



# Healthy pregnancy for women with asthma

An information paper for health professionals



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The prevalence of asthma among pregnant women is increasing.<sup>1</sup> Over 50% of Australian women with asthma are likely to experience at least one exacerbation during pregnancy.<sup>2</sup>

Good asthma control is especially important during pregnancy to ensure adequate oxygen supply to the foetus and the best possible outcomes for mother and baby. A substantial body of data from observational studies indicates that poorly controlled asthma poses significant risks to both mother and baby.<sup>3</sup> Asthma episodes that are sufficiently severe to necessitate hospitalisation, and the absence of regular preventive inhaled corticosteroid (ICS) treatment during pregnancy, are major risks for low birth weight.

### Effects of pregnancy on asthma

Physiological changes occurring during pregnancy may affect asthma control.<sup>4</sup> In some women, pregnancy itself causes a deterioration in asthma, but the mechanisms are not well understood.<sup>3</sup> Asthma can recur during pregnancy in women who have not experienced asthma symptoms since childhood.<sup>5</sup>

Approximately 20% of pregnant women with asthma experience exacerbations that require medical intervention, and approximately 6% require hospital admission, according to a recent systematic review of published studies assessing exacerbations during pregnancy.<sup>1</sup> High exacerbation rates have been reported in Australia. In a prospective cohort study, exacerbations sufficiently severe to necessitate hospital admission, emergency department

## Non-adherence to inhaled corticosteroid (ICS) medication is a major risk factor for asthma exacerbations during pregnancy.

presentation, unscheduled medical visits or a course of oral corticosteroids occurred in 65% of women with severe asthma, 47% of those with moderate asthma and 8% of women with mild asthma.<sup>6</sup>

Worsening of asthma can occur at any stage of pregnancy, but is most common between 17 and 36 weeks' gestation.<sup>1</sup> Non-adherence to ICS medication is a major risk factor for asthma exacerbations during pregnancy.<sup>1</sup> Viral respiratory tract infection is another major contributor, with the highest risk during winter.<sup>1,6</sup> The risk of exacerbation does not appear to be affected by maternal age, lung function, body mass index or number of previous pregnancies.<sup>6</sup>

### Effects of asthma on pregnancy outcomes

Overall, evidence from historical studies, prospective cohort studies and case-control studies suggests that babies born to women with asthma have a higher risk of low birth weight and pre-term delivery.<sup>3</sup> Optimal birth weight is an important goal, given the substantial body of evidence linking low birth weight to increased risk for type 2 diabetes, hypertension, coronary artery disease, stroke, and neurodevelopmental and psychiatric disorders.<sup>8,9</sup> The risk of pre-eclampsia is higher in women with asthma than those without asthma.<sup>3</sup> Asthma-related factors

that might affect pregnancy outcomes include maternal hypoxia, release of inflammatory mediators and altered placental function.

Emerging evidence indicates that documented adverse outcomes are mainly related to poorly controlled asthma, particularly the absence of ICS. Asthma medications including ICSs are now thought to protect foetal growth rate rather than contribute to low birth weight.<sup>3</sup> A recent meta-analysis of clinical studies of asthma in pregnancy (including data for 1453 pregnant women with asthma and more than 156,000 non-asthmatic pregnant women) found a highly statistically significant increase in the risk of low birth weight among women with asthma who **did not** receive ICS treatment during pregnancy (relative risk 1.55 compared with women without asthma). In contrast, meta-analysis of studies that included women receiving ICSs showed **no** association between the diagnosis of asthma and low birth weight.<sup>3</sup>

Asthma exacerbations during pregnancy increase the risk of poor outcomes, particularly low birth weight and pre-term delivery.<sup>3</sup> A recent systematic review of studies reporting pregnancy and asthma outcomes found that low birth weight (defined as <2500 g) was significantly more likely in women with asthma who experienced one or more severe exacerbations during pregnancy than in women with asthma who remained free of exacerbations during pregnancy. Asthma exacerbations during pregnancy did not appear to increase the risk of pre-term delivery (before 37 weeks' gestation) or pre-eclampsia in this large data set.<sup>1</sup>

The use of oral corticosteroids or theophyllines appears to increase the risk of pre-term labour and delivery, based on recent large, prospective cohort studies.<sup>3</sup> However, these medications should not be withheld when necessary, because a severe asthma attack represents the greater risk to the foetus, due to potential reduction in oxygen supply.

### Pregnancy and asthma facts

- Current evidence from large studies indicates that maternal asthma increases the risks of low birth weight, pre-term delivery and pre-eclampsia, and may increase the risk of perinatal mortality.<sup>3,7</sup>
- These risks are highest for women with more severe asthma and those who experience asthma exacerbations during pregnancy. The risk is lower among those with well-controlled asthma, especially where managed with ICS.<sup>7</sup> The use of ICS during pregnancy appears to protect against low birth weight.<sup>3</sup>
- Uncontrolled asthma has been associated with maternal death and foetal death.<sup>7</sup>

## Planned pregnancy and asthma

Women with asthma who are planning a pregnancy should be advised:<sup>10,11</sup>

- to stop smoking (refer women to the Quitline on 13 78 48)
- that asthma and pregnancy may interact – exacerbations during pregnancy usually occur between 17 and 36 weeks' gestation
- that good asthma control is especially important during pregnancy to minimise risk to the baby, so asthma control should be reviewed regularly
- that some commonly used asthma medications have a good safety profile and should be continued during pregnancy – failure to continue taking ICS medication as planned is a risk to the baby.

## Principles of asthma care during pregnancy

At all stages of pregnancy planning and care, health professionals should emphasise that poorly controlled asthma poses significant risk to the foetus. Good asthma control is especially important during pregnancy, given that asthma exacerbations increase the risk of low birth weight.<sup>1</sup> Inadequately managed asthma can result in maternal and foetal hypoxaemia, which increases the risk of pregnancy complications and compromises the baby's safety.<sup>4</sup>

Australian expert consensus statements report that there is no convincing evidence that any of the drugs commonly used to manage asthma cause any particular problems during pregnancy (See *Drug safety considerations in pregnancy*, below).<sup>4,11</sup> As a general principle, the lowest dose required to control symptoms and maximise lung function should be used.<sup>11</sup>

### Avoid asthma exacerbations

Health professionals involved in the care of pregnant women with asthma should reinforce the importance of continuing to take prescribed regular preventer treatment throughout pregnancy to reduce the risk of

exacerbations.<sup>1</sup> Women should be advised to monitor their asthma closely if they experience a viral respiratory infection and to follow their asthma action plan if asthma control worsens.

### Avoid tobacco smoke

Smoking may contribute to the elevated incidence of low birth weight babies born to women with asthma, given that smoking rates are higher among people with asthma than the general population.<sup>3</sup> Maternal smoking increases the risk of sudden infant death syndrome and of respiratory infections, asthma and middle-ear disease in infants and children.<sup>12</sup> Prenatal exposure may be especially harmful.<sup>13</sup> Women should be informed that milk production may be reduced by as much as 250 mL per day in mothers who smoke.<sup>12</sup>

All pregnant women should be asked about smoking status at their first antenatal assessment to identify those who need further support to stop smoking.<sup>12</sup> Because smoking during pregnancy carries a social stigma, health professionals need to learn effective interviewing skills when asking pregnant women about smoking. Appropriately designed written questionnaires are useful in encouraging accurate disclosure of smoking status.<sup>12</sup>

### Arrange regular review

Regular monitoring of asthma status (every 4–6 weeks) is recommended throughout pregnancy.<sup>4,7</sup> Spirometry should be performed at regular visits to monitor lung function. Between visits, women can

## Be 'asthma aware' in pregnancy care

- Don't routinely reassure all women that a degree of dyspnoea can be normal during pregnancy – check first whether the woman has asthma or requires thorough diagnostic investigation for possible asthma.
- For women with asthma, advise (and, if possible, arrange) regular pre-emptive asthma check-ups. Ask about asthma control before week 24 and train women to self-monitor for signs of deterioration.

monitor their lung function using a peak flow meter, if required.

Dyspnoea due to pregnancy should be distinguished from dyspnoea caused by asthma. Women can wrongly attribute asthma symptoms to pregnancy, leading to under-medication and risk of hypoxaemia.<sup>4</sup>

Women should be advised to report any reduction in foetal activity. In women with suboptimally controlled asthma, consider regular foetal ultrasound check-ups from 32 weeks' gestation. If a severe exacerbation occurs, arrange a follow-up ultrasound.<sup>7</sup>

For women with severe asthma, it is important to establish cooperation between health professionals managing asthma (including GPs, asthma educators and respiratory physicians) and those managing the pregnancy and delivery (including obstetricians and midwives).

## Reinforce consistent messages about asthma medications

Reinforce messages about good asthma control using terms that will be familiar to women with asthma. Respiratory physicians, GPs and asthma educators use the following terms when speaking to patients about the classes of medication used to manage asthma.

- **Relievers:** rapid-onset bronchodilators (typically inhaled short-acting beta<sub>2</sub> agonists, e.g. salbutamol, terbutaline) – for managing acute symptoms of breathlessness or taken pre-emptively before exercise.
- **Preventers:** regular medications taken long term to modify airway inflammation – typically ICSs, e.g. fluticasone propionate, budesonide, beclomethasone dipropionate, ciclesonide.
- **Symptom controllers:** regular long-acting beta<sub>2</sub> agonists (LABAs) – often combined in a single inhaler with an ICS.



## Prescribe and adjust medications as for non-pregnant women

According to current expert consensus, asthma during pregnancy should be managed as for non-pregnant women, with these aims:<sup>3,4,10</sup>

- to achieve and maintain best possible lung function
- to back-titrate medication doses when asthma is well controlled, so as to maintain best lung function using the lowest effective doses
- to eliminate asthma symptoms
- to prevent exacerbations.

International expert consensus emphasises that inadequate control of asthma is a greater risk to the foetus than asthma medications. It is safer for a pregnant woman with asthma to use asthma medications than to risk asthma symptoms and acute episodes. Regular monitoring and adjustment of medications as required is necessary to ensure an adequate foetal oxygen supply.<sup>7</sup>

With good asthma control, a woman can expect to maintain a normal pregnancy with minimal risk to herself and her baby.<sup>7</sup>

## Continue regular preventer medication

Regular asthma treatment – including selected ICS – is recommended as appropriate to the current level of asthma severity.<sup>4</sup> The use of an ICS during pregnancy may reduce the risk of exacerbations<sup>14–16</sup> and is recommended for all women with persistent asthma. ICSs are better tolerated than theophylline and equally effective in preventing exacerbations during pregnancy.<sup>17</sup>

Non-adherence to ICS is one of the most common causes of exacerbation during pregnancy,<sup>1</sup> and is commonly due to the misconception that ICSs are harmful to the foetus.<sup>2</sup> Women need active encouragement to take ICSs, with reassurance that current data demonstrate that these medications are safe for both mother and foetus.<sup>3</sup>

## Manage exacerbations promptly and aggressively

Asthma exacerbations during pregnancy should be managed promptly and aggressively, just as for exacerbations



occurring at any other time.<sup>4,7,10</sup> During a severe acute asthma episode in a pregnant woman, the following approaches are recommended:<sup>1</sup>

- closely monitor lung function via spirometry
- monitor oxygen saturation and maintain above 95%
- consider foetal monitoring using ultrasound
- use oral corticosteroids if indicated.<sup>4,7,10</sup> (Although the safety of oral corticosteroids remains uncertain, there is convincing evidence that uncontrolled asthma exacerbations carry the greater risk to mother and baby.<sup>7</sup>)

After discharge from the emergency facility, the addition of ICS to a tapered course of oral corticosteroids, in combination with as-needed short-acting beta<sub>2</sub> agonist reliever, may reduce the risk of readmission in pregnant women compared with the use of oral corticosteroids plus reliever alone.<sup>16</sup>

## Identify and manage allergic rhinitis

Concurrent allergic rhinitis should be effectively managed because untreated rhinitis can contribute to asthma symptoms and compromise control. Intranasal corticosteroids at recommended doses pose a low risk of systemic effects.<sup>7</sup> If an oral antihistamine is required, loratadine or cetirizine are suitable during pregnancy.<sup>7</sup> The use of oral decongestants should be avoided because of their association with

increased risk of gastroschisis, a very rare congenital abnormality.<sup>7</sup>

## Provide thorough asthma self-management education

Australian data show that pregnant women with asthma generally have poor asthma knowledge and skills, and benefit from education on how to manage their asthma during pregnancy.<sup>18</sup> Effective asthma education involves verbal and written information about the proper use of medicines, encouraging women to adhere to regular preventer medication, and a written asthma action plan.<sup>4,19</sup> There is convincing evidence that asthma self-management education is effective in improving adherence to medications.<sup>3</sup>

An Australian study demonstrated that a self-management program tailored to pregnant women and delivered by an asthma educator achieved significant improvements in all aspects of asthma self-management, including inhaler technique, knowledge of prescribed medications and adherence to ICS. In women with severe asthma, night symptoms and reliever medication use significantly decreased after education. The provision of individually designed asthma action plans was associated with a significant increase in neonatal birth weight, compared with no action plan.<sup>18</sup>

Ask about and address women's concerns about medication use. Stress the safety of most modern asthma treatments during pregnancy, and the risks of poorly controlled asthma to the baby.<sup>4,19</sup> Concerns

## Write an asthma action plan

All pregnant women with asthma should be offered an individually tailored, written asthma action plan. An asthma action plan can be designed by the GP through discussion with the woman, in consultation with an asthma educator or respiratory physician. Templates and guidance on preparing an asthma action plan can be obtained from the Asthma Foundation of NSW ([www.asthmansw.org.au](http://www.asthmansw.org.au) or phone 02 9906 3233).

about ICSs are common among pregnant women and lead to anxiety and non-adherence,<sup>20,21</sup> which has been identified as a major risk factor for clinically significant exacerbations.<sup>6</sup> Reassure women that:

- some medications that are used to control asthma carry less risk to the mother and baby than a severe asthma episode<sup>4</sup>
- women with well-managed asthma can expect the same outcomes as women without asthma.<sup>1,4</sup>

## Drug safety considerations in pregnancy

There is extensive evidence for the safety of major drug classes used to treat asthma during pregnancy, including short-acting beta<sub>2</sub> agonists, some ICSs and theophylline (Table 1). The safety of oral corticosteroids is less clear. Before prescribing any medication during pregnancy, refer to Australian Drug Evaluation Committee safety categories for pregnancy.

### Inhaled corticosteroids

No studies to date – including large birth registries – have reported an association between ICS use and any increase in congenital malformations or other adverse perinatal outcomes.<sup>7</sup> Most evidence for safety of ICSs in pregnancy is for budesonide, which has not been associated with adverse pregnancy outcomes, even when high doses are required in women with severe persistent asthma.<sup>7</sup> There are fewer or no data for newer ICSs or for LABA-ICS combinations.<sup>3,7</sup> Budesonide is currently recommended in international guidelines as the preferred ICS in pregnancy.<sup>7</sup> There are no data specifically indicating that the other ICSs are unsafe in pregnant women. Patients whose asthma

is already well controlled on another ICS with some safety data for pregnant women might be advised to continue, especially if changing formulations might compromise asthma control.<sup>7</sup>

Findings from a recent small Australian study suggest that ICS treatment for asthma is associated with normal birth weight neonates.<sup>2</sup> The foetus is normally protected from high maternal systemic corticosteroid concentrations by the actions of placental 11 $\beta$ -HSD2 enzyme, which provides a barrier by converting active cortisol to inactive cortisone.<sup>22</sup> In women with asthma, the activity of this enzyme appears to increase in response to ICS use, and may explain findings of normal foetal growth and birth weight despite ICS use.<sup>2</sup>

### Oral corticosteroids

Available data suggest that oral corticosteroids are associated with increased incidence of cleft lip with or without cleft palate (absolute increase from approximately 0.1% to 0.3% of population), especially when given during the first trimester. However, available evidence is from a small number of pregnant women requiring oral corticosteroids, and from studies that were not purposely designed to assess this risk. Insufficient data are

available to assess the effects of dose, timing, and length of course.<sup>7</sup>

Two recent large, prospective cohort studies found an association between oral corticosteroid use and increased risk of pre-term delivery.<sup>3</sup> The use of oral corticosteroids during pregnancy in women with asthma is associated with an increased incidence of pre-eclampsia and low birth weight, but it is not possible to ascertain whether this is due to the effect of severe or poorly controlled asthma or the effect of medication.<sup>7</sup>

## Considerations for delivery and post-partum care

Exacerbations of asthma are uncommon during labour and delivery.<sup>4</sup> Close co-operation between the respiratory physician, midwife, obstetrician and anaesthetist is particularly important at this time.

Except in the most severe cases, asthma should not preclude a vaginal delivery.<sup>10</sup> There is no increase in the induction of labour, use of forceps or emergency caesareans in women with asthma.<sup>4</sup> 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 controlled.<sup>4</sup>

Acute asthma attacks in labour are rare. Symptoms of asthma during labour are generally easily controlled with standard asthma therapy.<sup>4</sup> The use of prostaglandin F<sub>2</sub> $\alpha$  and ergometrine in the induction of labour, the initiation of the third stage of labour or for placental separation should be avoided due to the risk of bronchoconstriction.<sup>23</sup> There is no evidence that oxytocin causes bronchoconstriction.<sup>4</sup>

## Reassure women that asthma medications are safe in pregnancy

- Advise women that many asthma medications are generally safe to use during pregnancy, with the exception of prolonged courses of high-dose oral corticosteroids.
- For women already using an ICS who are planning a pregnancy, consider switching to budesonide (Category A for pregnancy). Asthma control should be reviewed after any change in the medication regimen.<sup>10</sup>
- Severe exacerbations should be treated promptly and as for non-pregnant women.

**Table 1.** Summary of safety data for asthma medications in pregnancy<sup>3,7,10</sup>

Class	Evidence	Comments
Inhaled corticosteroids	Large body of evidence supports safety in pregnancy	<ul style="list-style-type: none"> <li>• Large safety database for budesonide</li> <li>• Inadequate evidence of safety for fluticasone, beclomethasone in pregnancy. No adequate studies of ciclesonide in pregnancy</li> <li>• Limited data for LABA-ICS combinations</li> </ul>
Short-acting beta <sub>2</sub> agonists (salbutamol, terbutaline)	Overall safety profile favourable	Salbutamol preferred due to excellent safety profile and most pregnancy data
Long-acting beta <sub>2</sub> agonists (salmeterol, eformoterol)	Limited data on use in pregnancy	<ul style="list-style-type: none"> <li>• If possible, LABAs should be avoided during the first trimester</li> <li>• The use of ICS-LABA combinations may be considered in pregnant women with moderate-severe persistent asthma, e.g. where expected to control symptoms and reduce ICS dose requirement</li> </ul>
Theophylline	Evidence for safety at recommended doses (to serum concentration of 5–12 mcg/mL)	Discontinuations due to adverse effects more likely than with ICS <sup>17</sup>
Sodium cromoglycate	Safety profile appears favourable on current evidence	
Leukotriene modifiers (montelukast)	Limited data on safety in pregnancy	
Anticholinergic bronchodilators (ipratropium bromide)	Limited data on safety in pregnancy	
Oral corticosteroids	Widely used during pregnancy for severe asthma	<ul style="list-style-type: none"> <li>• Can be life-saving in acute severe asthma</li> <li>• Associated with increased risk of cleft lip/palate during first trimester</li> </ul>
For information on medications during pregnancy and breastfeeding please call MotherSafe, Royal Hospital for Women on 02 9382 6539 (Sydney) or 1800 647 848 (NSW outside Sydney).		

## Post-partum phase

Regular review of asthma is recommended following delivery.<sup>10</sup> If a woman's asthma has worsened during pregnancy, it is less likely to be a problem after birth and usually returns to her

pre-pregnant level of severity within 3 months of delivery.<sup>4</sup>

Advice about primary prevention measures should be given if there is a strong genetic predisposition to atopic disease, as outlined below.<sup>10</sup>

- **A smoke-free environment should be recommended for all children.** Exposure to smoke appears to be an independent risk factor for allergic sensitisation,<sup>24</sup> while avoiding environmental tobacco smoke may reduce the risk of childhood asthma.<sup>10</sup>
- **Breastfeeding should be recommended.** Breastfeeding might lower asthma risk during early childhood, especially in children with a family history of atopy.<sup>25</sup> Australian data suggest that the introduction of milk other than breast milk before age 4 months increases the risk of asthma, wheezing and atopy.<sup>26</sup> However, data on breastfeeding and asthma risk are conflicting. If breastfeeding is not possible, infant feeding with hydrolysed milk formulae may slightly lower the risk of childhood allergy, wheezing and asthma, compared with use of other formulae.<sup>10</sup>

Current evidence suggests that the following measures **do not** protect against childhood asthma:<sup>10</sup>

- infant feeding with soy formulae
- omega-3 fatty acid supplementation of infant feeds
- avoidance of commonly allergenic foods during pregnancy or lactation
- measures to reduce exposure to dust mite – multifaceted environmental controls that include allergen avoidance, undertaken during infancy, may reduce asthma symptoms in young children, but have no effect on lung function or bronchial hyperresponsiveness
- long-term treatment with antihistamines.

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