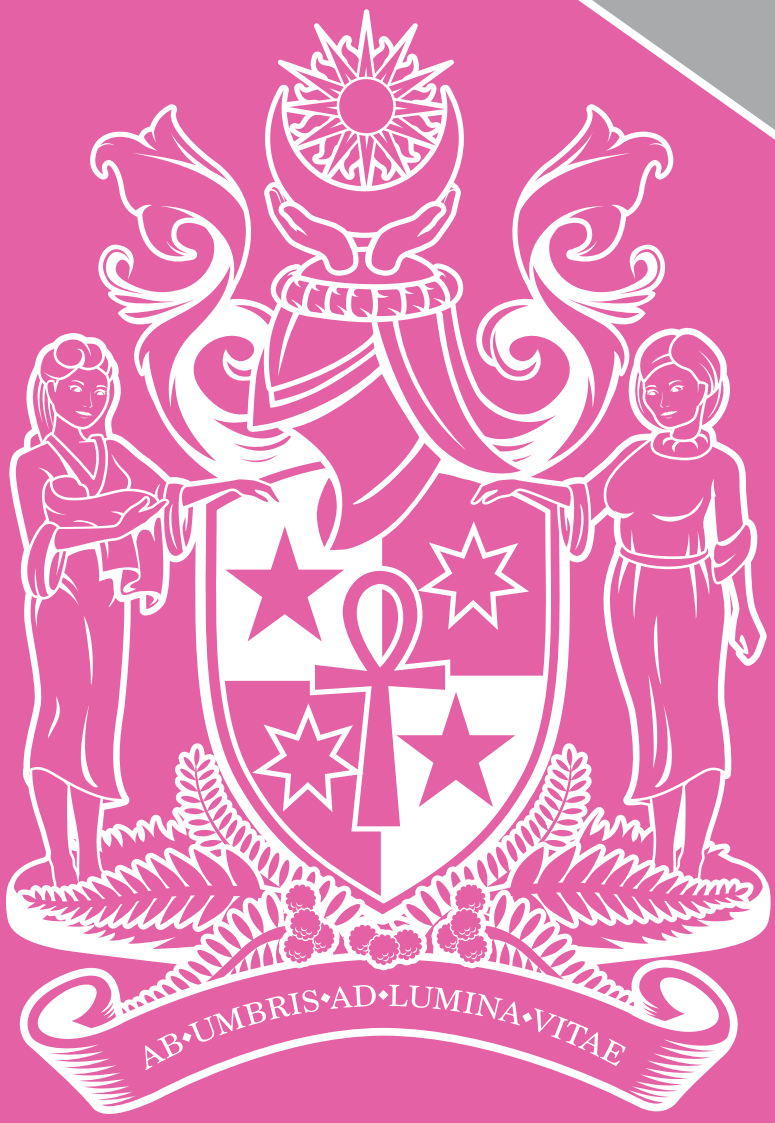
1. American Porphyria Foundation, 2020. Available from: https://porphyriafoundation.org/apf/assets/Image/patients/testing/enzymechart
2. Klose RT. Porphyria. Magill's Medical Guide (Online Edition), 2019. Available from: https://search.ebscohost.com/login.aspx?direct=true&AuthType=sso&db=ers&AN=86194445&site=eds-live&scope=site.
3. Sohail QZ, Khamisa K. Acute porphyria presenting as abdominal pain in pregnancy. *Canadian Medical Association Journal*. 2021;193(12):E419–E422. doi: 10.1503/cmaj.202384.
4. Edel Y, et al. The clinical importance of early acute hepatic porphyria diagnosis: a national cohort. Internal and Emergency Medicine: *Official Journal of the Italian Society of Internal Medicine*. 2021;16(1):133–9. doi: 10.1007/s11739-020-02359-3.

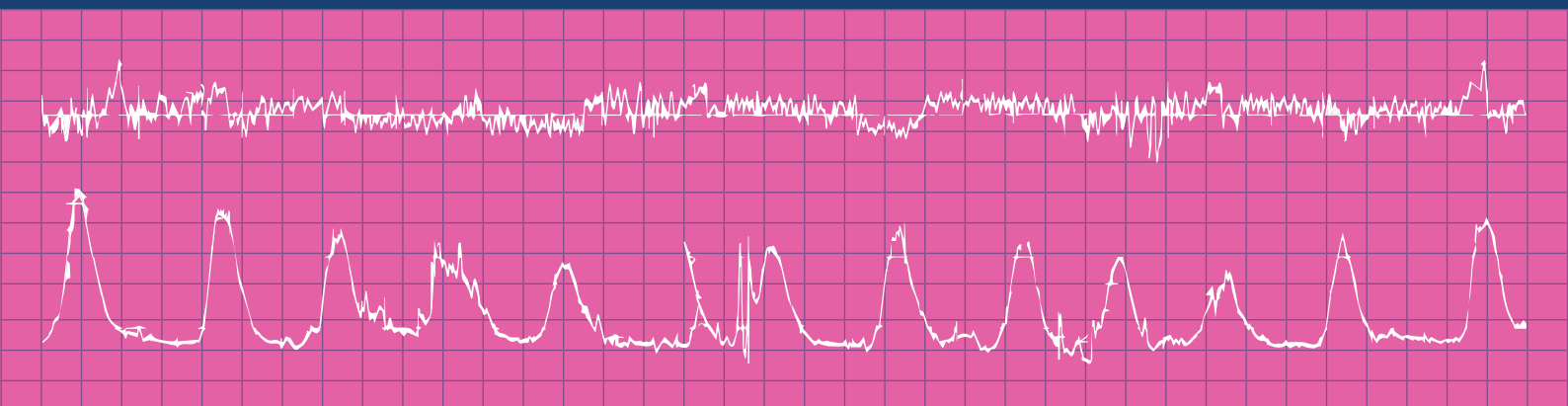
Intrapartum Fetal Surveillance

Clinical Guideline – Fourth Edition 2019

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists

AVAILABLE NOW!





Normal serum-ferritin in pregnancy: less is more

Dr Barton Smith
BSc (hons 1st), PhD, MBBS, FRANZCOG

Ferritin is a 12nm polypeptide comprised of 24 protein chains arranged as a hollow octahedral cage to imprison iron. It is designated H (heavy), or L (light), depending on protein structure, and binds iron cations to protein chains and converts the cations to stable iron-hydroxides in the core of the complex.[1,2] Serum-ferritin is ordinarily measured using a chemiluminescent antibody assay that quantifies ferritin, not the amount of iron it houses, which can be determined using mass spectrometry if need be.[2] Each protein complex can house as many as 4,500 iron atoms, but they are rarely this saturated.[1-5]

Ferritin is synthesised in the liver and spleen where production is regulated at a post-transcriptional level via an interaction with iron-responsive elements in the mRNA, so under iron homeostasis the rate of intracellular ferritin synthesis is constant.[6-8] Most ferritin is intracellular with only a small fraction of total body ferritin being found in the serum. Some is leached into the circulation from dead cells and some is actively secreted in the absence of apoptosis,[2] so it can be used as a crude surrogate for whole-body iron storage provided the rate of iron flux in and out of the circulation is constant. In practice this means inflammation must be quiescent, the patient must not be on iron supplements, primary or secondary iron overload pathology must be absent, there is no history of recent blood transfusions or significant bleeding, and the patient cannot be a neonate.

Serum-ferritin's primary purpose is to encapsulate and safely house circulating iron cations.[2] It can be high in the presence of true iron overload (hereditary haemochromatosis),[9] high when total body iron is normal (early neonates,)[10] or high despite true net iron stores being low (sepsis, cancer, trauma).[11] Conversely, serum-ferritin can be low despite iron poisoning (months after intravenous iron), low in the setting of adequate body iron stores (healthy young children),[12] and low in the presence of truly reduced body iron (women with menorrhagia). A protean protein.

Diminishing serum-ferritin is typical beyond the first trimester,[13,14] but this scarcity is maligned because the benefits of gestational iron restriction are unheralded. Dietary iron absorption during the first trimester is so low it fails to recoup obligatory integumentary and gastrointestinal losses, and does not meet basal requirements even once gestational amenorrhoea is taken into account.[15,16] The ensuing hypoferremia is often assumed to be pathological, but it serves two logical protective purposes:

1. Iron restriction is the host's primary defence against septicaemia.[10] Gestational immune tolerance mediated by beta human chorionic gonadotrophin[17] mitigates rejection of the confined semi-allogenic fetus, but at the expense of diminished cellular immunity, which in turn benefits iron-dependant obligate intracellular organisms during pregnancy (eg. Listeria, Klebsiella).[18,19] To compensate, iron scarcity impedes bacterial reproduction and also increases the relative abundance of apotransferrin, which then stringently binds any remaining iron and further enhances bacteriostasis by binding divalent cations other than Fe2+ on gram-negative cell walls, increasing susceptibility to host defences.[20,21]
2. Hypoferremia protects the embryo during critical organogenesis in the absence of the placental barrier by mitigating oxidative stress, since iron catalyses the Fenton Reaction[22] which generates free radicals that disrupt DNA synthesis.[23,24] In circulatory iron-overload pathologies, such as hereditary haemochromatosis, thalassemias, and sickle-cell disease, both miscarriage and infection rates are notorious in part due to the harmful effects of iron toxicity.[25-29]

Envisaging serum-ferritin as an emergency mop for spilt iron in the circulation rather than a marker of tissue iron stores is a useful analogy and provides a ready explanation for serum-ferritin oscillations. Neonates demonstrate the role of serum-ferritin vividly – within twelve hours of birth, a neonate effectively eliminates circulating iron, mainly by doubling serum-ferritin, to protect against sepsis.[10] Once dangerous ionic iron has been mopped up, serum-ferritin falls and remains very low throughout healthy childhood.[12] Administering parenteral iron to neonates is associated with increased mortality[30] and is contraindicated for this reason. Pregnancy serum-ferritin trajectory is similar, although the initial rise post-conception is more subtle, and the subsequent decline[13,14] more gradual than that seen in early neonates. If serum-ferritin is already low at conception[14] an initial serum ferritin surge is not seen (superfluous), and ferritin remains low for the entire pregnancy.

A dramatic example of ferritin oscillation is evident following intravenous iron administration. Serum-ferritin rises several hundred-fold within days of an iron infusion, but within weeks recedes from its peak to near pre-injection baseline levels despite virtually none of the injected iron exiting the

body.[31,32] Clearly this precipitous ferritin recoil cannot reflect iron deficiency. The likely explanation is that ferritin is urgently secreted into the circulation to encapsulate unliganded iron, and once sequestered, the levels of ferritin are then safely reduced back to baseline. Manufacturers of iron carboxymaltose (FCM) interpret this ferritin oscillation as supporting evidence for the safety and efficacy of their product.[31] However, it is contradictory to claim that FCM does not leach unliganded iron into the circulation, yet then claim raised serum-ferritin as evidence for the efficacy of the product, and then lay further claims that declining ferritin levels are evidence of successful iron transfer to the target organs. Serum-ferritin should not surge post-infusion if FCM is as robust as theoretically touted.

Studies of pregnant women randomised to varying levels of oral iron have shown that increased iron fortification during pregnancy yields higher initial postpartum serum-ferritin levels, but at six monthly follow-up these levels fall disproportionately relative to non-fortified patients.[33,34] This excess fall reflects cessation of excess iatrogenic iron receding with time rather than a drop in tissue iron stores. Again, the ferritin sequestrates excess iron, then recedes as it is no longer needed. Elevated serum-ferritin co-exists with chronic inflammation, and the effects of iron-leaching can be seen in the absence of iatrogenic iron. A common example relevant to obstetrics is that of gestational diabetes[35] – one likely mechanism is that high blood sugar concentration damages endothelium and ionic iron is then leached into the circulation, which is then encapsulated by ferritin. Diabetic patients are not preferentially endowed with iron, they likely need more circulating ferritin to impound the rogue iron.

Ferritin concentration is an excellent gauge of disease severity because it directly correlates with iron leaching into the circulation, and therefore approximates the degree of cellular damage. Ferritin accurately predicts mortality in patients infected with Covid-19,[36,37] and it also predicts mortality on admission to intensive care independent of disease aetiology.[11] It rises with ageing[12] because raised ferritin reflects elderly disease prevalence, not antique iron storage. Geriatrics do not bequeath an iron surplus. The ferritin protein cage itself is normally benign, but in the setting of iron overload it binds to erythrocyte membranes causing premature lysis and increases the propensity to clot.[2] Raised ferritin during pregnancy should never be comforting, save a transient rise to reduce circulating iron in the first few weeks of gestation.

A collation of two-million Australian ferritin assays demonstrates that around one-quarter to one-third of reproductive aged females who have had serum ferritin analysed have a level less than a nominal value of 30ug/L.[12] Admittedly, this is a skewed representation of the population as an unknown number of these tests would have been undertaken to investigate presumed iron deficiency – some being genuinely anaemic, and some not. Regardless, serum ferritin has an extraordinarily wide statistical dispersion for a biochemical marker,[2] analogous to the Gini coefficient of Brazil. It has a non-Gaussian distribution that is both age and sex dependent, which in turn reflects normal physiological life-stages, as well as a range of disease states. The unrealistic lower limit of 30ug/L adopted by Australian chemical pathologists[12] and used by most obstetricians in Australia is purely arbitrary and statistically baseless. Studies that have been done throughout pregnancies without interference from iatrogenic iron clearly show that a serum-ferritin less than 30ug/L is entirely normal for a gravid women, regardless of the analytical platform used.[13,14]

Unsurprisingly, there has never been an agreed lower limit of serum-ferritin during pregnancy,[38] and nor should there be a need for one, unless low circulating iron is proven detrimental to pregnancy. At present, refining the reputed sensitivity of serum iron assays in an effort to diagnose iron deficiency with alternative markers such as serum transferrin receptor concentration[2] is futile, as any test that directly or indirectly quantifies circulating iron will inevitably conclude that normal pregnant women have innate biology geared towards restricting circulating iron. Similarly, invasive efforts to truly estimate net body iron stores with a liver biopsy (contraindicated in pregnancy) or a calibrated MRI are pointless. There is no good reason to measure serum-ferritin, transferrin, or serum-iron during pregnancy. Invariably, ferritin will be reduced, together with raised transferrin, and a healthy increased iron binding capacity, but none of this is evidence that a pregnant women is pathologically deficient in iron. Treating the number rather than the patient is poor practice. In privileged settings such as Australia with low prevalence of severe anaemia, low pregnancy serum-ferritin accompanies healthy hypoferremia and appropriate haemodilution, not necessarily deficient disease. Mild to moderate anaemia by World Health Organization standards[39-42] is consistent with favourable pregnancy outcomes, and by inference, so is the normal pregnancy iron debt.

Oral iron in early pregnancy is poorly absorbed, and causes black stools, constipation and worsens haemorrhoids. Unfortunately, this instructive clinical gift is often misinterpreted by well-meaning clinicians as treatment malfunction rather than malfunctional treatment, reduced serum-ferritin is misconstrued as evidence for iron deficiency, and the affliction of intravenous iron follows suit. Tellingly, there is no evidence intravenous iron supplementation during pregnancy improves any tangible obstetric outcomes,[43,44] but it is a lucrative pharmaceutical. Cunning and persistent marketing backed by drug funded research[32,45,46] has hoodwinked the Australian federal government into a pharmaceutical benefits listing, in the process bankrolling $257.52 AUD per infusion. Vifor Pharma reported an annual increase in Ferrinject sales in Europe, Australia and New Zealand of 22% in 2021, totalling $480million AUD. Not all of this pertains to pregnancy therapy, but a sizeable proportion does.

Obstetricians do not treat mid-trimester hypotension with intravenous inotropes just because the patient feels a bit faint. Until a large double-blinded placebo controlled trial proves otherwise, permissive tolerance of gestational hypoferremia should also be encouraged in antenatal care, rather than reverting to 1000mg of intravenous iron just because the patient asked for it, or because she feels understandably tired, or because her serum-ferritin is healthy for pregnancy – low.

References

1. Theil EC. Ferritin: the protein nanocage and iron biomineral in health and in disease. *Inorg Chem.* 2013;52(21):12223. doi:10.1021/ic400484n
2. Kell DB, Pretorius E. Serum ferritin is an important inflammatory disease marker, as it is mainly a leakage product from damaged cells. *Metallomics*. 2014;6(4):748-73. doi:10.1039/c3mt00347g
3. Knovich MA, Storey JA, Coffman LG, et al. Ferritin for the clinician. *Blood Rev.* 2009;23(3):95-104. doi:10.1016/j.blre.2008.08.001

Full Reference list available online

Anaemia: often overlooked

Dr Ella Houston
BSc, MBBS (Hon)
ANZCA Advanced Trainee,
Townsville University Hospital

Perioperative anaemia is commonly encountered in patients undergoing major elective surgery with a reported prevalence of 30–60%. It is defined as a haemoglobin less than 130 g/L in males and less than 120 g/L in non-pregnant females. The early identification of anaemia is particularly relevant given its association with worse outcomes after surgery, including increased mortality, morbidity, allogeneic blood transfusion and longer length of stay.[1-3] The aim of this article is to summarise major guidelines and recent literature on this topic with the hope it will provide the impetus to identify this at-risk cohort early, investigate and institute appropriate management.

Absolute and functional iron deficiency

The aetiology of anaemia in surgical patients is complex and often multi-factorial, which further complicates its diagnosis and management. The most common cause of anaemia is absolute iron deficiency, secondary to increased demand, decreased supply or increased loss. Another large subset of surgical patients exist in a state of chronic inflammation, resulting in functional iron deficiency or iron sequestration. In this setting, enteric iron is unable to be absorbed and body iron stores are inaccessible due to upregulation of the regulatory protein hepcidin. Distinguishing between the two is paramount, as although iron is necessary in both instances, intravenous iron to bypass the enteric route, often in combination with erythropoiesis stimulating agents, is required in the setting of inflammation. The key to diagnosing iron deficiency and distinguishing between absolute and functional iron deficiency lies in interpretation of iron studies.

Demystifying iron studies

In the first instance, interpretation of iron studies begins with assessment of ferritin levels. A ferritin level <30 µg/L is indicative of absolute iron deficiency, with a sensitivity and specificity of 92% and 98% respectively. Ferritin between 30–100 µg/L and either transferrin saturation <20% or CRP >5 mg/L is also suggestive of absolute iron deficiency. Ferritin >100 µg/L in combination with transferrin saturation <20% suggests functional iron deficiency, that is, the presence of adequate iron stores that are inaccessible to the body. In addition to investigation of the underlying cause, subsequent management of iron deficiency will depend on the urgency of surgery, tolerance and response to oral iron therapy.

What to do?

An international consensus statement on the management of perioperative anaemia and iron deficiency recommends a trial of oral iron with dietary advice in the first instance, if time to surgery is greater than 6–8 weeks, with reassessment of efficacy after 4 weeks. Conversely, administration of intravenous iron is recommended if non-deferrable surgery is scheduled within 6–8 weeks.[4] Peak increase in haemoglobin after intravenous iron is anticipated at 3 weeks. Practice guidelines also recommend iron replacement in patients with suboptimal iron stores (ferritin <100 µg/L) if significant blood loss (>500 mL) is anticipated.[5] In this setting, intraoperative blood loss culminating in a postoperative haemoglobin decrease of 30 g/L or greater would exhaust body iron stores. Importantly, in order to facilitate these recommendations, appropriate investigations must be ordered and reviewed when patients are initially booked for surgery including full blood count, iron studies, a measure of inflammation (eg. serum CRP) and renal function.

A spanner in the works

Recommendations from major guidelines have been described above; however, a discussion of anaemia and iron deficiency would not be complete without mention of the recently published Preoperative intravenous iron to treat anaemia before major abdominal surgery (PREVENTT) trial.[6] This large multicentre randomised controlled trial was published in the Lancet in September 2020. It investigated the effect of administration of intravenous iron 10–42 days prior to major elective open abdominal surgery in patients with anaemia on the composite outcome of death or transfusion events 30 days postoperatively. In summary, there was no difference between the intervention and placebo group with respect to the primary outcome, despite a modest increase in haemoglobin preoperatively. Secondary endpoints suggested some benefits with respect to decreased readmissions for complications, which will be further investigated in a follow-up study. This trial suggests that a blanket approach to preoperative anaemia with administration of intravenous iron is not superior to placebo and advocates that tailored strategies aimed at treating the underlying cause may be more appropriate.

The big picture: Patient Blood Management

Investigation and correction of anaemia and iron deficiency is just one part of the broader picture of Patient Blood Management (PBM). PBM principles aim to reduce unnecessary administration of blood products and associated transfusion-related risks via adoption of a three-pillar approach. These three pillars apply throughout the perioperative journey and encompass optimisation of red cell mass (as outlined in this article), minimisation of blood loss and improving patient tolerance of anaemia.[5] We all have a role to play in implementing these recommendations, from investigating and treating anaemia throughout the perioperative period, minimising blood loss with evidence-based intraoperative haemostatic techniques and by applying a considered approach to ordering of blood investigations, as well as adopting restrictive transfusion strategies. The perioperative period serves as an opportunity to identify and manage modifiable risk factors such as anaemia with the hope of improving patient-centred outcomes.

Full Reference list available online

Iron deficiency in clinical practice

Dr Scott Cullen
MBBS, BBiomed (Hons)
Obstetrics and Gynaecology Resident

Dr Erin O'Reilly
RACP/RCPA
Haematology Advanced Trainee (Paediatrics)

Ms Emma Cameron
Accredited Practising Dietitian,
Mercy Hospitals Victoria Ltd

Iron deficiency (ID) is the most common micronutrient deficiency worldwide, contributing significantly to the global burden of disease.[1] ID is poorly defined in the O&G setting, with variations in diagnostic thresholds, investigative frameworks and management strategies.[2-3] ID can occur with or without anaemia, and remains the most common cause of anaemia in pregnancy worldwide.[4] Anaemia in pregnancy is defined by The World Health Organization as a haemoglobin (Hb) of <110g/L in the first 20 weeks, and <105g/L in the second 20 weeks of pregnancy.[5] In this article, we aim to cover the essentials of ID for students and clinicians alike, with a focus on providing a framework for the investigation and management of ID in pregnancy and the early postpartum period.

ID has important implications for both maternal and fetal health. For women of reproductive age, 14–22% have ID.[6] Women with ID can experience impairment to muscle, immune and neurological function, and have lower reported quality of life.[7-8] In Australia, 18% of pregnant people have iron deficiency anaemia (IDA), associated with a two- to threefold increase in iron requirements during pregnancy.[9-10] This occurs largely due to an increase in maternal red cell volume and fetal erythropoiesis (see Figure 1).[11] Inadequate iron stores are associated with immediate neonatal complications including preterm birth, low birth weight, and reduced iron stores in the newborn.[4,12] In the longer term, ID in pregnancy has been associated with neurodevelopmental concerns, including cognitive and behavioural difficulties.[4] Anaemia additionally has an impact on lactation, including reduced milk supply and lower rates of breastfeeding at six months.[13-14]

Outside of pregnancy, heavy menstrual bleeding (HMB) is a common, under-recognised cause of ID in the O&G setting. It affects 25% of menstruating people, increasing in prevalence in the perimenopausal period.[7,15] ID in patients with HMB may go untreated as clinicians are focused on managing the HMB in isolation.[16] Typically women experience >400 menstruations in their lifetime, depending on contraceptive and family choices, which can have a significant impact on blood loss and iron requirements.[17] Historically, women experienced 100–150 menstruations over a lifetime due to increased parity; hence establishing amenorrhea to reduce overall iron losses may be a more physiological treatment option for those not wishing to conceive. It is important to recognise that neither HMB or pregnancy in isolation are likely to cause significant or refractory IDA, and further investigation is required in most cases.[18] Guidance on the management of HMB can be found in the Australian Heavy Menstrual Bleeding Clinical Care Standard (2017).[19]

Interpretation of the full blood examination (FBE) and ferritin in pregnancy are challenging due to the normal reduction in some parameters due to physiological haemodilution. These changes are most significant from 28–36 weeks, which is similar to the timeframe of greatest iron requirement.[10] It is important to recognise the difference between ID that has onset in later stages of pregnancy, where pregnancy factors are the likely cause, versus ID identified in the first trimester or non-pregnant state. We suggest checking ferritin levels as part of routine prenatal care. During preconception counselling, clinicians have an opportunity to discuss optimisation of iron status prior to pregnancy, and additionally identify and manage potential causes of ID. Of note, patients with ferritin levels >80ug/L in the first

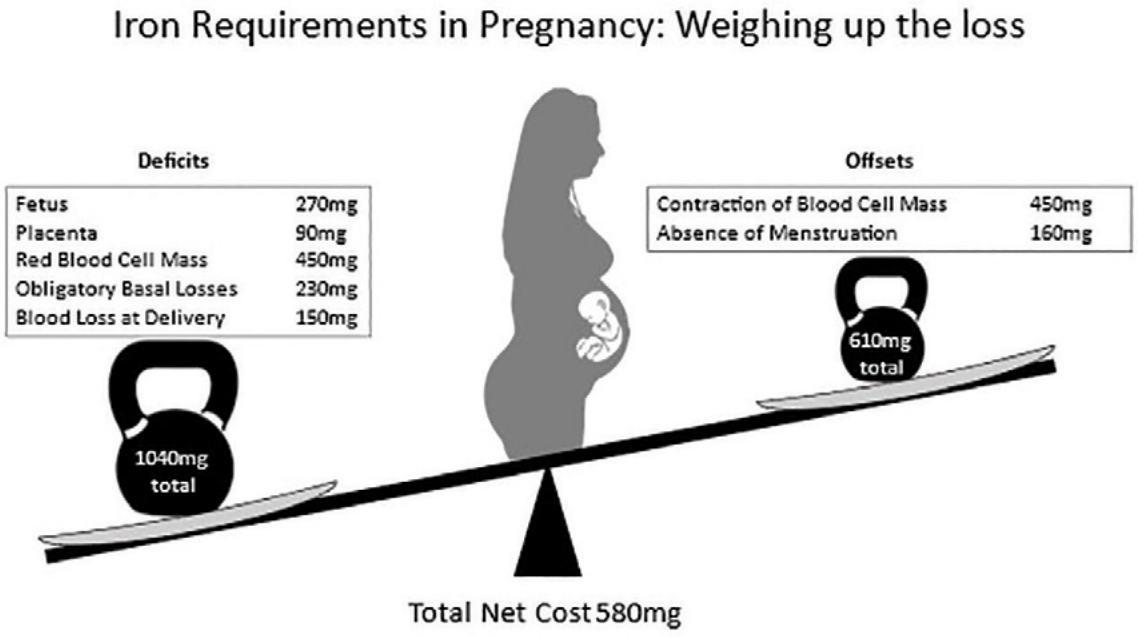


Figure 1. Iron requirements of pregnancy. *Adapted from tables provided in reference 11.*

trimester are likely to have adequate iron stores for the remainder of their pregnancy.[20]

ID can be confirmed in pregnancy on the basis of a serum ferritin level <30ug/L. Complete iron studies are not typically required and are significantly more expensive (see Table 1). Serum iron levels have significant diurnal variation and can reflect recent iron intake. The FBE will confirm anaemia, and the red cell indices (MCV and MCH) and blood film can help confirm ID (ie. microcytic, hypochromic red cells), and distinguish from thalassaemia trait.[21] Haemoglobinopathies, including thalassaemia and abnormal haemoglobins (eg. sickle cell disease), are increasing in prevalence in the Australian context due to immigration patterns.[22] Occasionally, IDA is confused with thalassaemia trait as both conditions present with microcytic, hypochromic red cells, and it is possible for these conditions to co-occur. Individuals with anaemia in pregnancy due to thalassaemia trait do not require iron supplementation, unless they have proven co-existing iron deficiency.[23]

Table 1. Cost of pathological investigations as per MBS schedule.

Test	Cost ($)
Full blood examination	7.85
Iron studies	32.55
Ferritin	18.88
Coeliac serology	49.50
Coeliac gene testing	118.85
B12 total/Active	23.60/42.95
Folate	23.60
Haemoglobin electrophoresis/ chromotography	90.20
Alpha/Beta Thalassaemia Gene Analysis	100–1000

Where ID is identified, particularly where refractory to iron replacement, potential causes should be carefully considered. A diet history is essential as approximately 40% of Australian women of reproductive age do not have adequate dietary iron intake.[24] In premenopausal women with ID, British guidelines (endorsed by the gastroenterological society of Australia) recommend screening for Coeliac disease (CD), as this cohort of patients represent 4% of ID cases and are typically refractory to oral iron supplementation.[25-27] In Australia, the prevalence of CD is approximately 1.4%, with a significant portion undiagnosed. Dietary gluten must remain for accurate testing via serology.[27] HLA gene testing on gluten-free patients may assist as 99.6% of the CD population have genes coding HLA-DQ2 or HLA-DQ8; thus, a negative test largely excludes the possibility of CD.[27] Identifying CD as a cause of ID in patients is important, as it has implications for fertility including recurrent miscarriage.[28] Those at risk of mixed nutritional deficiency should have B12 and folate levels assessed. This includes patients with restrictive intake, malabsorption or refugee background where there is emerging B12 and folate deficiency.[29-30]

Table 2. Management options for side effects of oral iron therapy.

Side effect	Intervention
Nausea/vomiting	Divided dosing, alternate formulation (eg. liquid, anti-emetics)
Constipation	Divided dosing, aperients
Teeth staining	Avoid liquid formulation
Reflux	Divided dosing, PPI therapy

Table 3. Key factors to consider when screening patients at risk of iron deficiency.

Factors	Examples
Does the patient have increased iron requirements?	• Pregnancy: recommended dietary intake (RDI) of 27mg/day, compared to 18mg/day for menstruating people aged 19–50yrs[36] • Heavy menstrual bleeding
Does the patient follow a diet reliant on non-haem iron sources?	• Vegetarian • Vegan
Could the patient have impaired absorption of iron?	• Newly diagnosed coeliac disease • Inflammatory bowel disease • Previous bowel resections or short gut syndrome • Bariatric surgery
Does the patient have any other nutrition impact symptoms?	• Anorexia • Nausea • Vomiting • Early satiety • Diarrhoea/constipation

Recommended approach to managing iron deficiency in obstetric patients

Dietary sources are inadequate to replace iron stores for pregnant people with established ID, hence first-line therapy is oral iron supplementation. The Australian recommendations are to commence treatment where ferritin levels are <30ug/L.[31] Recent data indicates that second daily iron dosing may be superior to daily dosing, with fewer side effects, and a higher total and fractional iron absorption.[32] Whilst 100mg iron supplementation has a greater fractional absorption compared to 200mg, the total absorption is greater with 200mg, and as such would be advisable in IDA. Consideration should be given to lower doses (minimum 60mg elemental iron) for patients that are not anaemic.[31] We suggest a trial of iron for four weeks, followed by repeat FBE and ferritin level. An earlier FBE at two weeks may be prudent in the setting of significant anaemia in early pregnancy, concerns regarding ongoing blood loss and/or uncertainty about the diagnosis. Treatment compliance should be reviewed on an ongoing basis, with consideration being given to missed doses and optimising tolerability (see Table 2). In anaemic patients, failure of oral therapy should be demonstrated by a lack of Hb response after four weeks of therapy. Pregnant people with Hb <70g/L or those who are hemodynamically unstable require prompt review and urgent referral to a Haematologist. Lifeblood's flowchart 'Hb assessment and optimisation in pregnancy' is a useful management guideline.[31]

In later stages of pregnancy, where there are significant bleeding risks or where oral iron has been inadequate/not tolerated, intravenous (IV) iron replacement may be more appropriate. IV iron and its indications have been previously discussed in *O&G Magazine* along with potential side effects.[33] Hypophosphatemia is a potential serious side effect of treatment with ferric carboxymaltose; however, is less well recognised compared to anaphylaxis, extravasation, and delayed serum sickness.[34] Clinicians should be familiar with all potential side effects, and refer to their local guidelines prior to administering IV iron. The need for a blood transfusion should be considered based on clinical symptoms and a patient's Hb level, and is generally appropriate in the postpartum setting where the Hb is <70g/L. When transfusion is indicated, a single red cell unit should be transfused with re-evaluation of the Hb and clinical status, unless clinically significant haemorrhage. The risk of transfusion and the potential for red cell alloimmunisation should be balanced against the potential of minimal benefit. Iron infusions may be given in addition to blood transfusion where additional iron is needed to support post pregnancy recovery, including for lactation. Of note, a single unit of red cells typically contains 250mg of iron. Lifeblood guidelines recommend oral iron therapy in the postpartum setting if Hb >80g/L in the non-transfused population for a minimum of six weeks.[31]

For all pregnant people, and those trying to conceive, it is essential to discuss dietary contributions to iron deficiency. Early identification of patients at risk of ID is important to facilitate a preventative rather than curative strategy. Key risk factors for ID are outlined in Table 3, and particular attention should be paid to patients with multiple risk factors. These patients should be considered for referral to an accredited practising dietitian. Dietary iron is differentiated as haem and non-haem, with haem iron having the greatest bioavailability (see examples of each in Table 4). Consider dietary intake of substances that inhibit or promote iron absorption. Phytates, including unprocessed bran, polyphenols including tea and coffee, and calcium decrease the absorption of non-haem iron particularly and should be spaced apart.[35] In contrast, ascorbic acid found in foods such as citrus fruits, berries, broccoli, tomato and capsicum increases non-haem iron absorption, as does co-ingestion of haem iron foods. The possibility that an individual's microbiome may lead to variations in iron absorption is the subject of ongoing research.

Table 4. Examples of dietary sources of haem and non-haem iron.

Haem	Non-haem
Red meat (eg. lamb, beef and pork)	Legumes
Poultry (eg. chicken, turkey)	Nuts (including nut butters)
Fish	Green leafy vegetables
Offal	Iron fortified cereals

Conclusions

ID is a treatable cause of anaemia in pregnancy. We suggest clinicians focus on optimising iron stores prenatally where possible by providing clear dietary advice, and commencing oral iron supplementation where serum ferritin levels are low. For those who are already pregnant, second daily oral iron should be considered to improve both absorption and tolerability. In cases where there is refractory iron deficiency, or perceived higher risks of anaemia, IV iron replacement may be more appropriate. In all cases, ongoing review for treatment compliance and monitoring for the common side effects of oral iron replacement should be undertaken. Screening for common causes of ID in premenopausal people, including HMB and CD, may help to improve not only a patient's iron status, but also their pregnancy outcome and overall quality of life.

Table 5. The dos and don'ts of iron deficiency in pregnancy.

Do	Don't
Give clear dietary advice to all patients trying to conceive or who are already pregnant	Attempt to treat iron deficiency by changing diet alone
Utilise oral iron supplements as first-line treatment for iron deficiency	Forget to check for side effects of oral iron supplements
Check FBE and ferritin four weeks post initiating treatment	Routinely order full iron studies in pregnancy
Consider screening for Coeliac disease	Forget to consider second daily oral iron supplementation
Screen for Thalassemia when there are microcytic, hypochromic red cell indices and a normal ferritin	Forget your local guideline for IV iron and potential side effects including hypophosphatemia
Check B12 and folate for mixed nutritional deficiency where appropriate	Presume it's not your job if it's not an obstetric cause

References

1. Bailey RL, West KP, Black RE. The epidemiology of global micronutrient deficiencies. Ann Nutr Metab. 2015;66(suppl 2):22-33.
2. Daru J, Allotey J, Pena-Rosas JP, et al. Serum ferritin thresholds for the diagnosis of iron deficiency in pregnancy: a systematic review. Transfus Med. 2017;27(3):167-74.
3. Stoffel NU, Zeder C, Brittenham GM, et al. Iron absorption from supplements is greater with alternate day than with consecutive day dosing in iron deficient anaemic women. Haematologica. 2020;105(5):1232-9.
4. Juul SE, Derman RJ, Auerbach M. Perinatal iron deficiency: implications for mothers and infants. Neonatology. 2019;115(3):269-74.
5. WHO. Iron Deficiency Anaemia, Assessment, Prevention, and Control: a Guide for Programme Managers. Geneva: World Health Organization. 2001.
6. Stevens, GA, Finucane MM, De-Regil LM, et al. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995-2011: a systematic analysis of population representative data. Lancet Glob Health. 2013;1(1):e16-25.
7. Karlsson TS, Marions LB, Edlund MG. Heavy menstrual bleeding significantly affects quality of life. Acta obstet gynecol scand. 2014;93(1):52-7
8. Fraser IS, Mansour D, Breymann C, et al. Prevalence of heavy menstrual bleeding and experiences of affected women in a European patient survey. Int J Gynaecol Obstet. 2015;128(3):196-200.
9. Khalafallah A, Dennis A, Bates J, et al. A prospective randomized controlled trial of intravenous versus oral iron for moderate iron deficiency anaemia of pregnancy. J Intern Med. 2010;268(3):286-95.
10. Soma-Pillay P, Nelson-Piercy C, Tolppanen H, et al. Physiological changes in pregnancy. Cardiovasc J Afr. 2016;27(2):89-94.
11. Bothwell TH. Iron requirements in pregnancy and strategies to meet them. Am J Clin Nutr. 2000;72(1 suppl):257S-264S.
12. Aub-ouf NM, Jan MM. The impact of maternal iron deficiency and iron deficiency anaemia on child's health. Saudi Med J. 2015;36(2):146-9.
13. Henley SJ, Anderson CM, Avery MD. Anaemia and insufficient breast milk in first-time mothers. Birth. 1995;22(2):86-92.
14. Chua S, Gupta S, Curnow J, et al. Intravenous iron vs blood for acute post partum anaemia (IIBAPPA): a prospective randomisted trial. BMC Pregnancy and Childbirth. 2017;17(1)424.
15. Royal College of Obstetricians and Gynaecologists. National heavy menstrual bleeding audit. London: RCOG; 2014.
16. Mansour D, Hofmann A, Gemzell-Danielsson. A review of the clinical guidelines on management of iron deficiency and iron deficiency anaemia in women with heavy menstrual bleeding. Adv Ther. 2021;38(1):201-25.
17. Strassman B. The biology of menstruation in homo sapiens: total lifetime menses, fecundity and nonsynchrony in a natural fertility population. Curr Anthropol. 1997;38(1):123-9.
18. Sinclair M. Iron deficiency: clinical update [internet].2nd ed. Mulgrave (AU): Gastroenterology Society of Australia; 2015.
19. Australian Commission on Safety and Quality in Health Care. Heavy Menstrual Bleeding Clinical Care Standard. Sydney: Australian Commission on Safety and Quality in Health Care; 2017.
20. Hallberg L, Bengtsson C, Lapidus L, et al. Screening for iron deficiency: an analydis based on bone marrow examinations and serum ferritin determinations in a population of sample women. Br J Haematol. 1993;47(120):875-9.
21. Van Vranken M. Evaluation if microcytosis. Am Fam Physician. 2010;82(9):1117-22.
22. Tan YL, Kidson-Gerber G. Antenatal haemoglobinopathy screening in Australia. Med J Aust. 2016;203(6):226-30.
23. Verma S, Gupta R, Kudesia M, et al. Coexisting iron deficiency anaemia and Beta thalassemia trait: effect of iron therapy on red cell parameters and hemoglobin subtypes. ISRN Hematol. 2014;2014:e1-5.
24. Australian Bureau of Statistics. Australian health survey: usual nutritional intakes. Belconnen (AU): Australian Bureau of Statistics; 2015:44.
25. Snook J, Bhala N, Beales ILP, et al. British society of gastroenterology guidelines for the management of iron deficiency anaemia in adults. Gut. 2021;70(11):2030-51.
26. Hershko C, Camaschella C. How I treat unexplained refractory iron deficiency anaemia. Blood. 2014;123(3):326-33.
27. Tye-Din J. Interpreting tests for coeliac disease: tips, pitfalls and updates. Aust J Gen Pract. 2018;47(1-2):28-33.
28. Martinelli P, Troncone R, Paparo F, et al. Coeliac disease and unfavourable outcome of pregnancy. Gut. 2000;46(3):332-5.
29. Benson J, Phillips C, Kay M, et al. Low vitamin B12 levels among newly-arrived refugees from Bhutan, Iran and Afghanistan: a multicentre Australian study. PLoS one. 2013;8(2):e57998.
30. Brown RD, Langshaw MR, Uhr EJ, et al. The impact of mandatory fortification of flour with folic acid on the blood folate levels of an Australian population. Med J Aust. 2011;194(2):65-7.
31. Australian Red Cross Lifeblood. Haemoglobin assessment and optimization in maternity. Melbourne: Australian Red Cross Lifeblood. 2020.
32. Stoffel NU, Zeder C, Brittenham GM, et al. Iron absorption from supplements is greater with alternate day than consecutive day dosing in iron-deficient anaemic women. Haematologica. 2020;105(5):1232-9.
33. Cutts B. Q&A: Iron infusions in pregnancy. O&G Magazine (RANZCOG). 2016;18(2). Available from: www.ogmagazine.org.au/18/2-18/qa-2/
34. Ifie E, Oyibo S, Joshi H, et al. Symptomatic hypophosphataemia after intravenous iron therapy: an underrated adverse reaction. Endocrinol Diabetes Metab Case Rep. 2019(1):19-0065.
35. Hurrell R, Egli I. Iron bioavailability and dietary reference values. Am J Clin Nutr. 2010;91(5): 1461S-1467S.
36. National Health and Medical Research Council [NHMRC]. Nutrient Reference Values for Australia and New Zealand: Iron. 2006 [updated 2014]. Available from: www.nrv.gov.au/nutrients/iron

Thalassaemia and haemoglobinopathy screening in pregnancy

Dr Cara Lacey
Royal Children's Hospital

Haemoglobinopathies encompass both the thalassaemia syndromes (alpha and beta thalassaemia) and structural haemoglobin variants. It is important to offer screening for pregnant women, ideally prior to conception, with the aim of detecting asymptomatic carriers so a couple may be counselled on reproductive risks and clinical implications to the fetus and child. Screening should include a full blood evaluation (FBE) and blood film, ferritin, and high-performance liquid chromatography (HPLC) or haemoglobin (Hb) electrophoresis.

Haemoglobin

The Hb molecule is a stable heterotetramer consisting of two pairs of globin polypeptide chains and a haem (iron component). The four globin chains determine the Hb type. Three main types of Hb are found in adults: Haemoglobin A (HbA), Fetal Haemoglobin (HbF) and Haemoglobin A2 (HbA2). HbA is made up of two alpha and two beta globin chains (α2/b2). HbF is made up of two alpha and two gamma globin chains (α2/g2). HbA2 is made up of two alpha and two delta globin chains (α2/d2).

Haemoglobinopathies

Genetic changes in the globin chains may result in altered production, structure, or function of Hb molecule. Over 1000 genetic variations have been described in the different globin chains.[1]

Thalassaemia is specific to alpha and beta globin chain production whereby it is reduced or ineffective. Mutations in alpha globin genes result in alpha thalassaemia and mutations in beta globin genes cause beta thalassaemia. Alpha and beta globin chains are normally produced in an exact ratio, and this is tightly regulated. When an individual has thalassaemia, this ratio is disrupted, leading to an imbalance of globin chains. This imbalance in globin chains contributes to the patient's symptoms or clinical phenotype. Genetic mutations that result in an abnormal haemoglobin structure are called haemoglobin variants, including HbS, HbC, HbD, HbE, HbO and Hb Lepore. An individual may be both a carrier of thalassaemia and a carrier of a Hb variant.

Alpha thalassaemia

Alpha globin chain production is controlled by four genes (two genes on each chromosome 16). A deletion in one alpha globin gene results in a silent alpha carrier status (normal Hb with a normal or mildly reduced mean corpuscular volume [MCV]). A two gene alpha deletion usually results in a normal Hb with a reduced MCV and reduced mean corpuscular haemoglobin (MCH), termed alpha thalassaemia trait. Deletions in three alpha globin genes is termed Haemoglobin H (HbH) disease, due to the production of HbH (formed from four beta globin chains [b4]. HbH disease is associated with a moderately severe microcytic anaemia and haemolysis but varies in severity depending on the specific gene mutations. When all four alpha globin genes are deleted, resulting no alpha globin chain synthesis and production, Hb Barts (four gamma globin chains [g4]) is made. Bart's hydrops fetalis is associated with non-immune hydrops and frequently fatal in utero and associated with significant maternal complications including hypertension, oedema, proteinuria, and mortality.[2] A summary of the alpha globin gene mutations is provided in Table 1.

Beta thalassaemia

There are two beta globin genes, one inherited from each parent. An individual with a mutation in one beta globin gene will typically have a mild microcytic hypochromic anaemia and is referred to as a carrier of beta thalassaemia (beta thalassaemia trait). Beta thalassaemia trait is associated with an elevated HbA2 due to reduced beta globin chains needed to make HbA and is usually diagnosed by HPLC. The degree of HbA reduction depends on the nature of the gene mutation, some cause reduced production of the beta globin chains whereas some result in no production.

If an individual has two beta globin gene mutations, they will have reduced or absent beta chain production, the severity of their disease will depend on the amount of normal beta chains produced and the specific genetic defects. Severely reduced beta globin gene production results in severe anaemia and requires regular blood transfusion and is termed beta thalassaemia major or transfusion-dependent beta thalassaemia.

Clinical manifestations of beta thalassaemia extend beyond anaemia to symptoms of increased and ineffective erythropoiesis such as bony expansion, hepatosplenomegaly and haemolysis. Ineffective erythropoiesis increases iron absorption which

Table 1. Alpha globin gene mutations and expected clinical phenotype.

Number of mutations	Genotype	Clinical Phenotype
0	αα/αα	Normal/Healthy
1	-α/αα	Silent Carrier/ Healthy
2	-α/-α or --/αα	Carrier – reduced MCV and MCH
3	--/-α	HbH disease – Mild to severe haemolytic anaemia
4	--/--	Hb Barts – Hydrops fetalis

contributes to iron overload. Iron overload effects many organs including the heart, liver, kidneys, thyroid, pancreas, bone marrow and reproductive organs. Increased haemolysis increases gallstone production. Individuals with beta thalassaemia major also have a reduced life expectancy.[3]

Structural haemoglobin variants

There are a number of structural variants of clinical significance that may cause severe disease when inherited in the homozygous form (HbS/HbS – sickle cell disease) or in a compound heterozygote form with beta thalassaemia (eg. Hb E/beta thalassaemia). Many carriers of a Hb variant may have a normal FBE, including those who are heterozygous for HbS, HbC, HbE and HbD. These variants are often easily detected on Hb electrophoresis as they have different electrophoretic mobility compared with normal adult Hb.

Thalassaemia screening

Australia's population is ethnically diverse and due to ongoing migration, thalassaemia carriers are increasing in our community.[4] Carriers of thalassaemia or a structural variant may be asymptomatic and unaware of their risk in having an affected child. Prenatal screening allows health professionals to identify couples at risk of having a child with a major haemoglobinopathy. It is recommended that all pregnant women in Australia are offered testing, as selective testing based on ethnicity can be inaccurate.[5,6]

How does a Thalassaemia screen work?

Thalassaemia screening should be requested at the earliest possible timepoint, usually with the first trimester bloods, or prior to conception. This should include a FBE (to evaluate the Hb, MCV and MCH) and film, a ferritin to evaluate for iron deficiency and HPLC to quantify the percentages of HbA, HbA2 and HbF and detect for any Hb variants and/or Hb electrophoresis to help identify the structural variant.[7] Thalassaemia screening will detect an individual who has iron deficiency, who is a carrier of beta thalassaemia trait (raised HbA2) or a structural Hb variant (eg. HbS) or raise suspicion that they are a carrier of alpha thalassaemia trait if they have a normal ferritin, normal HbA2 and still have microcytic, hypochromic red cell indices. Alpha thalassaemia gene testing requires DNA evaluation of the alpha globin genes and consent should be obtained for this genetic testing.

If maternal testing indicates normal red cell indices and normal HPLC (eg. does not have beta thalassaemia trait or a Hb variant), no further partner testing is required.

Iron is required for haemoglobin synthesis, and a FBE and blood film can be difficult to interpret in women with a low serum ferritin.[8] A women may need repeat thalassaemia screening when the iron stores are replete. It is important to treat any women found to have iron deficiency in pregnancy. In the instance of iron deficiency, the partner should undergo testing whilst she is being treated. If the partner has no evidence of being a carrier for thalassaemia or a haemoglobinopathy (normal MCV/MCH and normal HPLC) then no further investigation is required.

If both partners are suspected to be carriers of thalassaemia or a Hb variant, urgent genetic counselling and testing for both individuals are recommended. Genetic counselling or guidance should be consulted when there is a chance that a fetus may inherit a combination of mutations that results in severe clinical disease.

Prenatal diagnosis may be offered to couples at risk. It is important that even when prenatal diagnosis is not undertaken and a couple is at risk of an affected baby that appropriate evaluation occurs after delivery. For example, in the case of Sickle cell disease, so that an infant may be appropriately commenced on Penicillin.

Conclusion

Haemoglobinopathies are increasing in Australia. Making testing available to all women allows families to understand their risk of having a child affected by a haemoglobinopathy. It is often a two-stage process with an initial examination of the FBE, ferritin and Hb analysis of the mother, followed up by genetic and partner testing if a risk is identified. A third stage of testing, prenatal testing, may be offered if genetic testing of parents reveals a potential for a severe or life-threatening haemoglobinopathy to the fetus. We suggest that maternal thalassaemia screening occurs as early as possible so that couples are appropriately informed and counselled and so that prenatal testing can be offered.

References

1. Hardison RC, Chui DH, Giardine B, et al. HbVar: A relational database of human hemoglobin variants and thalassaemia mutations at the globin gene server. *Human Mutation*. 2002;19:225.
2. Songdej D, Babbs C, Higgs DR. An international registry of survivors with Hb Bart's Hydrops Fetalis Syndrome. *Blood*. 2017:129(10):1251-9.
3. Modell B, Khan M, Darlison M, et al. Improved survival of thalassaemia major in the UK and relation to T2 cardiovascular magnetic resonance. *Journal of Cardiovascular Magnetic Resonance*. 2008:10;42.
4. Crighton G, Wood E, Scarborough R, et al. Haemoglobin disorders in Australia: where are we now and where will we be in the future? *Internal Medicine Journal*. 2016:46 (7);770-9.
5. Dyson SM, Culley L, Gill C, et al. Ethnicity questions and antenatal screening for sickle cell/thalassaemia [EQUANS] in England: a randomised controlled trial of two questionnaires. *Ethn Health*. 2006;11(2):169–89.
6. RANZCOG. Genetic Carrier Screening. March 2019. Available from: https://ranzcog.edu.au/statements-guidelines/obstetrics/genetic-carrier-screening-(c-obs-63)
7. Metcalfe SA, Barlow-Stewart K, Campbell J, Emery J. Genetics and blood: Haemoglobinopathies and clotting disorders. *Australian Family Physician*. 2007;36(10):812-9.
8. Bowden DK. Screening for thalassaemia. *Australian Prescriber*. 2001:24(5);120-3.

Q&A

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

Q How close are we to intrapartum molecular testing for GBS status in Australia and New Zealand?

Dr Kelly O'Donovan
MBBS (Hons), DRANZCOG
O&G Senior Registrar,
King Edward Memorial Hospital

Dr Michelle Porter
Microbiologist/Infectious Disease Physician

A

Current strategies for reducing neonatal Group B Streptococcal disease

Group B Streptococcus (GBS) is still the most common pathogen responsible for early-onset sepsis in neonates in developed countries.Early-onset GBS (EOGBS) disease, including sepsis, meningitis and pneumonia, is a leading cause of infant morbidity and mortality.[1]

Prevention strategies of EOGBS disease in neonates rely on reducing or eliminating vertical transmission of GBS to the newborn with systemic administration of intrapartum antibiotic prophylaxis (IAP). IAP for at least four hours during labour has reduced, but not eliminated, the incidence of EOGBS disease in neonates.[1-3]

There are currently two strategies in established practice for identifying women eligible for IAP. This entails either performing universal culture-based screening for GBS colonisation (for term deliveries) or identifying the presence of clinical risk factors for GBS transmission.[1,2] Both strategies are deemed acceptable for reducing EOGBS disease as per the current RANZCOG Statement.[4]

GBS carriage detection by bacterial culture

The current gold standard test for maternal GBS carriage detection is bacterial culture of a specimen obtained by vaginal-rectal swab, which is typically performed at 35–37 weeks gestation. The culture method for GBS detection has several disadvantages: limited sensitivity, a high turnaround time of 36–72hrs, the need for an experienced technician to perform the test, and the low predictive value of antenatal culture findings for GBS colonisation at delivery.[5,6] Evidence has shown that approximately 10% of women screened negative using antenatal culture screening were found to be GBS positive at the time of delivery.[7]

Due to the variability of GBS colonisation, the widespread use of antibiotics may not always be warranted.[3,8] Concerns exist about antibiotic resistance in the community and the influence of early antibiotics on dysbiosis of the infant's microbiome which may lead to adverse health effects in later life.[9]

Real-time polymerase chain reaction (PCR) testing for GBS at the onset of labour is a potential solution to these problems.[10]

Intrapartum molecular testing for GBS status

Point-of-care intrapartum testing, based on nucleic acid amplification, can provide qualitative analysis of the presence of GBS in the genitourinary and gastrointestinal tract at the time of delivery, both before and after rupture of membranes.[11]

Intrapartum PCR testing has been shown to be both highly sensitive (84–99%) and specific (76–99%) for detection of GBS and comparable to GBS culture.[3,6,7,12,13] Out of many testing systems globally, the GeneXpert® GBS test (Cepheid, Sunnyvale, CA,USA) is approved by TGA Australia and is promising because it can yield a result in 30–50 minutes with high diagnostic accuracy, and is characterised by a low workload.[3,8,14]

A 2015 European consensus conference recommended IAP based on universal intrapartum GBS screening using a rapid real-time PCR-testing method.[8] Use of PCR testing for GBS at the time of preterm rupture of membranes has shown a 50% reduction in IAP usage.[14,15] A 2019 French study compared EOGBS rates in a hospital prior to and after introduction of an intrapartum PCR screening protocol and demonstrated a significant reduction in the rate of proven EOGBS disease cases from 1.01/1000 live births to 0.21/1000 live births. Intrapartum PCR testing also reduced the number of days of antibiotic usage for EOGBS by 60%.[7]

One disadvantage to the use of the intrapartum PCR testing is the absence of information about antimicrobial susceptibility. This is particularly important in the setting of maternal beta-lactam allergy. The recommended use of clindamycin in this setting is problematic in that clindamycin resistance continues to increase in Australia, with resistance rates of up to 40% reported in Western Australia.[16,17] Therefore, antimicrobial susceptibility testing remains essential for penicillin-allergic women with a high anaphylaxis risk. Future improvements to the PCR test may be the combined detection of GBS and of mutations likely to confer resistance to clindamycin.[8]

Table 1. Summary of potential benefits and limitations of the routine use of intrapartum GBS PCR testing.

Benefits	Limitations

• Further reduce the incidence of EOGBS disease in the newborn
• Evaluate the GBS colonisation status of women at the time of labour
• Guide IAP decisions for women with no antenatal care, preterm delivery, preterm prelabour rupture of membranes
• Reduce the number of women receiving antibiotics for no benefit with possible long-term impacts on antibiotic resistance and effects on infant microbiome
	• Lack of information on antimicrobial susceptibility
	• Logistical challenge of providing 24-hour rapid testing service in an onsite laboratory if not performed as point of care test
	• Costs and resource implications:
	  ◦ Equipment
	  ◦ Laboratory staff availability and workload
	  ◦ Clinical staff training
	  ◦ Policy change

The cost of a GBS PCR test is more expensive compared to antenatal culture.[3,18] Costs involving implementation of the test into routine care are also significant, relating to equipment, clinical and laboratory staff training and availability. An option to deal with the increasing demand on laboratory staff is to train midwifery staff to use a point-of-care machine on the labour ward (this has been done successfully in some European centres).[7,10,18] One study showed a higher number of invalid tests when performed by midwifery staff compared to trained laboratory staff. This highlights that adequate training of non-laboratory staff is important to achieve sensitivity required for point-of-care testing in labour wards.[19] The point-of-care tests are simple to perform but require an administrative burden of quality control, training and result entry, which may be difficult for the midwifery workforce to absorb.

Table 1 summarises the potential benefits and limitations of the intrapartum PCR test.

Introducing intrapartum PCR testing into routine obstetric care in Australia and New Zealand

National Australian and New Zealand guidelines do not yet recommend the use of intrapartum PCR testing. The RANZCOG guideline on Maternal GBS in Pregnancy, last updated 2019, expresses concerns about the cost of the test and laboratory accessibility for PCR analysis after-hours.[4] Available evidence in recent publications is convincing in terms of overall benefits and safety of the test, and validates current technology. However, there are human and hospital infrastructure requirements still being navigated in an Australian and New Zealand context before routine implementation is possible. The 2019 guideline also states concerns about the timeliness of the PCR test to provide IAP within four hours of delivery. However, studies have addressed this showing that most test results are available four hours prior to delivery allowing for timely IAP.[3,8,19]

Cost effectiveness still needs to be evaluated in the Australian and New Zealand healthcare systems. European studies have demonstrated intrapartum GBS PCR testing to be cost-effective or at least cost-neutral.[7,20] The additional cost of PCR testing is balanced against the cost of routine intrapartum antibiotics, the significant reduction in early onset GBS disease and costs associated with treatment and admission of neonatal EOGBS sepsis.[7,8,20] If the test is introduced into clinical practice, the cost of the test will likely decrease and be similar or lower than the cost of antepartum culture.[3]

There is no available published data on the stages of implementation of this test across Australia and New Zealand. It is likely that pilot studies and cost analyses are being conducted at an institutional level at this stage.

Changes to established protocols, that have significant resource and logistical implications, will take time. The process of implementing intrapartum PCR testing for GBS status into routine care is in its infancy and it will likely be years before this is routine practice. Collaboration between units may be useful to fully appreciate the current state of implementing intrapartum PCR testing for GBS status across Australia and New Zealand.

References

1. Hasperhoven GF, AlNasiry S, Bekker V, et al. Universal screening versus risk-based protocols for antibiotic prophylaxis during childbirth to prevent early-onset group B stretococcal disease: a systemic review and meta-analysis. *BJOG*. 2020;126(6):680-91.
2. Li Q, Wang D, Li H, Liu J. Screening-based and Risk-based Strategy for the Prevention of Early-onset Group B Streptococcus/Non-group B Streptococcus Sepsis in the Neonate: A Systematic Review and Meta-analysis. *Pediatr Infect Dis*. 2020;39(8):740-8.
3. Pichiassi E, Coata G, Babucci G, et al. Intrapartum test for detection of Group B Streptococcus colonization during labour. *J Matern Fetal Neonatal Med*. 2018;31(24):3303-10.
4. RANZCOG. Maternal Group B Streptococcus in pregnancy: screening and management. 2013, updated 2019. Available from: https://ranzcog.edu.au/statements-guidelines/obstetrics/maternal-group-b-streptococcus-(gbs)-in-pregnancy
5. Verani JR, McGee L, Schrag SJ. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). Prevention of perinatal group B streptococcal disease - revised guidelines from CDC. *MMWR Recomm Rep*. 2010;59(RR-10):1-36.
6. El Helali N, Nguyen JC, Giovangrandi Y, Trinquart L. Diagnostic accuracy of a rapid real-time polymerase chain reaction assay for universal intrapartum group B streptococcus screening. *Clin Infect Dis*. 2009 49(3):417-23.
7. El Helali N, Habibi F, Azria E, et al. Point-of-Care Intrapartum Group B Streptococcus Molecular Screening: Effectiveness and Costs. Obstet Gynaecol. 2019;00:1-6.
8. Di Renzo GC, Melin P, Berardi A. Intrapartum GBS screening and antibiotic prophylaxis: a European consensus conference. *J Matern Fetal Neonatal Med*. 2015;28(7):766-82.
9. Neuman H, Forsythe P, Uzan A, et al. Antibiotics in early life: dysbiosis and the damage done. *FEMS Microbiol Rev*. 2018;42(4):489-99.
10. Dakin A, Ferguson W, Drew R, et al. Assessing standards for prevention of early onset group B streptococcal (GBS) disease in Ireland. *Ir J Med Sci*. 2021;14:1-7.
11. Bergeron M, Danbig K, Menard C, et al. Rapid Detection of Group B Streptococci in Pregnant Women at Delivery. *N Engl J Med*. 2000;343:175-9.
12. Feuerschuette O, Silveira S, Cancelier A, et al Diagnostic yield of real-time polymerase chain reaction in the diagnosis of intrapartum maternal rectovaginal colonization by group B streptococcus: a systematic review with meta-analysis. *Diagn Microbiol Infect Dis*. 2018;91(2):99-104.
13. Nielson SY, Moller JK, Khalil MR. A comparison of GenomEra GBS PCR and GeneXpert GBS PCR assays with culture of GBS performed with and without broth pre-enrichment. *Eur J Clin Microbiol Infect Dis*. 2020;39(10):1945-50.
14. Helmig RB, Gertsen JB. Intrapartum PCR-assay for detection of Group B Streptococci (GBS) European Journal of Obstetrics and Gynaecology and Reproductive Biology: X. 2019;4:1-4.

Full reference list available online

Global Health

Preventable stillbirths in the Solomon Islands

Dr Rangi De Silva
MBBS, MReproMed, FRANZCOG

Dr Leeanne Panisi
MMed (O&G), Pacific Associate Member RANZCOG

The Solomon Islands is Australia's close neighbour, only a 3.5-hour plane trip away from Brisbane. It is a beautiful country spread across an idyllic archipelago of over 990 islands with a rich history and strong culture. Despite its beauty, it faces significant geographical, socioeconomic and cultural barriers to achieving health equity. I was fortunate enough to spend six months in Honiara in 2018 as an Australian Volunteers International (AVI) volunteer as a Senior O&G registrar at the National Referral Hospital (NRH). NRH is the only tertiary referral hospital servicing a population of over 600 000. Unsurprisingly, the O&G department is the busiest in the hospital, seeing over 70% of the hospital's admissions and up to 6000 deliveries a year. The department is led by Dr Leeanne Panisi, an inspirational leader and the only female O&G consultant in the country. Dr Panisi is supported by only three other consultants and limited junior medical and midwifery staff – a fraction of the human resources a tertiary hospital in Australia or New Zealand would have, and far less than what is needed.

The morning handover is where the events of the last 24 hours are summarised for the whole team – the total births, caesarean sections, maternal deaths, maternal morbidity, neonatal deaths and stillbirths. The stories and numbers are sobering, particularly when discussing stillbirths. Stillbirth is a significant global public health issue, with approximately 98%

Table 1. The ICD-PM stillbirth classification system.

MAIN PERINATAL CAUSE OF DEATH IN ICD-PM GROUPS	
Antepartum death	**Intrapartum death**
A1: Congenital malformations, deformations and chromosomal abnormalities	**I1:** Congenital malformations, deformations and chromosomal abnormalities
A2: Infection	**I2:** Birth trauma
A3: Antepartum hypoxia	**I3:** Acute intrapartum event
A4: Other specified antepartum disorder	**I4:** Infection
A5: Disorders related to fetal growth	**I5:** Other specified intrapartum disorder
A6: Fetal death of unspecified cause	**I6:** Disorders related to fetal growth
	I7: Intrapartum death of unspecified cause
MATERNAL CONDITION	
M1: Complications of placenta, cord and membranes	
M2: Maternal complications of pregnancy	
M3: Other complications of labour and delivery	
M4: Maternal medical and surgical conditions	
M5: No maternal condition	

Table 2. Causes of antenatal and intrapartum stillbirth (ICD-PM classification) at the National Referral Hospital over a two-year period of 2017–2018 for all cases of stillbirth where cause was documented (n-198).

Cause of death	Total (%)
Antepartum deaths	**170 (85·9)**
A1: Congenital malformations, deformations and chromosomal abnormalities	8 (4·7)
A2: Infection	19 (11·2)
A3: Antepartum hypoxia	19 (11·2)
A4: Other specified antepartum disorder	13 (7·6)
A5: Disorders related to fetal growth	43 (25·3)
A6: Unspecified cause	68 (40)
Intrapartum deaths	**28 (14·1)**
I1: Congenital malformations, deformations and chromosomal abnormalities	4 (14·3)
I2: Birth trauma	1 (3·6)
I3: Acute intrapartum event	13 (46·4)
I4: Infection	1 (3·6)
I5: Other specified intrapartum disorder	0
I6: Disorders related to fetal growth	5 (17·9)
I7: Unspecified cause	4 (14·3)

occurring in low- and middle-income countries (LMICs), like the Solomon Islands.[1-3] Each of these lives lost results in a huge emotional burden for these women, families, and communities. For Dr Panisi and her team, these stories are all too familiar. Like many of its counterparts in the Asia-Pacific, the Solomon Islands has poor perinatal outcomes, with a recent study showing a high rate of preventable maternal mortality[6] and an estimated stillbirth rate of 17.6 per 1000 births in 2015 from World Health Organization (WHO) data. Whilst most stillbirths occurring in LMICs are preventable, progress in reducing these numbers has been poor and under prioritised compared to other perinatal outcomes[1,2] and there has been no previous targeted research investigating preventable causes of stillbirths in the Solomon Islands.

In many LMICs, the lack of diagnostics tools makes ascertaining timing and cause of death especially challenging.[1,5,6] As a result, many countries do not have a national registration system for perinatal deaths, particularly in the Asia-Pacific region.[2,10,11] While stillbirths are not nationally classified, monthly audits at NRH presented an opportunity to glimpse the state of stillbirth in the country. Thus, with the aim of identifying key opportunities for intervention, we conducted a retrospective review in 2019 investigating all stillbirths (those ≥20 weeks estimated gestation or >500g birth weight) occurring at NRH over two years (2017 and 2018). Using the WHO International Classification of Diseases applied it to the perinatal period (WHO ICD-PM) (Table 1), we identified timing of death, primary cause and linked each death with the main contributing maternal condition.[6,7]

With 341 stillbirths and 11 056 births over two years, we uncovered a high institutional incidence of 30.8 per 1000 births.[8] This is nearly double that of its closest neighbour, Papua New Guinea (15.9 per 1000 births, nation-wide) and a stark contrast to the stillbirth rates of Australia (6.8 per 1000 births) and New Zealand (8 per 1000 births).[8,9] Whilst suspected cause of death was available for 198 stillbirths (Table 2), 58% of case files were missing, highlighting the difficulties with accurate data collection in LMICs. The majority of women were multiparous (62%). We deemed 72% to be preventable – those with an estimated gestation over 28 weeks, birthweight >1500g and no congenital abnormalities. There were five stillbirths associated with a maternal death. Most fetal deaths occurred antenatally (86%) and 80% occurred in the third trimester. Unsurprisingly, risk factors, such as low birthweight (<2500g) and preterm birth (<37 weeks estimated gestation) were common (59% and 62%, respectively). Hypertensive disorders and infection were present in almost half of antenatal stillbirths with 10 fetuses showing overt signs of congenital syphilis. Although we found almost 80% of mothers attended at least one antenatal visit, sadly, many simple interventions were completely lacking. Only a quarter of women who experienced a stillbirth received an early ultrasound, discussions of reduced fetal movements were not documented in half of all cases and haemoglobin levels were only recorded in 56%. Only 90 women (63%) were tested for syphilis and of those who tested positive, only 30% completed treatment. These findings suggest many crucial gaps in care. But they also provide hope that simple, cost-effective interventions may have the potential to significantly reduce stillbirths nationwide.

Importantly, progress is being made. The Solomon Islands Ministry of Health and the WHO have recently launched an updated national Antenatal Care Package, which emphasises interventions for many of these issues and provides a standard expected quality of care. It incorporates focused health worker education and resource provision, such as improved

access to antenatal ultrasounds and point-of-care syphilis and haemoglobin testing. This initiative acknowledges the socioeconomic return of investing in stillbirths[1] and is a fundamental step in reducing the burden of stillbirths in the Solomon Islands.

Without a national surveillance system for stillbirths, the true magnitude of perinatal deaths remains under-reported and under-investigated, as we have only included data from the hospital setting in this study. Our study was also limited by its retrospective nature and incomplete data. Alarmingly, the disruption of health systems as a result of the COVID-19 pandemic will potentially increase these losses, as has already been found in other regions.[12,13] Furthermore, Honiara has suffered recent disruptions to service provision with civil unrest. Despite this, Dr Panisi and her team continue to work tirelessly and advocate for the women of the Solomon Islands. We remain hopeful that we may be able to uncover why stillbirths are occurring and what can be done to prevent them with ongoing research efforts. Only with accurate data can we hope to inform public health reforms and tackle this ongoing global issue.

References

1. Blencowe H, Cousens S, Jassir FB, et al. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. *Lancet Global Health*. 2016;4:e98-e108.
2. Lawn JE, Blencowe H, Waiswa P, et al. Stillbirths: rates, risk factors, and acceleration towards 2030. *Lancet*. 2016;387:587-603.
3. McClure EM, Saleem S, Goudar SS, et al. Stillbirth rates in low-middle income countries 2010 - 2013: a population-based, multi-country study from the Global Network. *Reprod Health*. 2015;12 Suppl 2:S7.
4. De Silva M, Panisi L, Maepioh A, et al. Maternal mortality at the National Referral Hospital in Honiara, Solomon Islands over a five-year period. *ANZJOG*. 2020;60:183-7.
5. Patterson JK, Aziz A, Bauserman MS, et al. Challenges in classification and assignment of causes of stillbirths in low- and lower middle-income countries. *Semin Perinatol*. 2019;43:308-14.
6. International Stillbirth Alliance Collaborative for Improving Classification of Perinatal D, Flenady V, Wojcieszek AM, et al. Classification of causes and associated conditions for stillbirths and neonatal deaths. *Semin Fetal Neonatal Med*. 2017;22:176-85.
7. Allanson ER, Vogel JP, Tuncalp, et al. Application of ICD-PM to preterm-related neonatal deaths in South Africa and United Kingdom. *BJOG*. 2016;123:2029-36.
8. De Silva M, Panisi L, Manubuasa L, et al. Preventable Stillbirths in the Solomon Islands - a hidden tragedy. Commentary. *The Lancet Regional Western Pacific*. 2020;5.
9. World Health Organization Statistic - Stillbirth (Western Pacific Region). Vol. 2020: World Health Oragnization, 2015.
10. Goldenberg RL, McClure EM, Saleem S. Improving pregnancy outcomes in low- and middle-income countries. *Reprod Health*. 2018;15:88.
11. McClure EM, Garces A, Saleem S, et al. Global Network for Women's and Children's Health Research: probable causes of stillbirth in low- and middle-income countries using a prospectively defined classification system. *BJOG*. 2018;125:131-8.
12. Roberton T, Carter ED, Chou VB, et al. Early estimates of the indirect effects of the COVID-19 pandemic on maternal and child mortality in low-income and middle-income countries: a modelling study. *Lancet Global Health*. 2020;8:e901-e8.
13. Ashish K, Gurung R, Kinney MV, et al. Effect of the COVID-19 pandemic response on intrapartum care, stillbirth, and neonatal mortality outcomes in Nepal: a prospective observational study. *Lancet Global Health*. 2020;8(10):e1273-81

RANZCOG Women's Health Foundation

Scholarship, Fellowship and Travel Grant recipients for 2022

The RANZCOG Women's Health Foundation proudly supports promising medical researchers and scientists pursuing high-quality, innovative research and training in women's health. Research scholarships, fellowships and travel grants are awarded annually across Australia and New Zealand in recognition of those committed to continuous improvement in the fields of obstetrics, gynaecology, and the reproductive sciences. The Foundation strives to recognise researchers at different stages of their careers and in particular young researchers, to assist them as they progress their careers.

The RANZCOG Women's Health Foundation is pleased to announce its successful grant recipients commencing in 2022.

Arthur Wilson Memorial Scholarship

Recipient: Dr Janelle James-McAlpine

Institution: Griffith University

Project: Micronutrient supplementation and birth outcomes in Queensland women

Ferring Research Grant

Recipient: Dr Mooska Raoofi

Institution: Epworth Freemasons and Royal Women's Hospitals

Project: A comparison of the imaged preoperative versus the visualised intraoperative uterosacral ligament in women undergoing laparascopic uterosacral ligament suspension for the management of pelvic organ prolapse

Recipient: Dr Evelyn Smith Romero

Institution: Liverpool and Campbelltown Hospitals

Project: Immediate postpartum contraception information and provision: the impact of consumer and healthcare provider education and training on uptake – a before and after study

Fotheringham Research Fellowship

Recipient: Dr Louie Ye

Institution: University of Melbourne

Project: Genome-wide scale functional screen to identify microRNAs essential for human endometrial receptivity

Norman Beischer Clinical Research Scholarship

Recipient: Dr Bassem Gerges

Institution: Nepean Hospital

Project: Diagnostic accuracy of transvaginal ultrasound, magnetic resonance imaging and positron emission tomography-computed tomography with 16α-[18F]fluoro-17β-oestradiol for the diagnosis of rectosigmoid deep endometriosis

RANZCOG NSW State Committee Trainee Research Grant

Recipient: Dr Komal Chohan

Institution: Royal North Shore Hospital

Project: The use of chorionicity-specific growth charts to improve pregnancy outcomes

Recipient: Dr Zanna Franks

Institution: University of Newcastle

Project: Investigating the associations between chronic disease and infertility - A window for change

Recipient: Dr Cansu Uzuner

Institution: Nepean Hospital

Project: Contrast Enhanced Ultrasound with Pulse Inversion Technology in Gynaecology

NSW State Committee Traveling Scholarship

Recipient: Dr Philip Cellich

Institution: Port Moresby General Hospital, PNG

Project: 6-month clinical Fellowship working in general obstetrics and gynaecology in a low resource setting.

Robert Wrigley Pain Research Scholarship

Recipient: Dr Supuni Kapurubandara

Institution: University of New South Wales

Project: Women with persistent pelvic pain: a lived experience

UroGynaecological Society of Australasia (UGSA) Research Scholarship

Recipient: Dr Ellen Yeung

Institution: Royal Brisbane and Women's Hospital

Project: Histological analysis and imaging of explanted pelvic mesh

Obituary

Dr Justin Frederick Nasser
1967–2021

It is with deep regret that RANZCOG informs members of the death of Dr Justin Nasser on 14 November 2021.

Justin was born 9 March 1967 to his parents Malcolm and Helene, a paediatrician and GP respectively. Raised in Queensland, Justin completed his primary and secondary school education in Brisbane, attending Our Lady of the Rosary School Kenmore (1973–1975), St Joseph's College Nudgee Junior Indooroopilly (1976–1979), St Joseph's College Gregory Terrace (1980–1984) and Indooroopilly State high school (1985).

Justin was awarded a Bachelor of Medicine and Bachelor of Surgery (MBBS) from the University of Queensland in 1991 and became a Fellow of RANZCOG in 2003.

After obtaining his specialist qualifications in Obstetrics and Gynaecology, he spent two years of subspecialty training in Obstetrical and Gynaecologic Ultrasound at the Royal Women's Hospital and the Mercy Hospital for Women in Melbourne. During this time, he obtained a Diploma in Diagnostic Ultrasound (DDU) from the Australasian Society for Ultrasound in Medicine (ASUM).

He returned to the old Gold Coast Hospital as a Staff Specialist and developed the first local tertiary level Obstetrical and Gynaecologic ultrasound service. He continued his interests in clinical and academic medicine, and in 2010 obtained a Masters of Reproductive Medicine.

He worked in both the public and private sectors in the fields of obstetrics, gynaecology, reproductive medicine, and women's imaging. Our hearts and thoughts are with his wife Pam and children Yasmine, Mia and Kelly, and his loving extended family.

We have lost a great friend and colleague.

Vale Justin.

Dr Benjamin Bopp
President, RANZCOG

Remembering Our Fellows

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

- **Dr Peter Harry Crowe**, NSW, February 2021
- **Dr David Michael Bowers**, NSW, July 2021
- **Dr Robert James Gaal**, NSW, July 2021
- **Dr Berna Jean Madill**, NT, December 2021
- **Dr Thomas Guy Wright**, Qld, February 2022