

Asthma, Allergic and Immunologic Diseases During Pregnancy

A Guide to Management

Jennifer A. Namazy

Michael Schatz

Editors



Springer

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Preface

The management of the pregnant allergic patient presents a challenge to the attending physician. It is a barbed challenge replete with therapeutic pitfalls and dangers strewn all along the way from early pregnancy through childbirth...

– Angelo Maietta, MD, FACA, *Annals of Allergy* 1955

More than 60 years later, this statement is still relevant. The “therapeutic pitfalls” exist because many of the commonly used medications have very little human safety data. The “dangers strewn along the way” today consist of fear of possible adverse outcomes to mother and baby from medications or the disease themselves. This “phobia” of medication use during pregnancy has led many women and clinicians to discontinue much needed medications during pregnancy. And, despite this, over the last three decades, first-trimester use of medications by pregnant patients has increased more than 60% [1].

We hope this book will provide primary care providers and specialists with a common understanding of asthma, allergic, and immunologic diseases during pregnancy. With a general understanding of allergic disease, providers may perform adequate preconception planning, manage patients effectively, and consult with specialists when needed.

This book brings together world-renowned experts with a broad spectrum of clinical experience and research interests to provide the reader with a comprehensive review of asthma, allergic, and immunologic diseases during pregnancy. Drs. Woessner and Brauer begin the book with an overview of nonpharmacologic management of allergic diseases during pregnancy, particularly of respiratory conditions. Next is Dr. Chambers’ review of the safety of asthma and allergy medications during pregnancy. Dr. Murphy then provides an overview of the interrelationships between asthma and pregnancy followed by a summary of the management of asthma during pregnancy by Dr. Namazy. This is followed by a series of chapters devoted to the management of other specific conditions during pregnancy: rhinitis and sinusitis by Drs. Carroll, Bulkhi, and Lockey; anaphylaxis by Dr. Calabria; atopic and contact dermatitis by Drs. Fonacier and Mawhirt; urticaria and angioedema by Drs. Joshi and Khan; hereditary angioedema by Drs. Zuraw and Christiansen; drug allergy by Dr. Macy; and primary immunodeficiency by

Drs. Kakkar and Hajjar. These chapters are followed by a discussion of the obstetric management of high-risk allergic patients by Dr. Dombrowski. Finally, Dr. Leonard provides a chapter on the prevention of asthma and allergic diseases during childhood.

And let us remember the additional wise words of Dr. Maietta, “The allergic expectant mother may be fearful lest her allergic symptoms disrupt pregnancy or the pregnancy aggravate her allergy. These emotional reactions should be understood and treated continuously with cheerful reassurance....” We hope that this book will give readers confidence in their gestational management such that they can provide optimal care as well as this needed “reassurance.”

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Contents

1	Non-pharmacologic Aspects of Management: “Asthma and Allergic and Immunologic Diseases During Pregnancy – A Guide to Management”	1
	David Lawrence Brauer and Katharine Margaret Woessner	
2	Safety of Asthma and Allergy Medications During Pregnancy	15
	Christina Chambers	
3	Asthma: Interrelationships with Pregnancy	29
	Vanessa E. Murphy, Megan E. Jensen, Linda E. Campbell, and Peter G. Gibson	
4	Asthma: Management	47
	Jennifer A. Namazy	
5	Rhinitis and Sinusitis	61
	Michael P. Carroll Jr., Adeeb A. Bulkhi, and Richard F. Lockey	
6	Anaphylaxis in Pregnancy	87
	Christopher W. Calabria and Christopher A. Coop	
7	Atopic Dermatitis and Allergic Contact Dermatitis in Pregnancy	101
	Stephanie L. Mawhirt and Luz Fonacier	
8	Urticaria and Angioedema	123
	Shyam R. Joshi and David A. Khan	
9	Hereditary Angioedema	141
	Bruce L. Zuraw and Sandra C. Christiansen	
10	Drug Hypersensitivity	157
	Eric Macy	
11	Primary Immunodeficiencies in Pregnancy	175
	Ekta Kakkar and Joud Hajjar	

12 Obstetric Management of High-Risk Asthmatic, Allergic Patients and Anaphylaxis 193
Mitchell Dombrowski

13 Prevention of Asthma and Allergic Diseases During Childhood 203
Stephanie A. Leonard

Index 243

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Chapter 1

Non-pharmacologic Aspects of Management: “Asthma and Allergic and Immunologic Diseases During Pregnancy – A Guide to Management”



David Lawrence Brauer and Katharine Margaret Woessner

Introduction

Pregnancy represents a unique physiologic state that makes management of chronic disease more challenging, particularly when considering use of pharmacologic therapies in the context of risk for possible teratogenicity and poor maternal-fetal outcomes [1]. Allergic diseases are among the most commonly encountered disorders affecting 18–30% of women in the United States during their childbearing years, with asthma and allergic rhinitis being the most common [2]. Allergic rhinitis, asthma, and atopic dermatitis represent the three main allergic disease states that can be expected to be encountered during pregnancy. Non-pharmacologic approaches to the management of atopic disorders in pregnancy need to be a key part of any disease state management plan. This need is the greatest during the first trimester. This chapter focuses on effective avoidance strategies and other non-pharmacologic approaches to the management of common allergic disease in the pregnant patient, allowing for better outcomes while at the same time limiting exposure to unnecessary medical therapy.

Allergic Rhinitis

Nasal symptoms are common in the pregnant population, occurring in about 30% of pregnant women. Apart from pre-existing conditions, hormones associated with pregnancy can affect nasal blood flow and local mucus glands leading to either the

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appearance of previously nonexistent symptoms or worsening of pre-existing nasal disease. Among the etiologies responsible for nasal symptoms during pregnancy, allergic rhinitis, vasomotor (non-allergic) rhinitis, sinusitis, and rhinitis medicamentosa are the most common that require treatment. The course of pre-existing allergic rhinitis during pregnancy is somewhat unpredictable and unique to each individual patient. Allergic rhinitis that has existed prior to pregnancy is known to improve, worsen, or remain stable during pregnancy [2]. Allergic rhinitis typically presents in patients with prominent nasal and ocular symptoms, such as rhinorrhea, nasal pruritus, sneezing, ocular pruritus, and ocular irritation. Allergic rhinitis can be commonly triggered by environmental factors such as pollens, dust mites, molds, and animal dander. As such, avoidance of allergens is a key modality of treatment in patients with allergic rhinitis. Although allergy skin testing can be beneficial for identifying causative allergens, due to the very small risk of systemic reaction, skin prick testing should be avoided during pregnancy. Serum IgE testing for environmental allergens is now widely available and represents a safer alternative for evaluation of causative allergens in pregnant women [3].

Asthma

Asthma typically can present with symptoms such as shortness of breath, wheezing, cough, and chest tightness. Confirmation of the diagnosis is ideally made through demonstrating evidence of reversible airway obstruction, which can be quantified by spirometry or pulmonary function testing that shows a forced expiratory volume in 1 s (FEV1) increase of greater than or equal to 12% after inhalation of a short-acting bronchodilator such as albuterol. An elevated fraction of exhaled nitric oxide (FeNO) can also be suggestive of the diagnosis in the right clinical context. Although in nonpregnant patients, a methacholine challenge test can be used to establish the diagnosis of asthma, this is not recommended in pregnant women [3]. Similarly, patients with asthma have improvement, worsening, or unchanged severity of disease during pregnancy, with each possibility occurring in approximately one third of patients. In regard to asthma, it is vitally important to maintain optimal management during pregnancy, as poor asthma control can be associated with premature birth, preeclampsia, low birth weight, and neonatal and maternal hypoxia [2, 4].

Atopic Dermatitis

Atopic dermatitis is a multifaceted disease involving a spectrum of skin barrier dysfunction, skin dryness, inflammation, and pruritus. The onset is typically early in life and is thought to often represent the first step in the “atopic march” followed in many cases by food allergy, asthma, and allergic rhinitis. Although there is an allergic and

inflammatory component to atopic dermatitis, epidermal skin barrier dysfunction is thought to represent the primary pathologic mechanism [5]. The treatment of atopic dermatitis in both pregnant patients and the general population is cutaneous hydration and use of emollients. Adequate cutaneous hydration and use of emollients can help protect and restore the barrier of the stratum corneum and thus decrease the need for additional therapy. It is recommended for patients to take soaking baths that are lukewarm for a minimum of 20 min, to be immediately followed by application of occlusive emollient, which can both help retain moisture and decrease symptoms. Effective emollients such as petrolatum can be found in a variety of moisturizing agents, with thicker ointments and higher concentrations of petrolatum likely to provide more significant improvement. For atopic dermatitis lesions that are not improving with therapy, the use of wet dressings can also be employed. For patients who are pregnant, bathing should be restricted to only once per day, consisting of warm or cool water, and when possible, it is recommended that soap be restricted to the scalp, feet, armpits, and groin and that brushes or washcloths not be used. The use of a non-soap cleanser may prove less damaging to the skin barrier. After the patient has rinsed, skin should be dried by patting, and then immediately an emollient should be applied. All of these interventions are safe to perform during normal pregnancy. Due to the skin barrier dysfunction and skin fissuring that results in atopic dermatitis, the skin can develop small passages via which allergens may enter and thus worsen inflammation [6]. As such, the avoidance of plant- or biologic-based products to the skin is advised. Allergen avoidance as discussed below can play an important role in the management of atopic dermatitis as well.

Allergen Avoidance Measures (Table 1.1)

In general, the initial non-pharmacologic treatment approach for allergic rhinitis, asthma, and atopic dermatitis in pregnancy does not differ from that in nonpregnant patients. The avoidance of known irritants and allergens is a cornerstone of allergic rhinitis and allergic asthma therapeutic strategy and should be recommended to all patients first [2]. In the following sections, many of the major allergens and appropriate avoidance measures will be described.

Table 1.1 Allergen avoidance measures summary

Allergen	Avoidance measures
Pet dander	Pet removal, limited avoidance, frequent pet washing, HEPA filters
Mouse/cockroach	Integrated pest management
Mold	Mold removal, water leak repair, improved ventilation
House dust mites	Dust mite pillow/mattress covers, frequent vacuuming, minimize carpet in home, HEPA filters

Pet Dander Allergens

Pregnant patients with known pet dander sensitivity should be advised that removal of the pet from the environment is the most effective environment control measure. In particular, dogs and cats are significant indoor allergen sources common to many allergic patients. *Fel d1* (*Felis domesticus* allergen 1) is an important cat allergen and is carried through the air in particles greater than 2.5 μ in size. *Fel d1* is known to stay airborne for significantly extended periods of time. The major allergenic dog proteins, *Can f1* and *Can f2* (*Canis familiaris* allergens 1 and 2), are similar although not as persistent in the air as those from cats. Both cat and dog allergens are found in their excretions and secretions and on their dander [7]. In a study looking at 20 patients with allergic asthma and pet sensitivity, of the patients who removed their pet and then were followed up at 1 year, none of these patients required inhaled corticosteroids, as opposed to 9/10 of the patients who retained their pets in the control group [8]. In many cases, complete removal of the pet is either impractical or undesired. Clinicians often recommend frequent washing of cats and dogs in an effort to reduce pet dander allergen levels in the home and thus also decrease allergic rhinitis symptoms. It has been demonstrated that the level of *Can f1* in the home as well as on the dog themselves and their dander can be decreased significantly with at least twice per week shampooing and blow drying of the dog. It has been shown that *Can f1* levels return to prewashed levels within a 3–4-day period [9]. In regard to cats, it has been demonstrated that washing cats weekly results in a limited decrease of *Fel d1* both in the patient's home and on the cat, in particular after 1 week [10]. Considering the difficult nature of frequently washing animals, this strategy has not found widespread acceptance [11]. More likely to be successful in some instances would be a strategy of limited avoidance, such as ensuring the patient's pet be limited to the outdoor area of the home or at least restricted from entering the patient's bedroom. The use of air purifiers with high-efficiency particulate air filters (HEPA filters) in the management of animal dander allergy is discussed below.

Mouse and Cockroach Allergens

In regard to pest allergens, such as mouse and cockroach which are especially problematic in low-income and urban environments, environmental non-pharmacologic control measures are also of significant importance [11]. For mouse allergen exposure, studies have typically employed the use of integrated pest management to reduce the concentration of mouse allergen. Integrated pest management (IPM) involves an approach consisting of a multifaceted intervention, which includes the sealing up of cracks and holes in the home, the setting of mouse traps, the meticulous disposal of food, intensive cleaning procedures, and, when required, the use of rodenticide. The studies that have looked at IPM had

used a variety of approaches ranging from providing education regarding IPM strategy to the actual professional implementation of these interventions [12]. It has been shown that a reduction in mouse allergen of at least 50–75% in the home is directly linked to significant improvements in clinical asthma outcomes [13–15]. Some of these studies have also shown that professionally performed IPM has led to a reduction in home mice allergen concentrations of 70–75%, while one study showed that a comparable reduction was achieved with the provision of IPM education to patients alone. However, it should be noted that a second study only showed minimal change in mouse allergen concentration when looking at IPM education-only interventions compared to controls [13–16]. As such, it appears that professionally delivered IPM interventions are effective at achieving clinically relevant reductions in mouse allergen concentration levels in the home; however the efficacy of IPM education-only interventions for patients has yet to be definitively proven as reliable [11]. For pregnant patients with known mouse sensitivity and concurrent allergic rhinitis and/or asthma, IPM education or the recommendation to obtain professionally delivered IPM interventions, when necessary, is highly advisable.

Similar to mouse allergen environmental control measures, for patients sensitized and exposed in the home to cockroach allergen, integrated pest management (IPM) strategies are often employed as well. Although there are over 4500 cockroach species, only four are indoor pests, *Periplaneta americana*, *Blatta orientalis*, *Blattella germanica*, and *Supella longipalpa*, with the major allergens being *Bla g1*, *Bla g2*, and *Per a1* [7]. As with mouse allergen strategies, cockroach IPM consists of a multifaceted interventional approach that can include the sealing of holes and cracks in the home, the use of pesticide, intensive cleaning targeted at reducing the reservoir of cockroach allergen, and disposal of food in a meticulous manner. These interventions have been demonstrated to provide a significant decrease in home cockroach allergen level compared to controls in the homes of children with asthma in urban, low-income areas. In fact, it has been shown that the levels of cockroach allergen can be decreased significantly by 80–90% using IPM strategies [17–21]. Furthermore, there has been demonstrated clinical benefit correlated to reduced cockroach allergen exposure in the home, with data showing a clinical benefit when a reduction of at least 50–90% in either allergen concentration of cockroach or mean number of trapped cockroaches was achieved [19, 22]. There is also a suggested clinical benefit observed in children with asthma but without cockroach sensitivity, who are exposed to cockroach allergen in their home environment. However, the benefit is not as pronounced as shown in children who are cockroach allergen sensitive [22]. Thus, as with mouse allergen exposure, it can be extrapolated that IPM should be part of the comprehensive management strategy advised to cockroach-sensitive pregnant patients affected by allergic rhinitis and/or asthma. Insecticide sprays should not be used, either by the patient themselves or by professional IPM services, in an effort to avoid the irritant effects of these chemical aerosolized compounds which can exacerbate airway disease [11].

Other Animal Allergens

Other animals, such as horses, birds, and rabbits, are also common allergens that can exacerbate patient symptoms. The major allergen from horses, *Equ c1*, has been found in horse salivary glands, urine, and dander [23]. Although there is very little research performed looking at bird sensitization, a recent study showed bird sensitization to be lower than that found to a dog or cat, possibly due to the smaller number of pet birds [24]. Other smaller pets that are furry, such as hamsters, rabbits, and guinea pigs, have become more commonplace in recent decades, with upwards of 5% of households in the United States and Europe having a small furry pet. However, quantitative measurements of these allergens in house dust are suboptimal [23]. As with other animal allergens, avoidance measures are advised for sensitized and symptomatic patients.

Mold

Asthma morbidity has been linked with mold and/or damp home environments in multiple studies [25–27]. Mold is known to become problematic in home environments affected by an excess of moisture. Moisture excess can be secondary to a number of factors, including ventilation problems, intrusion of water, plumbing problems, and other structural issues. It has been demonstrated that levels of carbon dioxide correlate with fungal allergen concentration, supporting the concept that ventilation deficiencies promote mold growth. Mold allergen concentrations are most elevated in ambient temperatures ranging from 20 to 22.5 °C [28]. The allergenic fungi that are most studied are *Aspergillus*, *Alternaria*, *Penicillium*, *Fusarium*, *Cladosporium*, and *Epicoccum* [7]. It has been shown that asthma outcomes improve following mold and dampness remediation interventions. These interventions include a variety of approaches: stopping intrusion of rainwater, removing mold from surfaces, repairing leaks in plumbing, and installing proper ventilation. These interventions have been demonstrated in studies to improve asthma outcomes, including decreased medication use, less symptom days, and decreased utilization of health-care resources [29–31]. Respiratory symptom risk and exposure to mold are associated, whether the patient has mold allergen sensitization or not. Fungal allergen sensitization is thought to increase the morbidity risk [32, 33]. It is recommended that patients with mold sensitization and allergic asthma use a central heating, ventilation, and air conditioner (HVAC) system with appropriately changed filters in an effort to reduce the movement of fungal spores from the outdoors to inside the home. When employing mold remediation, it is recommended by the National Institute of Occupational Safety and Health to use at least an N-95 mask during removal of visible mold due to the risk of aerosolized particulates [11]. Thus, for patients with allergic rhinitis and known mold sensitization, or for patients with allergic asthma regardless of mold sensitization, it is advisable to enact mold

remediation measures for a home environment known to be susceptible to significant mold colonization.

House Dust Mites

House dust mites are ubiquitous in many environments around the world. The principal allergen is derived from the mite feces, which are typically 20–30 μ in diameter, with the major mite species being *Euroglyphus* and *Dermatophagoides*. Dust mites are especially prevalent in warm (greater than 20 °C), humid, and dark environments, such as pillows, mattresses, stuffed animals, and carpets [7, 34]. In patients with known house dust mite sensitivity and related symptoms, environmental control measures are both commonplace and highly recommended. Interventions focused on the bedroom, due to the large percentage of time spent there, are typically emphasized [34]. The encasement of the mattress and pillows in a finely woven fabric capable of preventing dust mite feces passage is the primary intervention. It is also recommended that bedding be washed in warm or hot water on a regular basis, and it is known that if a clothing dryer is used, virtually all dust mites are killed [35–37]. Dust mite growth is well known to be facilitated by humid environments. Although it is understood that relative humidity level thresholds of 45–50% are usually needed to achieve control, trials investigating dehumidification have shown mixed results, possibly due to the fact that even a short period of higher humidity can be enough to allow reproduction and survival of house dust mites [38–40]. In regard to carpets and upholstery, it is recommended that for dust mite-allergic patients, the amount of carpet in the home be minimized and that carpet be regularly vacuumed, cleaned, and sun dried if possible. Furthermore, if high humidity is difficult to control, it is suggested to avoid upholstered material as much as possible [34]. Activities such as vacuuming and manipulating bedding, furniture, or other materials known to harbor dust mites can disturb the allergen and cause it to become airborne [41]. It is advisable that vacuuming be performed by a person other than the dust mite-allergic patient if possible.

High-Efficiency Particulate Air Filters

Another strategy considered by many patients is the use of air filters. Many different types of air filters exist, with the most highly recommended being the high-efficiency particulate air filters (HEPA filters). Other types of air filters, such as electrostatic precipitators and ionizers, function by electrically charging air particles in order to remove them. However, it is known that these devices emit ozone and as such should be avoided [42]. When considered for cases of known pet-allergic patients, it has been shown that HEPA filters have led to about a 30–40% decrease in cat allergen that is airborne when compared to placebo filters. However, it does not appear that

HEPA filters seem to significantly affect settled pet allergen dust levels, and most importantly, the use of these filters does not seem to significantly improve either allergic rhinitis or asthma symptoms [43, 44]. In fact, it is known that cat allergen in particular can be found in homes long after the cat has been removed, due to the allergen's inherent adherent nature. Despite these findings, a single study did show that the combined practice of frequent vacuuming in conjunction with the use of HEPA filters that were free-standing and placed in multiple rooms in the home did have an association with asthma outcome improvement, even though there was only minimal change in the actual levels of settled dust allergen [45]. As such, it is possible that the combination of high-efficiency particulate air filters in conjunction with other environmental controls such as vacuuming to reduce settled dust allergen may have a clinical benefit in both allergic rhinitis and asthmatic pregnant patients with known pet dander-allergic sensitivity; however to date there does not seem to exist overwhelming evidence to support this supposition.

In regard to the use of HEPA filters to decrease house dust mite allergens, a previous 8-week randomized double-blinded study examined the potential of these filters to reduce bedroom particulates, symptoms, and medication use in patients who had known sensitivity to house dust mites. The study did demonstrate that HEPA filters did in fact reduce bedroom particulates; unfortunately the improvement in the patient's symptoms was minimal [46]. These findings in part could be due to the fact that dust mite allergen is typically not airborne unless disturbed. However, another study that was also randomized, double-blinded, and placebo-controlled looked at patients with a history of allergic rhinoconjunctivitis and a known allergic sensitivity to dog, cat, or house dust mite. In the study, the combined uses of HEPA filter in the patient's bedroom along with dust mite bed pillow barrier encasings demonstrated a significantly decreased level of bedroom dust particles compared to placebo. In addition, there was a significant improvement in ocular and nasal symptoms at nighttime in the patient group receiving the combined environmental interventions; however it should be noted that daytime symptoms did not improve in this patient group [47]. Altogether this suggests that the benefit of high-efficiency particulate air filters in allergic rhinitis and/or asthmatic patients is best realized in combination with other environmental control measures.

Allergen Immunotherapy

Apart from other non-pharmacologic interventions, desensitization of allergic disease utilizing allergen immunotherapy also has a proper role in the treatment of allergic rhinitis and allergic asthma during pregnancy. Subcutaneous immunotherapy (also known as "allergy shots") has been used for treatment of allergic disease for approximately 100 years and has been shown to be highly effective for allergic rhinitis, allergic asthma, and insect venom allergies. Subcutaneous immunotherapy consists of a series of subcutaneous injections with known environmental or venom allergens, initially starting with increasing dosages until a maintenance dose is

achieved. The maintenance dose can be continued for several years or indefinitely, depending on the patient and the particular allergens. Previous studies have demonstrated the safety of continuing subcutaneous immunotherapy during pregnancy. The first study published by Metzger et al. in 1978 demonstrated that out of a total of 121 pregnancies, no significant change in prematurity, hypertension, congenital malformations, or proteinuria was demonstrated. Also, no abnormal births were found to result from the seven generalized reactions that occurred [48]. The safety of continuing immunotherapy was further verified by a retrospective study published in 1993. With this study, the incidence of proteinuria, HTN, and prematurity was actually lower for the group of women continuing subcutaneous immunotherapy, and no birth complications were observed with the three patients who experienced systemic reactions [49, 50]. In many patients, subcutaneous immunotherapy results in sustained desensitization to the allergens, even after discontinuation of immunotherapy. More recently, the use of sublingual immunotherapy (grass, ragweed, or dust mite tablets dissolved daily under the tongue) has entered mainstream practice as an alternative in some instances as well. The safety of sublingual immunotherapy has been previously investigated, with a study of 155 patients during 185 pregnancies receiving sublingual immunotherapy with dust mite or a five allergen mixture, with 6-year follow-up demonstrating no systemic reactions in the sublingual immunotherapy patients, with only local reactions observed versus the control arms. Twenty-four of these patients were started on sublingual immunotherapy during pregnancy for the first time. Thus, the safety of sublingual immunotherapy has been suggested both for patients previously on sublingual immunotherapy before pregnancy and for those initiating sublingual immunotherapy during pregnancy [51].

Thus, pregnant patients who were previously on stable subcutaneous immunotherapy without significant complications can safely continue on immunotherapy maintenance dosing throughout their pregnancy. For women of childbearing age, the consideration for starting subcutaneous immunotherapy prior to pregnancy may be a wise proactive choice in some instances to avoid the need for medication during pregnancy, especially in allergic asthmatics. However, subcutaneous immunotherapy should not be initiated during pregnancy, and dosages should not increase during pregnancy due to the possibility of systemic reactions. In the event a patient becomes pregnant during the low-dose buildup phase of subcutaneous immunotherapy, injections should be discontinued. An unusual exception may be for the patient with a history of anaphylaxis secondary to venom hypersensitivity and an ongoing risk of exposure [2].

Irritant Exposures

Tobacco smoking is a well-established risk factor for a multitude of diseases in the worldwide general population. In pregnancy, smoking also has a wide variety of negative impacts on both maternal and fetal health, including in asthmatic pregnant

patients. Smoking has been associated with worsened asthma medication requirements and also decreased asthma pharmacologic therapy response. A recent study demonstrated that the relative risk of an asthma exacerbation during pregnancy was significantly higher in current and former smokers when compared to never-smokers, and it also showed that even never-smokers who had only passive exposure to tobacco had a significantly increased risk of asthma exacerbation during pregnancy [47]. The study reported that never-smokers who had passive exposure to tobacco had a significantly lower FEV1% predicted, when compared to patients who were never-smokers and did not have passive exposure to tobacco. Since it is known that asthma exacerbations are linked to an increased risk of poor pregnancy outcomes, it is absolutely critical that pregnant women be advised to stop smoking immediately and avoid exposure to secondhand smoke [52]. Furthermore, a correlation between smoke exposure in utero or in infancy and the childhood development of rhinitis and asthma has been established [53]. Beyond tobacco smoke, mothers with asthmatic disease should also avoid other potential irritants, such as pollutants and other noxious chemicals, as much as possible due to their potential to lead to exacerbations of disease [2].

Other Non-pharmacologic Approaches in Asthma and Allergic Rhinitis

A recent review of other non-pharmacologic approaches to asthma treatment in pregnancy evaluated the efficacy of certain approaches, such as education, a fraction of exhaled nitric oxide (FeNO)-based treatment algorithm, and progressive muscle relaxation (the deliberate application of tension to particular muscle groups followed by release of that tension), which did demonstrate some beneficial effects for management of asthma in pregnancy. However, the review in the end emphasized that no firm conclusions were able to be established regarding the true benefit of these approaches due to various limitations in prior studies [54]. Other non-pharmacologic approaches for improving asthma symptoms may also include stress reduction management and breathing exercises, as asthma symptoms can be worsened by psychological stress factors. Breathing exercises that have been previously suggested involve the use of breathing patterns that reduce hyperventilation as well as hyperinflation, thus leading to a normalization of carbon dioxide levels and theoretically then reducing the sensation of breathlessness and bronchospasm. However, when examined previously in children with asthma, clear evidence for its effectiveness has not been demonstrated [55]. In regard to psychological stress factors and asthma, appropriate psychiatric evaluation should be obtained for pregnant patients with asthma presenting with concurrent psychiatric illness, and for patients with stress-related symptoms, appropriate stress reduction measures should be considered.

For allergic rhinitis, the use of saline rinses can facilitate mucous passage and reduce nasal congestion in some patients. Also, the use of external nasal strips may

help relieve nasal passage obstruction in some cases. For the treatment of allergic disease and asthma, although some patients may consider the use of probiotics as a supplement to standard medical care, there are no studies in pregnant women that show a therapeutic benefit for probiotics in regard to allergic sensitization, asthma, or atopic dermatitis. Furthermore, at this time there are no society recommendations supporting the use of probiotics to treat allergic manifestations or asthma [56, 57]. In regard to other nontraditional interventions such as acupuncture, no studies to date have been performed to evaluate the effects of acupuncture on allergic disease or asthma in the pregnant patient.

Conclusion

The approach to the non-pharmacologic treatment of allergic diseases in pregnancy closely reflects the non-pharmacologic approach to management of these conditions in the general population. In the pregnant patient, the importance of avoiding unnecessary medical therapy is of the utmost importance due to concerns of the effects of pharmacologic therapy on fetal health. It is strongly recommended to maximize non-pharmacologic approaches as appropriate in an effort to minimize pharmacologic interventions. In some instances, adequate relief may be achieved solely with non-pharmacologic interventions, and in many cases, the need for pharmacologic therapy can be reduced by concurrent use of non-pharmacologic approaches. At all times, it is critically important to appropriately ensure the well-being of both mother and baby. Due to the strong influence of the environment on allergic disease, environmental control measures and non-pharmacologic therapies can have a large impact on disease severity and patient symptoms in both a safe and effective manner.

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Chapter 2

Safety of Asthma and Allergy Medications During Pregnancy



Christina Chambers

Introduction

Asthma and allergy are among the most common conditions in women of reproductive age. Allergic diseases are thought to be present in approximately 20% of women who are in their childbearing years. Data also suggest that at least 8% of pregnant women have a current diagnosis of asthma and that the prevalence of asthma in pregnant women and women of reproductive age appears to be increasing [1, 2].

Maternal asthma itself, and in particular poorly controlled asthma, has been associated in some studies with increased risks of adverse pregnancy outcomes including spontaneous abortion, stillbirth, major birth defects, preeclampsia, pre-term delivery, and infants who are small for gestational age [3, 4]. While approximately one-third of asthmatic women will experience remission or reduction in asthma symptoms during pregnancy, at least one-third are likely to have symptoms worsen over the course of gestation. Data suggest that continued and appropriate management of asthma throughout pregnancy results in optimal outcomes for both mother and infant [5].

Appropriate management of asthma and allergy in pregnancy requires adequate information on the safety and/or risks associated with specific treatments for the developing fetus. This information is essential for the prescribing clinician but also important for the pregnant woman. In the absence of strong and reassuring evidence on the safety of specific medication treatments, women may avoid needed medication or undertreat symptoms against advice due to fear of harming the pregnancy [6].

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Guidelines for asthma and allergy treatment are provided by professional practice groups and in general suggest that pregnant women should be treated the same as nonpregnant women [7]. However, the quantity and quality of human safety data for some specific medications can help inform treatment choices within those guidelines.

In this chapter, four topics will be reviewed: (1) current methods for studying medication safety in pregnancy and the strengths and weaknesses of each of these approaches, (2) the current level of safety data for selected commonly used medications to treat asthma and allergy conditions in women of reproductive age, (3) an overview of the changes to the pregnancy label section of the package insert for pharmaceutical products marketed in the USA and how these changes are being implemented, and (4) a list of resources that clinicians and their patients can use for current pregnancy safety data.

Approaches to Studying Medication Safety in Pregnancy

The goal of pregnancy safety studies is to rule out, with a reasonable level of confidence, that a medication is a human teratogen, i.e., is causally related to adverse pregnancy outcomes including major birth defects in the prenatally exposed infant. Typically, known human teratogens, such as thalidomide, are associated with increased risks for patterns of adverse outcomes including clusters of specific birth defects.

Many human teratogens have been identified through a series of case reports linking prenatal use of a specific drug to an unusual birth outcome. However, observational studies are needed to demonstrate that the association is not coincidental (e.g., above the background risk of 3–5% for major birth defects) and to better understand the magnitude of the risk and critical period of susceptibility to that exposure in pregnancy. Observational studies are the primary source of safety data that guide clinical practice in pregnancy, as randomized clinical trials in pregnant women to evaluate medication safety are rarely conducted for ethical reasons. Currently in the USA, there is no universal systematic method for evaluating pregnancy safety for pharmaceuticals. Individual studies are conducted as required by regulatory authorities or as initiated by investigators.

There are four general observational study designs currently used for medication safety studies in pregnancy: pregnancy registry, cohort, case-control, and database/claims data studies. Pregnancy registries represent prospectively collected exposure and outcome data for a series of pregnancies exposed to a specific medication. Registries are often the first source of data available for a new drug. These studies are usually too small to detect anything but large effects for rare outcomes, such as specific major birth defects, but can identify early