

South Australian Perinatal Practice Guidelines

Asthma in Pregnancy

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Literature review

- > A recent analysis of the SA Perinatal database identified that maternal asthma contributes to the burden of 20 % of all preterm births, 15 % of all intrauterine growth restricted fetuses and 15 % of all stillbirths in South Australia. These outcomes are likely to be reduced with well managed asthma
- > Women with well managed asthma can expect the same outcomes as women without asthma^{1,2}
- > Physiological changes occurring during pregnancy may affect asthma control²
- > Overall, prospective cohort studies in Australian women identified that asthma
 - > improves for about 20 % of women with asthma
 - > remains stable for 20 % of women with asthma
 - > worsens in about 60 % of women with asthma⁶
- > During pregnancy, medical intervention for asthma exacerbations occurs in about 60 % of women with asthma, with approximately 6 % being admitted to hospital. These exacerbations may occur any time during pregnancy but predominantly between 17 and 34 weeks gestation. The major triggers are viral infection and non-adherence to inhaled corticosteroid medication¹. However pregnancy itself may be a trigger for worsening asthma
- > Since most pregnant women have increased dyspnoea in pregnancy, all pregnant women with asthma, even those with mild and / or well controlled disease, should be monitored by clinical assessment and regular tests of lung function³
- > Severe asthma may be associated with a number of perinatal complications including:
 - > preterm birth
 - > caesarean delivery
 - > intrauterine growth restriction
 - > Associated maternal morbidities include:
 - > pre-eclampsia
 - > urinary tract infection
 - > gestational diabetes
 - > postpartum haemorrhage
 - > and mortality^{3, 4}
- > Adverse outcomes are lower among those with well - controlled asthma, especially where managed with inhaled corticosteroids (ICS)⁵
- > The use of ICS during pregnancy appears to protect against low birth weight⁶
- > There is no evidence that asthma drugs increase the risk of birth defects⁷ or complications in labour
- > Many women decrease or cease their asthma therapies when pregnant due to their concerns about safety of medications in pregnancy¹⁴. However, it is safer for pregnant women to maintain control of their asthma with appropriate medications than for them to have asthma symptoms and exacerbations⁵

- > An asthma education program tailored to pregnant women and delivered by an asthma educator can contribute to significant improvements in all aspects of asthma self – management including inhaler technique, knowledge of and adherence to prescribed medications⁸. It is recommended that the best approach to asthma

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management during pregnancy may be with the use of a combined obstetric and respiratory clinic. The provision of individualised asthma action plans are an important aspect of asthma self-management and associated with a significant increase in neonatal birth weight, compared with no action plan⁸

Assessment of asthma control

- > Effective long term control of asthma requires continual reassessment of control throughout pregnancy⁹
- > The level of control of asthma is based on the most severe category (see table 2 below)^{3,14}
- > Reliever use and the frequency, severity and effect of symptoms on sleep and usual activities should be based on the woman's recall over the past 2- 4 weeks. A measure of pulmonary function should also be undertaken using either spirometry or peak flow with spirometry being the preferred option^{9,14}

	Daytime asthma symptoms	Night-time asthma symptoms	Exacerbations	Spirometry
Intermittent	< weekly	< 2 per month	> Infrequent > Brief	FEV ₁ at least 80% predicted FEV ₁ variability < 20%
Mild persistent	> weekly and < daily	> 2 per month but not weekly	> Occasional > May affect activity or sleep	FEV ₁ at least 80% predicted FEV ₁ variability 20-30%
Moderate persistent	Daily	Weekly or more often	> Occasional May affect activity or sleep	FEV ₁ 60-80% predicted FEV ₁ variability > 30%
Severe persistent	> Daily > Physical activity is restricted	Frequent	Frequent	FEV ₁ 60% predicted or less FEV ₁ variability > 30%

Table 1: Classification of asthma severity Adapted from GINA 2004¹⁹

An individual's asthma pattern is determined by the level in the table that corresponds to the most severe feature present. Other features associated with that pattern need not be present

Variable	Well controlled asthma	Not well controlled asthma	Very poorly controlled asthma
(a) Frequency of symptoms	(a) ≤ 2 days a week	(a) > 2 days a week	(a) Throughout the day
Frequency of night time awakening	≤ 2 times a month	1-3 times a week	≥ 4 times a week
Interference with normal activity	None	Some	Extreme
Use of short acting β-agonist for symptom control	≤ 2 days a week	> 2 days a week	Several times a day

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Use of short acting β-agonist for symptom control

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Table 2: Assessment of asthma control Adapted from Ernst P, Fitzgerald JM, Spier S, 1996¹⁵

FEV₁: Forced expiratory volume in 1 second; FVC: Forced vital capacity obtained by spirometry; PEF: Peak expiratory flow obtained with a portable peak flow meter. Not well controlled is when at least one characteristic is present in column 2. Very poorly controlled is when at least one characteristic is in column 3

Pre-pregnancy counselling

- > Women with asthma who are planning to become pregnant should stop smoking
- > Assess level of asthma control and severity (see Tables 1, 2, 3, 4 and 5) and ensure the woman is well controlled with an appropriate asthma medication before becoming pregnant
- > Reassure women with asthma that most asthma medications, including most inhaled corticosteroids (ICS), have a good safety profile and can be continued during pregnancy
- > In women who are planning a pregnancy and are already using ICS, budesonide is recommended because it is rated Category A by the Australian Drug Evaluation Committee (ADEC). More data on use in pregnant women are available for budesonide than for other ICS. However, there are no data indicating that other ICS are unsafe during pregnancy
- > Long acting beta two agonists (LABA) (e.g. salmeterol and eformoterol) found in combination therapies (i.e. combined with ICS) are rated Category B3 and are, if possible, best avoided in the first trimester. Therefore consider changing women on combination therapies to an inhaled corticosteroid alone. However, the benefits of asthma control outweigh any potential for an adverse pregnancy outcome from LABA therapy
- > Review asthma control after any change in the medication regimen
- > Identify significant triggers and discuss avoidance strategies
- > Encourage good asthma self - management by training in self-monitoring for signs of deterioration of asthma control (via symptoms and / or peak flow monitoring); ensure correct inhaler technique; review and update the asthma action plan and arrange regular asthma review
- > Assess need for influenza re-vaccination

Antenatal care

General Principles:

- > Pregnant asthmatic women should be treated in a manner similar to non-pregnant asthmatic women

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- > Breathlessness during pregnancy is common but should be assessed in women with asthma. Pre and post bronchodilator spirometry is safe to perform in pregnancy and can assist to determine the cause of breathlessness. Measures of lung function such as FEV1 and PEFr do not change substantially as a result of pregnancy¹⁴. The use of bronchial provocation tests for the diagnosis of asthma in pregnant or lactating women should only be performed on the advice of a respiratory specialist due to the lack of data on safety of these tests in pregnant women⁹
- > All pregnant women should be asked whether they have ever been prescribed asthma medication. Determining past and current treatment will assist to categorise level of asthma severity and will also assess potential problems and barriers to adherence since many women decrease or cease their asthma medications when pregnant¹⁴
- > Pregnant women with asthma should have regular evaluation and monitoring of asthma control throughout pregnancy. Poorly controlled asthma increases the risk of a poor outcome for the fetus. Good asthma control can reduce these risks³
- > The ultimate goal of asthma management in pregnancy is to maintain adequate oxygenation in the fetus by preventing hypoxic episodes in the mother
- > The principles of pharmacological treatment of asthma during pregnancy should be the same as for non-pregnant women. Doses of ICS should be the minimum necessary to control symptoms and maintain normal or best lung function
- > Identify and manage common co-existing conditions such as allergic rhinitis, sinusitis and gastro-oesophageal reflux that can aggravate asthma and compromise asthma control¹⁴
- > Close cooperation between all health professionals will ensure the best asthma management for the woman

Management:

Optimal management of asthma during pregnancy includes:

- > Assessing asthma control at each visit
- > Avoiding or minimising asthma triggers where possible and minimising exposure to known allergens and irritants (including cigarette smoke)
- > Individualising pharmacologic treatment to maintain normal pulmonary function
- > Self- management, education and provision of an asthma action plan
- > Regular review
- > Routine booking appointment / antenatal care
- > Assess asthma control (see Table 1 above)
- > Measure lung function - spirometry is preferable but peak expiratory flow measurement with a peak flow meter is also acceptable³
- > Review medications, check inhaler technique; review and update the asthma action plan
- > Assess need for influenza vaccination
- > Assess smoking status
- > In utero exposure to cigarette smoke is associated with reduced lung function and increased risk of respiratory illnesses including wheeze and asthma in children⁸
- > Review need for immediate obstetric / respiratory physician review especially in moderate or severe persistent asthmatics (see Table 1)
- > Arrange obstetric / respiratory physician review as indicated
- > Women with moderate or severe persistent asthma (see Table 1) or who are identified as very poorly controlled (see Table 2) should be managed in close consultation with a physician who has expertise in pulmonary medicine

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- > Arrange an antenatal anaesthetic referral / review for all women with severe and / or uncontrolled asthma
 - > Manage exacerbations promptly and aggressively with inhaled beta-2 agonists and oral corticosteroids
 - > Provide thorough asthma self – management education
 - > Reinforce the importance of maintaining good control of their asthma with appropriate medications, especially ICS, to reduce the risk of asthma exacerbations¹
 - > Explain to women that poorly controlled asthma and asthma exacerbations increases the risk of a poor outcome for the fetus. Good asthma control can reduce these risks¹²
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- > Explain to women that regular evaluation (about every 4 – 6 weeks) and monitoring of asthma control is recommended throughout pregnancy and that good asthma control is to ensure the oxygen supply required for normal fetal development, as well as to maintain maternal health and quality of life
 - > Explain to women that asthma exacerbations need to be treated promptly and aggressively
 - > Ensure all pregnant women who have asthma, regardless of the severity, have an up to date asthma action plan and understand how to use it
 - > Emphasise the importance of smoking cessation and assist smoking women to quit
 - > Remind parents that passive smoking increases the risk of childhood asthma and other respiratory conditions in their child. The link between exposure to environmental tobacco smoke in early childhood and increased risk of respiratory illnesses, including asthma, has been well documented in epidemiological studies. Avoidance of environmental tobacco smoke may reduce the risk of childhood asthma⁹

Managing asthma exacerbations

An exacerbation is a loss of control and can be classified as mild, moderate or severe

- > All asthma exacerbations need to be treated promptly and aggressively with inhaled beta agonists, an increase in ICS dose if it is a mild exacerbation and oral corticosteroids if clinically indicated
- > Clinical indicators of moderate or severe acute asthma include:⁹
 - > Unable to complete sentences
 - > Tachycardia (> 120 beats per minute)
 - > Raised respiratory rate (> 30 beats per minute)
 - > Moderate to severe wheeze (or chest can sound quiet)
 - > Oximetry less than 90 %
 - > Peak expiratory flow rate between 50-75 % predicted (or less than 100 litre per minute)
 - > FEV₁ between 50-75 % predicted (or less than 1 litre)
- > During a severe acute asthma episode in a pregnant woman:
 - > Closely monitor lung function via spirometry
 - > Monitor oxygen saturation and maintain above 95 %
 - > Consider fetal monitoring using ultrasound and CTG

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Monitoring

- > Review every four to six weeks throughout pregnancy to monitor asthma control and detect and treat any changes in respiratory function
- > Women with very poorly controlled asthma should be seen every 1 – 2 weeks until control is achieved¹⁴
- > Spirometry should be performed at regular visits to monitor lung function. Between visits, women can monitor their lung function using a peak flow meter, if required.
- > Discuss and agree on an asthma action plan to be followed if the woman's asthma deteriorates
- > Women should be advised to report any reduction in fetal activity
- > In women with sub-optimally controlled asthma, consider regular fetal ultrasound check up from 32 weeks' gestation. If a severe exacerbation occurs, arrange a follow-up ultrasound⁵
- > Consider a chest X-ray in the presence of respiratory compromise if respiratory complications are suspected following examination (very small fetal risk is far outweighed by the potential benefits for both the mother and fetus)¹⁰

Pharmacological treatment

Inhaled asthma medications can be used in pregnancy. A suggested treatment regimen associated with asthma severity is outlined in Table 2

Bronchospasm relaxants:

- > Inhaled short acting β_2 -agonists – SABAs - (ADEC [category A](#)) such as salbutamol and terbutaline have no associated teratogenic risks
- > Inhaled long acting β_2 -agonists - LABAs - (salmeterol, eformoterol ADEC [category B3](#) – usually combined with an ICS in “combination therapies”) should be avoided in the first trimester where possible⁹. However, do not withdraw LABAs in women who present after they have become pregnant if they are controlling symptoms as the benefits of asthma control outweigh any potential for an adverse pregnancy outcome
- > Theophyllines (ADEC [category A](#)) may aggravate nausea and reflux in pregnant women as well as causing transient neonatal tachycardia and irritability

Preventers:

Inhaled corticosteroids (ICS)

- > ICS are the mainstay of treatment for asthma and appear to be safe in pregnancy
- > Most evidence for safety is for budesonide (ADEC category A)
- > There is limited experience with the other ICS i.e. beclomethasone, fluticasone and ciclesonide (ADEC [category B3](#)). There is no data indicating that they are unsafe in pregnant women and may be used in pregnancy

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- > ICS should be administered to persistent asthmatics increasing dose with severity (Table 2). Moderate and severe persistent asthmatics will require medium to high doses of ICS in combination with LABA (refer Asthma Management Handbook 2006 and Table 2). A step wise procedure for increasing treatment in women identified to be uncontrolled is outlined in Table 3

Table 3: Recommended ICS dose⁹

Daily ICS dose				
Dose level	CIC*	BDP-HFA**	FP**	BUD**
Low	80-160 micrograms	100-200 micrograms	100-200 micrograms	200-400 micrograms
Medium	160-320 micrograms	200-400 micrograms	200-400 micrograms	400-800 micrograms
High	320 micrograms	Over 400 micrograms	Over 400 micrograms	Over 800 micrograms

ICS: inhaled corticosteroid; LABA: long acting beta 2 agonist; CIC: ciclesonide; BDP-HFA: beclomethasone dipropionate; FP: fluticasone propionate; BUD: budesonide

*ex actuator dose

**ex valve dose

Table 4: Asthma severity rating and medication required for control⁹

Asthma pattern	Asthma control	Medication required
Intermittent	Good	Reliever PRN
Mild persistent	Good	Reliever PRN Low-dose ICS
Moderate persistent	Good	Low-moderate ICS +/- LABA
Severe persistent	Good-fair (poor if very severe)	Moderate-high ICS + LABA +/- other

Adapted from Asthma Management handbook 2006⁹

PRN: when required; LABA: long acting beta2 agonists; ICS inhaled corticosteroids

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Table 5: Step up treatment regimen for ICS and LABA¹⁷

Step 1	Step 2	Step 3	Step 4
SABA as needed for symptom relief			
	Add low dose ICS	Continue low dose ICS and add LABA	Increase ICS to medium to high dose and continue LABA
		OR	OR
		Start low dose budesonide + eformoterol maintenance and reliever therapy	Continue budesonide + eformoterol maintenance and reliever therapy with higher maintenance dose
			More frequent routine review (at least 3 monthly) Specialist referral if no improvement

Adapted from: Respiratory Expert Group. Therapeutic guidelines: respiratory. Version 4. Melbourne: Therapeutic Guidelines Limited; 2009

Cromones

- > Sodium cromoglycate (ADEC [category A](#)): There are no known adverse fetal effects
- > Nedocromil sodium (ADEC [category B1](#)): No teratogenic effects have been shown in animal studies

Leukotriene receptor antagonists

- > Montelukast – Recent recommendations suggest not to be used during pregnancy

Oral corticosteroids

- > Are necessary for short periods of severe asthma in pregnancy especially to resolve an exacerbation or if high dose ICS in combination with LABA do not control asthma symptoms
- > Can be life saving in acute severe asthma with the benefits outweighing the risks

Intravenous corticosteroids

- > Are necessary for short periods of severe asthma in pregnancy especially to resolve an exacerbation or if high dose ICS in combination with LABA do not control asthma symptoms
- > Can be life saving in acute severe asthma with the benefits outweighing the risks

Intrapartum considerations related to asthma

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- > Exacerbations of asthma are uncommon during labour and birth²
- > Except in the most severe cases, asthma should not preclude a vaginal birth
- > Occasionally, women with very severe asthma may be advised to have an elective delivery (induction of labour or caesarean section) at a time when their asthma is well controlled²
 - > Plan after 37⁺⁶ weeks unless there are medical complications requiring earlier intervention
- > Expert opinion recommends adequate hydration and analgesia should be maintained during labour and birth¹⁴
- > Continue preventer medication
- > Symptoms of asthma during labour are generally controlled with standard asthma therapy²
- > Inhaled β -agonists do not impair uterine contractions or delay the onset of labour
- > Prostaglandin E₂ may be used to induce labour for women who have asthma¹⁴
- > Avoid using 15-methyl Prostaglandin F₂ alpha due to the risk of bronchoconstriction¹¹
- > There is no evidence that oxytocin causes bronchoconstriction²
- > Ergometrine has been reported to cause bronchospasm, especially if general anaesthesia is being used, but this does not appear to be an issue if Syntometrine is used for prophylaxis of postpartum bleeding
- > Regional anaesthesia is preferred over general anaesthesia (reduced risk of chest infection)

Use of intravenous hydrocortisone in labour

- > The major role of hypothalamic-pituitary-adrenal (HPA) axis is to control the synthesis and secretion of cortisol from the adrenal cortex. The antenatal administration of glucocorticoids (prednisolone) can result in HPA suppression¹⁸
- > For women taking regular oral glucocorticoids, in consultation with the physician, consider intravenous hydrocortisone to prevent adrenal crisis. Continue until after birth when it is suitable to recommence oral treatment
- > HPA axis suppression is unlikely in women taking the equivalent of < 5 mg prednisolone per day for any length of time or any dose of steroids for < 3 weeks over the past year. These women do not require prednisolone in labour¹⁸
- > Intravenous hydrocortisone is recommended in labour in the following:
 - > Women who have taken > 5 mg prednisolone per day for > 3 weeks in the past year
 - > Women on glucocorticoids at any dose and who are cushingoid in appearance¹⁸

Table 6: Intravenous hydrocortisone dose in labour¹⁸

Physiologic stress level	Representative surgeries	Recommended dose
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Minor surgical stress	D & C Vaginal birth	Hydrocortisone 25 mg IV (pre-op) or in labour, then resume previous dose
Moderate surgical stress	LSCS	Hydrocortisone 50-75 mg IV pre-delivery, then 25 mg every 8 hours for 1-2 days and then resume previous dose
Major surgical stress	Emergency LSCS, hysterectomy	Hydrocortisone 100-150 mg IV intra-operatively, then 50 mg every 8 hours for 2-3 days and then resume previous dose

Adapted from: Chen KK, Powrie R. Approach to the use of glucocorticoids in pregnancy for nonobstetric indications. In: Powrie RO, Greene MF, Camann W, editors. De Swiet's Medical disorders in obstetric practice. 5th ed. Oxford: Wiley-Blackwell; 2010. p. 736-741

Management of an acute asthma exacerbation in labour

- > This is a rare event possibly due to the high levels of endogenous steroids in labour
- > Requires early diagnosis and management
- > Assess for evidence of associated infection and treat accordingly
- > Clinical indicators of moderate or severe acute asthma include:⁹
 - > Unable to complete sentences
 - > Tachycardia (> 120 beats per minute)
 - > Raised respiratory rate (> 30 beats per minute)
 - > Moderate to severe wheeze (or chest can sound quiet)
 - > Oximetry less than 90 %
 - > Peak expiratory flow rate between 50-75% predicted (or less than 100 litre per minute)
 - > FEV₁ between 50-75 % predicted (or less than 1 litre)

Management

- > Upright position
- > Administer 100 % oxygen via Hudson mask
- > Continuously monitor oxygen saturation levels
- > In acute exacerbation, administer salbutamol via nebuliser (or 12 puffs via large volume spacer) with oxygen and repeat as indicated following physician / respiratory specialist medical review

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- > There is only theoretical evidence that nebulised β_2 -agonists will interfere with uterine contractions in labour
- > If there is no response to bronchodilators, in consultation with respiratory specialist or physician, consider intravenous hydrocortisone 100 mg every six hours and consult an intensivist at a hospital with adult intensive facilities
- > The baby of a woman who has had intravenous hydrocortisone may require paediatric review, early monitoring of blood sugar levels, + / - initial observation in the nursery
- > Consider intravenous β_2 -agonists, aminophylline or intravenous bolus magnesium sulphate as indicated and ordered by the physician / respiratory consultant. Assess the need for ventilatory support if inadequate response

Postpartum considerations related to asthma

Postpartum haemorrhage

- > Prostaglandin E₁ (misoprostol) may be used for the management of postpartum haemorrhage¹⁴
- > Use intramyometrial PGF₂ alpha (dinoprost) with caution as this may trigger bronchospasm¹¹

Breastfeeding

- > Breastfeeding should be encouraged as it may reduce the risk of childhood asthma, especially in children with a family history of atopy⁹
- > No contraindication to breastfeeding with any asthma medications⁹

Review asthma management

- > The decision to alter a successful medication regimen requires a balance between the benefit to the mother and risk to baby and agreement should be reached by the physician and woman concerned
- > Review asthma regularly after delivery

Education

- > Remind parents that passive smoking increases the risk of childhood asthma and other respiratory conditions in their child. The link between exposure to environmental tobacco smoke in early childhood and increased risk of respiratory illnesses, including asthma, has been well documented in epidemiological studies. Avoidance of environmental tobacco smoke may reduce the risk of childhood asthma⁹

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Useful websites:

National Asthma Council Australia. Available from URL:

<http://www.nationalasthma.org.au/index.php>

Inhaler technique (videos)

<http://www.nationalasthma.org.au/content/view/548/984/>

Inhaler technique (information paper)

http://www.nationalasthma.org.au/images/stories/manage/pdf/Inhaler_technique_in_adults_with_asthma_or_COPD.pdf

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www.asthmasa.org.au

Asthma action plan templates

<http://www.nationalasthma.org.au/content/view/249/639/>

Drugs In Pregnancy

<http://www.tga.gov.au/hp/medicines-pregnancy.htm>

Abbreviations

ACOG	American College of Obstetrics and Gynecology
ADEC	Australian Drug Evaluation Committee
Cat	Category
CTG	Cardiotocograph
et al.	And others
FEV	Forced expiratory volume
FEV ₁	Forced expiratory volume in 1 second
FVC	Forced vital capacity obtained by spirometry
GINA	Global initiative for Asthma program
ICS	Inhaled corticosteroid(s)
LABA	Long Acting Beta-two Agonist
mg	Milligram(s)
PEF	Peak expiratory flow obtained with a portable peak flow meter
PEFR	Peak expiratory flow rate
PRN	When required

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