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

CATEGORY: BEST PRACTICE STATEMENT

Prophylactic antibiotics in obstetrics and gynaecology

This statement has been developed and reviewed by the Women's Health Committee and approved by the RANZCOG Board and Council.

A list of Women's Health Committee Members can be found in Appendix A.

Disclosure statements have been received from all members of this committee.

Disclaimer This information is intended to provide general advice to practitioners. This information should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The document has been prepared having regard to general circumstances.

First endorsed by RANZCOG: November 2011
Current: March 2021
Review due: March 2024

Objectives: To provide advice on the use of prophylactic antibiotics in obstetrics and gynaecology.

Target audience: Health professionals providing maternity and gynaecological care, and patients.

Values: The evidence was reviewed by the Women's Health Committee (RANZCOG), and applied to local factors relating to Australia and New Zealand.

Background: This statement was first developed by Women's Health Committee in November 2011 and reviewed in March 2021.

Funding: The development and review of this statement was funded by RANZCOG.

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1. Plain language summary

Antibiotics are used to treat or prevent infections caused by bacteria. If you are having an operation, you may be given antibiotics to prevent infection. Always tell your doctor if you have had an allergic reaction to an antibiotic and remind them of your allergy before you receive any antibiotics.

2. Summary of recommendations

Recommendation 1	Grade
Prescribers should use the current *Therapeutic Guidelines: Antibiotic* when prescribing antimicrobials as the primary source of information, and these should be readily accessible to clinicians wherever antimicrobials are being prescribed[1].	Consensus-based recommendation Reference 1
Recommendation 2	**Grade**
Local guidelines should take into account recommendations in the Therapeutic Guidelines and also reflect local antimicrobial susceptibilities and availability.	Consensus-based recommendation
Recommendation 3	**Grade**
Consult the best available evidence and specialist clinicians for guidance on either prophylaxis or management of infections not covered in the Therapeutic Guidelines.	Consensus-based recommendation

3. Introduction

The use of prophylactic antibiotics in obstetric and gynaecological surgery is an important part of conventional practice. Many institutions and jurisdictions have their own established protocols which should take into consideration the advice of the Therapeutic Guidelines: Antibiotic. Where these exist, and provided they are consistent with accepted national guidelines, they should be followed.

In the absence of such guidelines, the Australia Therapeutic Guidelines Limited (2019) contains advice regaining prophylactic antibiotics for hysterectomy and termination of pregnancy[1].

4. Discussion and recommendations

4.1 Caesarean section

Traditionally, antibiotics at caesarean section have been given after cord clamping, due to several potential concerns; 1) exposure of the fetus to antibiotics could mask newborn positive bacterial culture results; 2) fetal antibiotic exposure could lead to an increase in colonization or infection with antibiotic-resistant organisms, and 3) to avoid the risk of severe fetal compromise in the rare event of maternal anaphylaxis.

Against these potential concerns needs to be weighed the strong evidence that antibiotics given prior to skin incision reduce the risk of post-operative endometritis and surgical site infection by approximately 50%. These trials have not observed any increase in neonatal sepsis rates among patients randomised to pre-incision antibiotics. Whether the magnitude of benefit is the same for elective as emergency caesarean section is unclear.

Accordingly, it is suggested that:

- Antibiotic prophylaxis should be given for all caesarean sections.

- Antibiotics administered prior to skin incision will minimise the risk of post-operative infectious morbidity, but consideration should be given to how the fetus could be delivered expeditiously in the rare event of maternal anaphylaxis.
- Surgical data suggests that for antimicrobial prophylaxis to be effective, ideally it should be administered at least 30 minutes before caesarean section, to ensure a bactericidal concentration is reached by the time of incision. This could occur at time of intravenous cannulation.
- Narrow-spectrum antibiotics that are effective against gram-positive and gram- negative bacteria with some anti-anaerobic activity are the most appropriate choice.
- A first-generation cephalosporin is recommended, such as 2g intravenous cefazolin. The dose should be increased to 3g for women weighing over 120kg. Consideration should also be given to a repeat dose if the procedure is prolonged (over 3 hours).
- For women with a history of immediate or delayed nonsevere hypersensitivity to penicillins, cefazolin, as above, remains appropriate.
- For women with a history of immediate or delayed severe hypersensitivity to penicillins, use Clindamycin 600mg iv plus Gentamicin 2mg/kg iv.
- For women colonised with Methicillin-resistant Staphylococcus aureas (MRSA) or at increased risk of being colonised with MRSA, add Vancomycin 15mg/kg iv.
- Azithromycin may be considered at caesarean sections performed during labour or at least four hours after rupture of membranes (2). Administration of azithromycin 500mg has been shown to reduce a composite outcome of endometritis, wound infection or other infection (3). However, a strong recommendation in favour of routine use is not yet warranted given the concerns around the external validity of the paper, inducing resistance to azithromycin and possible effects on the establishment of the indigenous microbiome.

Surgical prophylaxis should still be administered even if the patient is receiving antibiotics for prolonged rupture of the membranes.

4.2 Operative vaginal delivery

Operative delivery, much like caesarean section, is a risk factor for maternal sepsis. Historically insufficient evidence existed to recommend antibiotics prophylaxis for women undergoing operative vaginal birth. This changed in 2019 with the publication of the ANODE trial. The ANODE trial demonstrated that prophylaxis with a single dose of intravenous amoxicillin and clavulanic acid resulted in significantly fewer confirmed or suspected infections when compared to placebo. The dose given was 1g amoxycillin and 200mg clavulanic acid once intravenously[2].

4.3 Group B streptococcus

All women with known carriage or risk factors for Group B streptococcus should be treated with prophylactic antibiotics in labour as per RANZCOG College Statement C-Obs 19.

4.4 Preterm prelabour rupture of membranes (PPROM) to 36+6 weeks gestation

Antibiotic prophylaxis for women with PPROM is associated with prolonged pregnancy and reduced maternal and neonatal infection. However, evidence that antibiotic prophylaxis in PPROM alters perinatal mortality or longer-term outcomes is lacking. The use of antibiotic prophylaxis in women with preterm labour in the absence of membrane rupture is not supported by the[1]. There are two rationales for administering antibiotics in PPROM

(i) For GBS chemoprophylaxis due to the high risk of spontaneous preterm labour (a known risk factor for early onset GBS disease); and

(ii) To prolong gestation (increase latency period).

The antibiotic of choice and optimal duration of treatment are not clear:

- Erythromycin 250 mg four times a day for 10 days or until the woman is in established labour (whichever is sooner)[3].

OR

- Amoxicillin/ampicillin 2 g IV every 6 hours for 48 hours, followed by amoxicillin 250 mg oral every 8 hours for 5 days (for seven days total), PLUS erythromycin 250 mg oral every 6 hours for 10 days[1].

ALSO

- Azithromycin can be considered in lieu of a multiple-day course of erythromycin because of its ease of administration, improved gastrointestinal tolerance, favorable cost profile, and similar efficacy; this substitution is also endorsed by ACOG (4). In retrospective studies of women with PPROM given prophylaxis with erythromycin versus azithromycin as part of the antibiotic regimen, both drugs had similar pregnancy and neonatal outcomes (latency length; mean birth weight; rates of chorioamnionitis, low Apgar score, neonatal sepsis, and neonatal respiratory distress syndrome)[4].

The choice of prophylactic antibiotics in PPROM will also depend on whether clinical signs of chorioamnionitis are present. Therapies may be modified based on the results of investigations. For patients with a hypersensitivity to penicillins, refer to the Therapeutic Guidelines or seek expert advice.

4.5 Prophylactic antibiotics in obstetrics

In obstetrics, there are some issues that are not well clarified:

- There is insufficient evidence for or against the use of prophylactic antibiotics to reduce infectious morbidity for manual removal of the placenta[5].
- Available evidence does not support the use of prophylactic antibiotics to reduce infectious morbidity following elective or emergency cerclage[5].
- The evidence is not robust for the use of antibiotic prophylaxis to prevent perineal wound complications following third or fourth degree tears[5].

While there is inadequate evidence to dictate uniform antibiotic prescribing practice in the above situations, the decision regarding prophylactic antibiotics should be made in each case, based on the clinical situation and individual patient circumstances.

Women with pre-exisiting heart disease require additional consideration as prophylaxis is often required to reduce the risk of infective endocarditis. Specific details are beyond the scope of this statement but further information can be found in the Therapeutic Guidelines[1].

4.6 Prophylactic antibiotics in gynaecology

There are no recommendations for routine prophylactic antibiotics for the following gynaecological procedures in healthy women with no risk factors:

- Insertion of intrauterine contraceptive device (IUCD)[6];
- Patients undergoing diagnostic laparoscopy[7];
- Patients having hysteroscopic surgery[7];
- Hysterosalpingography (HSG) without a prior history of pelvic inflammatory disease (8); and
- Large Loop Excision of Transformation Zone (LLETZ)[7].

However, antibiotic therapy should be instituted in any of the procedures listed above if there is reason to suspect infection risk or if the findings at the procedure indicate risk of infection e.g. dilated fallopian tubes at HSG.

Antimicrobial prophylaxis should be used during major abdominal, laparoscopic or vaginal procedures. This includes synthetic mid-urethral sling procedures. Antibiotic prophylaxis should also be considered for surgical termination of pregnancy where STIs have not been excluded. The choice of antibiotics should be guided by local guidelines, recommendations in the Therapeutic

Guidelines and also reflect local antimicrobial susceptibilities.

- In general, cefazolin 2g iv PLUS metronidazole 500mg iv prior to surgical incision is appropriate[1].

- For women with a history of immediate or delayed nonsevere hypersensitivity to penicillins, the above regimen remains appropriate[1].

- For women with a history of immediate or delayed severe hypersensitivity to penicillins, use Clindamycin 600mg iv plus Gentamicin 2mg/kg iv[1].

- For prophylaxis of patients who have not been appropriately investigated before surgical termination of pregnancy use doxycycline 100mg orally prior to the procedure and 200mg orally after the procedure OR doxycycline 400mg orally with food 10-12 hours prior to the procedure. An alternative regimen is metronidazole 2g orally prior to the procedure PLUS 1g azithromycin orally prior to the procedure for patients at a high risk of infection[1].

5. References

1. eTG complete [Internet]. Melbourne (Vic): Therapeutic Guidelines Ltd; 2019.
2. Knight M, Chiocchia V, Partlett C, Rivero-Arias O, Hua X, Hinshaw K, et al. Prophylactic antibiotics in the prevention of infection after operative vaginal delivery (ANODE): a multicentre randomised controlled trial. The Lancet. 2019;393(10189):2395-403.
3. Excellence NIfHaC. Preterm labour and birth London2015.
4. Navathe R, Schoen CN, Heidari P, Bachilova S, Ward A, Tepper J, et al. Azithromycin vs erythromycin for the management of preterm premature rupture of membranes. American journal of obstetrics and gynecology. 2019;221(2):144.e1-.e8.
5. van Schalkwyk J, Van Eyk N. No. 247-Antibiotic Prophylaxis in Obstetric Procedures. Journal of Obstetrics and Gynaecology Canada. 2017;39(9):e293-e9.
6. Buppasiri P, Lumbiganon P, Thinkhamrop J, Thinkhamrop B. Antibiotic prophylaxis for third- and fourth-degree perineal tear during vaginal birth. Cochrane Database of Systematic Reviews. 2014(10).
7. Gynecologists. ACoOa. Practice Bulletin 2018. Available from: https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2018/06/prevention-of-infection-after-gynecologic-procedures.

6. Other suggested reading

Antimicrobial prophylaxis for cesarean delivery: timing of administration. Committee Opinion No. 465. American College of Obstetricians and Gynecologists. Obstet Gynecol 2010; 116: 791-2. Available at: https://journals.lww.com/greenjournal/Citation/2010/09000/Committee_Opinion_No 465 Antimicrobial.43.aspx

Clifford V, Daley A. Review article. Antibiotic prophylaxis in obstetric and gynaecology procedures: A Review. Australian and New Zealand Journal of Obstetrics and Gynaecology 2012; 52: 412-19.

Kittur ND, McMullen KM, Russo AJ, Ruhl L, Kay HH, Warren DK. Long-Term effect of infection prevention practices and case mix on caesarean surgical site infections. Obstet Gynecol 2012; 120: 246–51.2a

7. Links to other College statements

Screening and Treatment for Group B Streptococcus in Pregnancy (C-Obs 19)
https://ranzcog.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical-Obstetrics/Maternal-Group-B-Streptococcus-in-pregnancy-screening-and-management-(C-Obs-19).pdf?ext=.pdf

Appendices

Appendix A Women's Health Committee Membership

Name	Position on Committee
Professor Yee Leung	Chair and Board Member
Dr Gillian Gibson	Deputy Chair, Gynaecology
Dr Scott White	Deputy Chair, Obstetrics and Subspecialties Representative
Associate Professor Ian Pettigrew	Member and EAC Representative
Dr Kristy Milward	Member and Councillor
Dr Will Milford	Member and Councillor
Dr Frank O'Keeffe	Member and Councillor
Professor Sue Walker	Member
Dr Roy Watson	Member and Councillor
Dr Susan Fleming	Member and Councillor
Dr Sue Belgrave	Member and Councillor
Dr Marilyn Clarke	ATSI Representative
Associate Professor Kirsten Black	Member
Dr Thangeswaran Rudra	Member
Dr Nisha Khot	Member and SIMG Representative
Dr Judith Gardiner	Diplomate Representative
Dr Angela Brown	Midwifery Representative
Ms Ann Jorgensen	Community Representative
Dr Rebecca Mackenzie-Proctor	Trainee Representative
Prof Caroline De Costa	Co-opted member (ANZJOG member)
Dr Christine Sammartino	Observer

Appendix B Overview of the development and review process for this statement

7.1 Steps in developing and updating this statement

This statement was originally developed in November 2011 and was most recently reviewed in February 2021. The Women's Health Committee carried out the following steps in reviewing this statement:

- Declarations of interest were sought from all members prior to reviewing this statement.
- Structured clinical questions were developed and agreed upon.
- An updated literature search to answer the clinical questions was undertaken.
- At the March 2021 committee meeting, the existing consensus-based recommendations were reviewed and updated (where appropriate) based on the available body of evidence and clinical expertise. Recommendations were graded as set out below in Appendix B part iii)

7.2 Declaration of interest process and management

Declaring interests is essential in order to prevent any potential conflict between the private interests of members, and their duties as part of the Women's Health Committee.

A declaration of interest form specific to guidelines and statements was developed by RANZCOG and approved by the RANZCOG Board in September 2012. The Women's Health Committee members were required to declare their relevant interests in writing on this form prior to participating in the review of this statement.

Members were required to update their information as soon as they become aware of any changes to their interests and there was also a standing agenda item at each meeting where declarations of interest were called for and recorded as part of the meeting minutes.There were no significant real or perceived conflicts of interest that required management during the process of updating this statement.

7.3 Grading of recommendations

Each recommendation in this College statement is given an overall grade as per the table below, based on the National Health and Medical Research Council (NHMRC) Levels of Evidence and Grades of Recommendations for Developers of Guidelines[1]. Where no robust evidence was available but there was sufficient consensus within the Women's Health Committee, consensus-based recommendations were developed or existing ones updated and are identifiable as such.

[1] eTG complete [Internet]. Melbourne (Vic): Therapeutic Guidelines Ltd; 2019.

Consensus-based recommendations were agreed to by the entire committee. Good Practice Notes are highlighted throughout and provide practical guidance to facilitate implementation. These were also developed through consensus of the entire committee.

Recommendation category		Description
Evidence-based	A	Body of evidence can be trusted to guide practice
	B	Body of evidence can be trusted to guide practice in most situations
	C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
	D	The body of evidence is weak and the recommendation must be applied with caution
Consensus-based		Recommendation based on clinical opinion and expertise as insufficient evidence available
Good Practice Note		Practical advice and information based on clinical opinion and expertise

Appendix C Full Disclaimer

Purpose

This Guideline has been developed to provide general advice to practitioners about women's health issues concerning prophylactic antibiotics in obstetrics and gynaecology and should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any person. It is the responsibility of each practitioner to have regard to the particular circumstances of each case. Clinical management should be responsive to the needs of the individual person with a need for of prophylactic antibiotics use and the particular circumstances of each case.

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The information available in the prophylactic antibiotics in obstetrics and gynaecology is intendedas a guide and provided for information purposes only. The information is based on the Australian context using the best available evidence and information at the time of preparation.
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