

Antibiotics in the Peripartum Period

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Note:

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

Explanation of the aboriginal artwork:

The aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant women. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.



Australian Aboriginal Culture is the oldest living culture in the world yet Aboriginal people continue to experience the poorest health outcomes when compared to non-Aboriginal Australians. In South Australia, Aboriginal women are 2-5 times more likely to die in childbirth and their babies are 2-3 times more likely to be of low birth weight. The accumulative effects of stress, low socio economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Despite these unacceptable statistics the birth of an Aboriginal baby is a celebration of life and an important cultural event bringing family together in celebration, obligation and responsibility. The diversity between Aboriginal cultures, language and practices differ greatly and so it is imperative that perinatal services prepare to respectively manage Aboriginal protocol and provide a culturally positive health care experience for Aboriginal people to ensure the best maternal, neonatal and child health outcomes.

Purpose and Scope of Perinatal Practice Guideline (PPG)

The purpose of this guideline is to provide clinicians with information on the antibiotic(s) to be used for prophylaxis in women during the peripartum period and also for treatment of specific sites of infection during this time. It includes information on the dosage, frequency and route of administration but does not include dilution and administration duration information. Refer to local hospital guidelines or the Australian Injectable Drugs Handbook.



Antibiotics in the Peripartum Period

Table of Contents

Purpose and Scope of Perinatal Practice Guideline (PPG)	1
Summary of Practice Recommendations	3
Abbreviations	3
Definitions	3
Prophylactic Antibiotic Use in the Peripartum Period	4
Group B Streptococcus (Intrapartum prophylaxis)	4
Indications:	4
Practice Considerations:	4
Recommended antibiotic treatment:	4
Caesarean Section	4
Indications:	4
Practice Considerations:	4
Recommended antibiotic treatment:	4
Manual Removal of the Placenta	5
Indications:	5
Practice Considerations:	5
Recommended antibiotic treatment:	5
3rd or 4th degree perineal tears	5
Indications:	5
Practice Considerations:	5
Recommended antibiotic treatment at time of repair:	5
Recommended postnatal antibiotic treatment:	5
Women with Cardiac Disease	6
Indications:	6
Recommended antibiotic treatment:	6
Bacterial Vaginosis	6
Recommended antibiotic treatment:	6
Prelabour Rupture of Membranes \geq 37 weeks (PROM)	7
Preterm Prelabour Rupture of Membranes (PPROM)	7
PPROM with no evidence of chorioamnionitis	7
Recommended antibiotic treatment:	7
PPROM with evidence of chorioamnionitis	7
Recommended antibiotic treatment:	7
Preterm Labour	7
Antibiotic Treatment of Infection	8
Chorioamnionitis	8
Indications:	8
Practice Considerations:	8
Recommended antibiotic treatment until birth:	8
Recommended continuation of postnatal antibiotic treatment:	8
Endometritis	9
Indications:	9
Practice Considerations:	9
Recommended Antibiotic Treatment:	9
Mastitis	10
Indications:	10
Practice Considerations:	10
Recommended Antibiotic Treatment	10
Sepsis where source is unknown	10
Indications:	10
Practice Considerations:	10
Urinary Tract Infection	11
Gentamicin use and dosing	11
Monitoring gentamicin levels	11
References	12
Useful Websites:	12
Appendix: Beta-lactam Assessment Tool	13
Acknowledgements	14



Antibiotics in the Peripartum Period

Summary of Practice Recommendations

Infection during pregnancy and the postpartum period may be caused by a combination of organisms, including aerobic and anaerobic cocci and bacilli.

Prophylactic antibiotics and standard infection prevention practices can reduce the risk of postpartum infectious morbidity.

When women with penicillin and cephalosporin allergy are screened for GBS during pregnancy, culture and sensitivity must also be included on the request form as there is increasing microbial resistance to beta-lactam antibiotic alternatives¹.

Blood cultures and other clinical specimens (as indicated) should be taken prior to the commencement of antibiotic treatment.

Systemically ill patients should commence broad spectrum, intravenous antibiotics (within 1 hour of recognition of severe sepsis)².

Women, who are suspected of or diagnosed as having an infection, should receive antibiotic treatment specific to their infection when known.

Selection of appropriate antibiotic treatment is complex. Consult an infectious diseases (ID) specialist if there is any uncertainty.

Penicillin hypersensitivity reported by a woman requires critical evaluation as beta-lactam antibiotics are frequently the drug of choice during the perinatal period³.

Use of the [beta-lactam allergy assessment tool](#) (Reproduced with permission from eTG complete [Internet]. Melbourne, Therapeutic Guidelines Limited; 2019)³ to determine whether penicillins are not recommended but cephalosporins are safe versus both penicillins and cephalosporins not recommended is essential to determine the most appropriate antibiotic in the context of self-reported beta-lactam allergy³.

Abbreviations

BMI	Body Mass Index
g	Gram
GBS	Group B Streptococcus
IBW	Ideal body weight
ID	Infectious Diseases
IV	Intravenous
kg	Kilogram
LSCS	Lower segment caesarean section
mg	Milligram
PROM	Prelabour rupture of membranes
PPROM	Preterm Prelabour Rupture of the Membranes
ROM	Rupture of membranes

Definitions

Allergy	Allergy occurs when a person's immune system reacts to substances in the environment that are harmless for most people
Antibiotic Prophylaxis	The use of antibiotics to prevent infections
Beta-lactam allergy	Includes allergy to penicillin derivatives (penams), cephalosporins (cephems), monobactams or carbapenems
Sepsis	Presence of both infection (invasion of tissue, fluid or a body cavity by pathogenic micro-organisms) and systemic manifestations of inflammatory response syndrome (SIRS)
Severe Allergy	Immediate hypersensitivity involving the development of urticaria, angioedema, bronchospasm or anaphylaxis within one to two hours of drug administration, or Delayed severe hypersensitivity (e.g. severe cutaneous adverse reaction or significant organ involvement such as acute interstitial nephritis)



Antibiotics in the Peripartum Period

Prophylactic Antibiotic Use in the Peripartum Period

Group B Streptococcus (Intrapartum prophylaxis)

Indications:

Woman screened Group B Streptococcus (GBS) positive during pregnancy
 Previous GBS neonatal sepsis
 Woman GBS negative or unknown with rupture of membranes (ROM) > 18 hours
 Women in preterm labour or with PPRM who are GBS positive or unknown
 For more information see the *Early Onset Neonatal Sepsis PPG* available at www.sahealth.sa.gov.au/perinatal

Practice Considerations:

Women who are GBS positive with intact membranes at the time of elective caesarean section do not require antibiotics.

GBS resistance to clindamycin has increased to approximately 30%¹. For women with penicillin and cephalosporin allergy, "Culture and sensitivity" must also be included on the laboratory request form along with "penicillin and cephalosporin allergy". If the results demonstrate resistance to clindamycin, prophylaxis with vancomycin is required¹.

Recommended antibiotic treatment:

Benzylpenicillin 3 g IV loading dose, then 1.2 g IV every 4 hours until birth

Penicillins not recommended but cephalosporins safe (see [beta-lactam allergy assessment tool](#))

Cefazolin 2 g IV every 8 hours until birth

Penicillins and cephalosporins not recommended (see [beta-lactam allergy assessment tool](#))

Clindamycin 600 mg IV every 8 hours until birth providing susceptible isolate

Or

If the GBS isolate is resistant to clindamycin or GBS susceptibility/sensitivity is unknown, replace clindamycin with

Vancomycin 25 mg/kg (based on actual body weight max 3g) IV as a loading dose (refer to [SA Health vancomycin monitoring guideline](#) for subsequent dosing)³

Caesarean Section

Indications:

Woman undergoing both elective and emergency caesarean section

Practice Considerations:

Single dose prophylactic antibiotic cover should be administered to all women having a caesarean section⁴.

The optimal timing for the administration of prophylactic antibiotics is before skin incision.

Recommended antibiotic treatment:

Cefazolin 2 g as a single IV dose (Consider increased dose of cefazolin (3g) if patient is obese (>120kg). Consult ID for advice)

Penicillins and cephalosporins not recommended (see [beta-lactam allergy assessment tool](#))

Clindamycin 600 mg as a single IV dose AND

Gentamicin 2 mg/kg as a single IV dose (see [gentamicin dosing](#))



Antibiotics in the Peripartum Period

Manual Removal of the Placenta

Indications:

Manual removal of the placenta

Practice Considerations:

Manual removal of the placenta is associated with an increased rate of postpartum endometritis. Despite this, there is no evidence to suggest routine antibiotic use following manual removal of the placenta is beneficial⁵.

However, single dose prophylaxis is currently recommended.

If possible, prophylactic antibiotics should be given 30 minutes before starting the procedure.

Recommended antibiotic treatment:

Cefazolin 2 g as a single IV dose (Consider increased dose of cefazolin (3g) if patient is obese (>120kg).

Penicillins and cephalosporins not recommended (see [beta-lactam allergy assessment tool](#))

Clindamycin 600 mg as a single IV dose AND

Gentamicin 2 mg/kg as a single IV dose (see [gentamicin dosing](#))

3rd or 4th degree perineal tears

Indications:

3rd or 4th degree perineal lacerations

Practice Considerations:

There are no randomised controlled studies comparing antibiotics with placebo for prevention of infection in 3rd or 4th degree perineal tears.

Infection carries a high risk of breakdown of the repair resulting in anal incontinence and fistula formation. Therefore, broad-spectrum antibiotics are recommended during and after the repair⁶.

Recommended antibiotic treatment at time of repair:

Cefazolin 2 g as a single IV dose (Consider increased dose of cefazolin (3g) if patient is obese (>120kg).

AND

Metronidazole 500 mg as a single IV dose

Penicillins and cephalosporins not recommended (see [beta-lactam allergy assessment tool](#))

Clindamycin 600 mg as a single IV dose AND

Gentamicin 2 mg / kg as a single IV dose (see [gentamicin dosing](#))

Recommended postnatal antibiotic treatment:

Oral Augmentin Duo Forte® (amoxicillin/clavulanic acid 875mg/125 mg) 12 hourly with food for 7 days

Penicillins not recommended but cephalosporins safe (see [beta-lactam allergy assessment tool](#))

Oral cefalexin 500 mg every 6 hours AND

Oral metronidazole 400 mg every 12 hours for 7 days

Penicillins and cephalosporins not recommended (see [beta-lactam allergy assessment tool](#))

Oral ciprofloxacin 500 mg every 12 hours AND

Oral clindamycin 450 mg every 8 hours for 7 days



Antibiotics in the Peripartum Period

Women with Cardiac Disease

Indications:

Intrapartum bacterial endocarditis prophylaxis is only recommended for vaginal birth, when one of the following cardiac conditions is present⁷:

- prosthetic cardiac valve or prosthetic material used for cardiac valve repair
- previous infective endocarditis
- congenital heart disease, but only if it involves:
 - unrepaired cyanotic defects, including palliative shunts and conduits
 - completely repaired defects with prosthetic material or devices, whether placed by surgery or catheter intervention, during the first 6 months after the procedure (after which the prosthetic material is likely to have been endothelialised)
 - repaired defects with residual defects at or adjacent to the site of a prosthetic patch or device (which inhibit endothelialisation)
- cardiac transplantation with the subsequent development of cardiac valvulopathy
- rheumatic heart disease in Indigenous Australians and individuals at significant socioeconomic disadvantage⁸.

Recommended antibiotic treatment:

Amoxicillin 2 g as a single IV dose as close as practical to the time of birth. Repeat dose after 8 hours if birth has not occurred

Penicillins and cephalosporins not recommended (see [beta-lactam allergy assessment tool](#))

Clindamycin 600 mg as a single IV dose as close as practical to the time of birth. Repeat dose after 8 hours if birth has not occurred

OR

Vancomycin 1 g (1.5 g > actual body weight 80 kg) IV, administered slowly (over at least one hour) and repeated after 12 hours if birth has not occurred

Bacterial Vaginosis

Antibiotic treatment for bacterial vaginosis does not reduce the risk of preterm birth before 37⁺⁰ weeks or the risk of preterm prelabour rupture of the membranes⁹.

For women undergoing cervical cerclage, consider antibiotic treatment for bacterial vaginosis (See *Cervical Insufficiency and Cerclage* PPG available at www.sahealth.sa.gov.au/perinatal)

Recommended antibiotic treatment:

Oral clindamycin 300 mg every 12 hours for 7 days OR alternatively if the woman is before 20 weeks' gestation

Clindamycin 2 % vaginal cream, 1 applicatorful at bedtime for 7 nights

Clindamycin not suitable

Oral metronidazole 400 mg every 12 hours for 5 days OR alternatively if the woman is before 20 weeks' gestation

Metronidazole 0.75 % vaginal gel, 1 applicatorful at bedtime for 5 nights



Antibiotics in the Peripartum Period

Prelabour Rupture of Membranes \geq 37 weeks (PROM)

Women who are known GBS positive should commence [GBS Prophylaxis](#).

Women who are GBS negative or unknown should commence [GBS prophylaxis](#) once membranes have been ruptured for 18 hours or more.

For more information, please refer to the *Prelabour Rupture of the Membranes (PROM) \geq 37 Weeks* PPG and the *Early Onset Neonatal Sepsis* PPG available at www.sahealth.sa.gov.au/perinatal.

Preterm Prelabour Rupture of Membranes (PPROM)

Use of prophylactic antibiotics for women with preterm rupture of the membranes is associated with prolongation of pregnancy and improvements in a number of short-term neonatal morbidities, but no significant reduction in perinatal mortality¹⁰.

However, [GBS prophylaxis](#) with the addition of oral erythromycin is recommended for women with PPROM¹⁰. Please note that the use of erythromycin may alter maternal vaginal flora and as a result adversely impact neonatal outcome in very preterm newborns¹¹.

PPROM with no evidence of chorioamnionitis

Recommended antibiotic treatment:

[GBS prophylaxis](#) if GBS positive or unknown

AND

Oral erythromycin 250 mg 4 times a day for a maximum of 10 days or until birth if this occurs sooner³

Note: Further benzylpenicillin prophylaxis, as above, is indicated whenever labour recurs

PPROM with evidence of chorioamnionitis

Recommended antibiotic treatment:

See treatment of [chorioamnionitis](#) below.

Note: The addition of alternative antibiotics should be based on the initial and subsequent weekly high vaginal swab results (in consultation with an ID consultant as indicated).

Preterm Labour

Women in active labour AND without symptoms/signs of infection should receive [GBS prophylaxis](#) if GBS positive or unknown.

Women should not routinely receive broad spectrum antibiotics in this situation¹² (see *Early Onset Neonatal Sepsis* and *Preterm Labour* PPGs at www.sahealth.sa.gov.au/perinatal).



Antibiotics in the Peripartum Period

Antibiotic Treatment of Infection

Chorioamnionitis

Indications:

Clinical suspicion of chorioamnionitis

Refer to *Sepsis in Pregnancy* PPG available at www.sahealth.sa.gov.au/perinatal

Practice Considerations:

The diagnosis of chorioamnionitis relies on the clinical presentation and may be difficult in its early manifestations.

If chorioamnionitis is confirmed, birth of the fetus is indicated.

Do not inhibit labour, but consider hastening birth under intravenous antibiotic cover.

Histological examination of placenta and membranes with evidence of acute inflammation may confirm diagnosis post birth.

Recommended antibiotic treatment until birth:

Amoxicillin 2 g IV every 6 hours AND

Gentamicin 5 mg/kg IV once a day (initial maximum 480 mg, see [gentamicin dosing](#)) AND

Metronidazole 500 mg IV every 12 hours

Penicillins not recommended but cephalosporins safe (see [beta-lactam allergy assessment tool](#))

Cefazolin 2 g IV every 8 hours for 48 (Note: No cover for enterococcus and listeria provided by cefazolin) AND

Gentamicin 5 mg/kg IV once a day (initial maximum 480 mg, see [gentamicin dosing](#)) AND

Metronidazole 500 mg IV every 12 hours

Penicillins and cephalosporins not recommended (see [beta-lactam allergy assessment tool](#))

Clindamycin 600 mg IV every 8 hours AND

Gentamicin 5 mg/kg IV once a day (initial maximum 480 mg, see [gentamicin dosing](#)) AND

Metronidazole 500 mg IV every 12 hours

Note: if the GBS isolate is resistant to clindamycin or GBS susceptibility/sensitivity is unknown, replace clindamycin with,

Vancomycin 25 mg/kg (based on actual body weight max 3g) IV as a loading dose (refer to [SA Health vancomycin monitoring guideline](#) for subsequent dosing)^{3,13}

Recommended continuation of postnatal antibiotic treatment:

Vaginal Birth

If there are no features of sepsis, cease antibiotic therapy following birth as the risk of postpartum endometritis is low³.

Caesarean Birth

If there are no features of sepsis, give one additional IV dose of each of the antibiotics commenced pre-operatively and then cease.

Consider continuing IV antibiotics for up to 24 hours following the caesarean if the woman is at increased risk of postpartum endometritis (e.g. PROM, obese women)³.



Endometritis

Indications:

Systemically ill patients should commence broad spectrum, intravenous antibiotics (within 1 hour of recognition of severe sepsis)².

Abdominal pain, fever (> 38°C), tachypnoea and sustained tachycardia (> 90 beats per minute) are indications for admission and intravenous antibiotics.

Practice Considerations:

Common symptoms of endometritis include abdominal pain, uterine tenderness and offensive lochia. The uterus may be subinvolved and slightly soft, with endometritis a cause of secondary postpartum haemorrhage.

In women with fever but no offensive lochia or uterine tenderness, other sources of infection should be considered.

Women with non-severe endometritis (infection is localised, woman is afebrile without systemic symptoms), only require oral antibiotic treatment³.

Women with severe endometritis (systemic features of infection), require IV antibiotic therapy.

For women with uncomplicated endometritis, cease antibiotics 24-48 hours following resolution of symptoms. Oral step-down is not required³.

For women with complicated infection (e.g. bacteraemia), IV therapy may be required for longer with oral step-down once clinically stable with normalising inflammatory markers³.

Consider modifying the therapy based on culture and susceptibility testing (when available) and clinical response.

Consult ID specialist after 72 hours if IV antibiotic therapy still required.

Recommended Antibiotic Treatment:

IV

Amoxicillin 2g IV every 6 hours AND

Gentamicin IV 5 mg/kg once each day (initial maximum 480 mg, see [gentamicin dosing](#)) AND

Metronidazole 500 mg IV every 12 hours

Penicillins not recommended but cephalosporins safe (see [beta-lactam allergy assessment tool](#))

Cefazolin 2 g IV every 8 hours for 48 (Note: No cover for enterococcus and listeria provided by cefazolin) AND

Gentamicin 5 mg/kg IV once a day (initial maximum 480 mg, see [gentamicin dosing](#)) AND
Metronidazole 500 mg IV every 12 hours

Penicillins and cephalosporins not recommended (see [beta-lactam allergy assessment tool](#))

Clindamycin 600 mg IV every 8 hours AND

Gentamicin 5 mg/kg IV once a day (initial maximum 480 mg, see [gentamicin dosing](#))

Note: If the GBS isolate is resistant to clindamycin or GBS susceptibility/sensitivity is unknown, replace clindamycin with,

Vancomycin 25 mg/kg (based on actual body weight max 3g) IV as a loading dose (refer to [SA Health vancomycin monitoring guideline](#) for subsequent dosing) AND

Metronidazole 500 mg IV every 12 hours

Oral

Total duration of therapy (total IV and oral) 7 days

Oral Augmentin Duo Forte® (amoxicillin/clavulanic acid 875mg/125 mg) 12 hourly with food

Penicillins and cephalosporins not recommended (see [beta-lactam allergy assessment tool](#))

Trimethoprim/sulfamethoxazole (160mg/800mg) every 12 hours AND

Metronidazole 400mg every 12 hours

Mastitis

Indications:

Evidence of mastitis with systemic symptoms

Practice Considerations:

In the absence of systemic symptoms, adequate drainage of the affected area in the breast via infant suckling, breast expression and massage may prevent progression.

If the woman shows signs of infection, early treatment with oral antibiotics is important to prevent abscess formation.

In women with cellulitis, breast abscess or not improving after 48 hours of oral treatment, admission and treatment with IV antibiotics is indicated³.

Recommended Antibiotic Treatment

Oral

Flucloxacillin 500 mg orally, every 6 hours for at least 5 days

Penicillins not recommended but cephalosporins safe (see [beta-lactam allergy assessment tool](#))

Cephalexin 500 mg orally, every 6 hours for at least 5 days

Penicillins and cephalosporins not recommended (see [beta-lactam allergy assessment tool](#))

Clindamycin 450 mg orally, every 8 hours for at least 5 days

IV

Flucloxacillin 2 g IV every 6 hours

Penicillins not recommended but cephalosporins safe (see [beta-lactam allergy assessment tool](#))

Cefazolin 2 g IV every 8 hours

Penicillins and cephalosporins not recommended (see [beta-lactam allergy assessment tool](#))

Vancomycin 25 mg/kg (based on actual body weight max 3g) IV as a loading dose (refer to [SA Health vancomycin monitoring guideline](#) for subsequent dosing)

OR

Clindamycin 600 mg IV every 8 hours

Sepsis where source is unknown

Indications:

Systemically ill patients should commence broad spectrum, intravenous antibiotics (within 1 hour of recognition of severe sepsis)^{1,14}.

Abdominal pain, fever (> 38°C), tachypnoea and sustained tachycardia (> 90 beats per minute) are indications for admission and IV antibiotics¹³.

Refer to *Sepsis in Pregnancy* PPG available at www.sahealth.sa.gov.au/perinatal

Practice Considerations:

Consult early with microbiologist or ID specialist for women with evidence of systemic infection.

The choice of antibiotic depends on the clinical suspicion, local flora and culture information.

If genital tract sepsis is suspected, prompt early treatment with a combination of high-dose broad-spectrum intravenous antibiotics may be lifesaving².

Empirical treatment should include broad spectrum antimicrobials active against Gram-negative bacteria, and capable of preventing exotoxin production from Gram-positive bacteria (according to local microbiology policy). Gram-positive cover is necessary if the likelihood of this infection is high¹⁴.

Refer to the principles of managing sepsis and septic shock in the [e-Therapeutic Guidelines](#)³.

Antibiotics in the Peripartum Period

Urinary Tract Infection

Detailed antibiotic information based on organism and clinical presentation is in the *Urinary Tract Infections in Pregnancy* PPG (see A-Z listing at www.sahealth.sa.gov.au/perinatal)

Gentamicin use and dosing

Gentamicin dosing frequency is generally once daily except for women with abnormal renal function, where the initial dose should be given once and advice obtained from Infectious Diseases regarding dosing frequency

Pregnant women should be dosed according to actual body weight as there are a number of pharmacokinetic changes, such as increased volume of distribution and renal clearance that could result in sub-therapeutic dosing if Ideal Body Weight (IBW) is used. However, caution should be used in overweight/obese women (pre-pregnancy BMI > 25) where dosing should be based on IBW

- Female Ideal Body Weight = 45.5 kg + 0.9 kg (for each cm over 152 cm)
- Initial starting doses should be capped accordingly, unless otherwise advised by an ID specialist.
- Women aged 16-60 years: 5 mg/kg dose (maximum of 480 mg)

Monitoring gentamicin levels

In the absence of a history of renal disease, short term treatment (2-3 days) with Gentamicin does not require levels

If levels are required, available evidence suggests the area under the curve (AUC) of plasma aminoglycoside concentration versus time may be a better predictor of toxicity and efficacy than the traditional peak and trough monitoring

Two blood samples taken at one hour and six hours after the first dose are required to calculate the AUC from these 2 plasma concentrations and dosage modifications recommended as necessary

- It is important to record the exact time the dose was given and the exact time of taking the blood samples on the request forms / collection tubes

Repeat levels are not usually required unless treatment is prolonged, in which case they should be done after 5-7 days. Potential efficacy or toxicity concerns may require earlier repeat levels

For further information refer to SA Health Policy - [Aminoglycoside: Recommendations for Use, Dosing and Monitoring Clinical Guideline](#)



Antibiotics in the Peripartum Period

References

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Useful Websites:

SA Health Antimicrobial Guidelines:

<https://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/clinical+resources/clinical+topics/medicines+and+drugs/antimicrobial+guidelines>

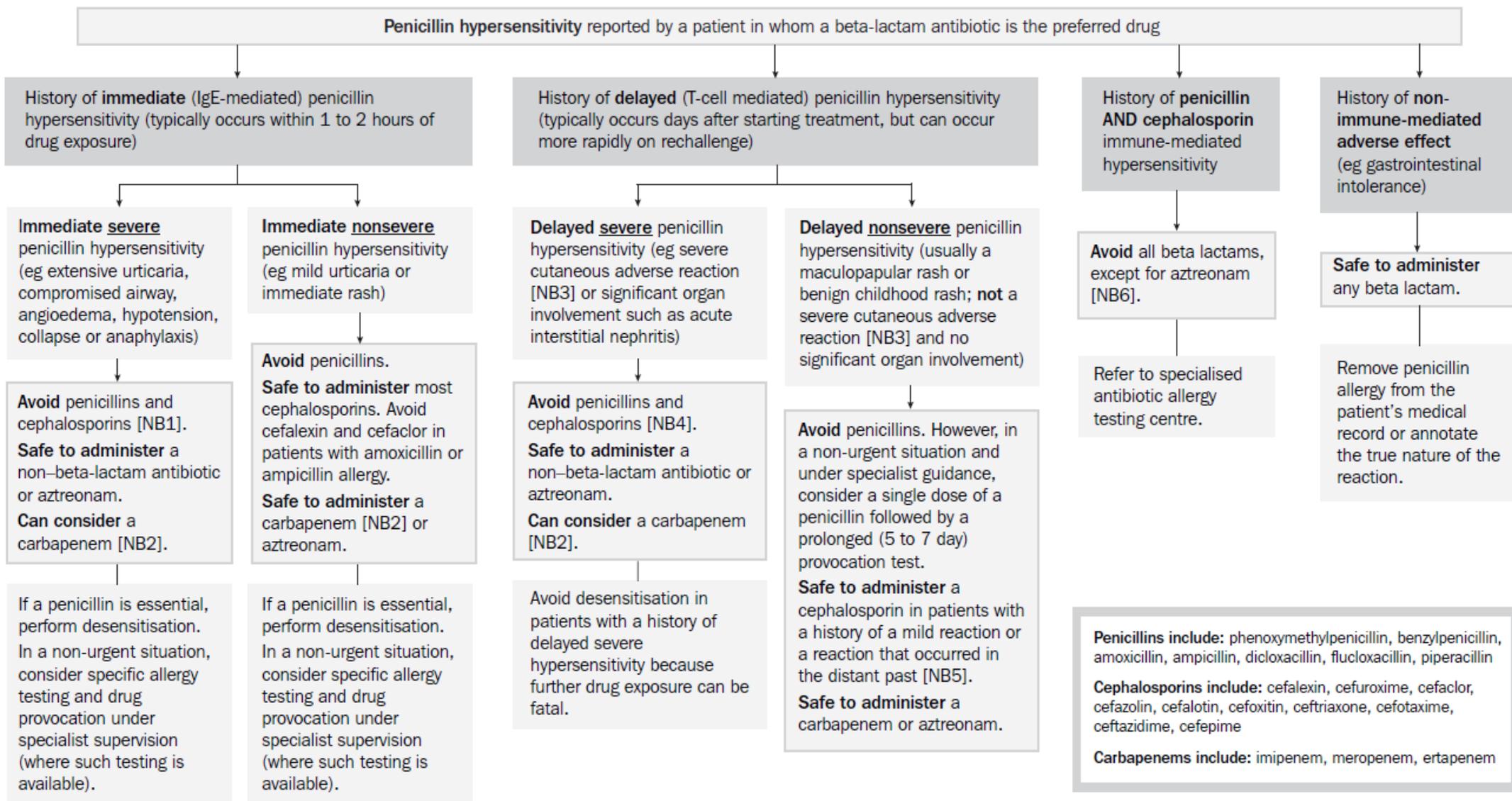
Australian Injectable Drugs Handbook (AIDH) - 7th Edition:

https://aidh.hcn.com.au/browse/about_aidh

Australian e-Therapeutic Guidelines Complete: Antibiotic:

<https://tgldcdp.tg.org.au>





Penicillins include: phenoxymethylpenicillin, benzylpenicillin, amoxicillin, ampicillin, dicloxacillin, flucloxacillin, piperacillin

Cephalosporins include: cefalexin, cefuroxime, cefaclor, cefazolin, cefalotin, cefoxitin, ceftriaxone, cefotaxime, ceftazidime, cefepime

Carbapenems include: imipenem, meropenem, ertapenem

NB1: In a critical situation, a cephalosporin can be considered in this group after undertaking a risk-benefit analysis and assessment of potential side-chain cross-reactivity. Seek expert advice.

NB2: In patients with penicillin hypersensitivity, the rate of immune-mediated cross-reactivity with carbapenems is approximately 1%; therefore, carbapenems can be considered in supervised settings. However, in patients with a history of a severe cutaneous adverse reaction (eg drug rash with eosinophilia and systemic symptoms [DRESS], Stevens-Johnson syndrome / toxic epidermal necrolysis [SJS/TEN], acute generalised exanthematous pustulosis [AGEP]), consider a carbapenem only in a critical situation when there are limited treatment options.

NB3: For example DRESS, SJS/TEN, AGEP.

NB4: There is limited evidence on the safety of cephalosporins in patients with a history of penicillin-associated acute interstitial nephritis (AIN). In a critical situation, directed therapy with a cephalosporin can be considered.

NB5: In patients who have had a recent reaction, consider avoiding cephalosporins with the same or similar R1 side-chain as the implicated penicillin.

NB6: However, avoid aztreonam in patients hypersensitive to ceftazidime; these drugs have the same R1 side-chain, so there is a risk of cross-reactivity.

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Antibiotics in the Peripartum Period

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