

Allergies and Adolescents

Transitioning Towards
Independent Living

David R. Stukus
Editor



Springer

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I would like to thank all of my adolescent patients and their families for their knowledge and insight; this book is a testament to how each of you successfully navigates every day.

Special thanks to Lee Budin, MD, for showing me the importance of questioning old mantras, to David Lang, MD, for instilling in me the importance of using evidence to base our decisions, and to Bryan Martin, DO, for inspiring me to pursue endeavors both challenging and worthwhile.

Finally, none of this would be possible without the never-ending love and support of my wife, Kristin, and our children, Jackson and Harper.

Foreword

Adolescence is a time of travel during which children stretch across the borders of their childhood, gain insights from irreverent and novel sources, and dip their toes in new waters. Teens gradually come to rely more upon themselves than ever before. It is therefore a time of differing risk not only for teens with life-threatening conditions, like food allergy-provoked anaphylaxis, but also for children with conditions that at first glance are seemingly benign, such as allergic rhinitis. Because the traverse of the teenage years comes with elevated risk, it is an obvious time of terror for those who care deeply about the well-being of a teen they love. This includes friends and family, but also physicians, nurses, and care teams who work hard to ensure a child thrives as that child emancipates out of childhood.

We all want adolescence to go so very well, but there are successes and failures as teens navigate their worlds and the elevated stakes. No longer are the risks a skinned knee, and no longer do children defer their environment and choices to their protective parents. Teens with allergic conditions have unique healthcare needs, and unique consequences occur when they are not included in their own care and not empowered to protect themselves.

The beauty here is that pediatric care teams and parents can help identify ways to enhance a teen's experience, knowledge, and know-how. This collection of evidence, wisdom, and practice advice can help you help an adolescent thrive.

All transitions in life come with a bit of heartache, just as all hand-offs in and out of the hospital come with risk. As teens' needs in their care change, as puberty takes hold, as sleep timing and sleep needs shift, as moods become more labile, as risk-taking advances, and as allergic symptoms morph, there are specific interventions—and noninterventions—that may not only improve the quality of life for a teen with allergies but also allow for a sense of control and an opportunity for a higher quality of care.

This collection of words and data, expertise, and insight proves a hearty tool with which to understand the unique opportunity we have with teens who have allergies. The overlay of depression, tobacco use, driving, sports involvement, and psychosocial stresses and demands of school during the teen years all deserve specific attention and care. Data supporting the “growing out of” and the “not growing out of”

allergies can help pediatric care teams and families surround a teen with bolsters of support.

The twenty-first century has offered a new medium for medicine. I see this optimistically. More than ever before, teens, parents, and clinical teams are learning about their health and about themselves online. We share and connect and learn now in novel ways from apps, online educational sites like FARE, teen-targeted media, social and traditional media, and content that arrive on our virtual doorstep every day.

Dr. David Stukus leads the way here for children, teens, and their families partnering in health care and wrestling with allergic conditions. Through his myth-busting and dedication to providing accurate information online and on Twitter to his illuminating the research specific to adolescence in this book, we are all afforded a new opportunity to do better.

May these words here and the research, experience, and expertise that brought them together reduce suffering for those you love and those for whom you care. I do not think adolescence will ever feel *steady* per se, but I am certain the knowledge housed here can help reduce the unease we all feel while supporting teens amid it.

Wendy Sue Swanson
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Preface

All adolescents face unique challenges when they leave home for the first time. Whether attending college or joining the work force, living independently can be a daunting task. Learning how to cook, do laundry, and manage a busy schedule constitute enough new “real life” experiences for the average teenager. Now imagine also being responsible for taking medications consistently, arranging medical appointments, and managing acute illness. This is difficult for most adults to manage, let alone adolescents learning how to juggle all the other aspects of living independently for the first time.

As a practicing allergist for the past 10 years, I have cared for thousands of patients with asthma, allergic rhinitis, eczema, food allergy, and immune deficiency. These are all chronic conditions that patients must learn to live with daily. As a pediatrician, I also help parents navigate the nuances of caring for children of various ages. Successful management strategies for toddlers are vastly different from those that apply to children in grade school and even more challenging in teenagers.

Unfortunately, there are very few, if any, evidence-based resources readily available for teenagers with allergic conditions and their parents to reference to as they prepare for leaving home. In addition, primary care providers and specialists caring for adolescents are rarely provided education regarding this topic and thus are often unprepared to help their patients transition to independence. My experiences in working with these families along with the lack of resources and research in this area inspired the development of this book.

Throughout this book, readers will learn about factors that are unique to the normal cognitive and social development of adolescents as well as be exposed to effective strategies for involving them in their own self-management. The many faces of nonadherence will be discussed in detail, including specific aspects pertaining to adolescents. Allergic rhinitis, asthma, food allergy, and eczema each have a chapter devoted to an in-depth discussion of basic concepts surrounding diagnosis and management; each of these chapters is then followed by a separate chapter providing details as to how that condition can specifically impact adolescents. Finally, the last

chapters of the book aim to provide practical tips that can be immediately implemented by adolescents and their families as well as clinicians.

The authors of each chapter are all experts within their respective fields and have graciously devoted their time to provide invaluable contributions. In addition, several of the authors are accomplished researchers, and all have experience working with adolescents. Throughout this book, the collective knowledge and understanding of our authors have been eloquently translated into a discussion written at a level that any reader can understand. References are provided throughout for those who desire more in-depth discussion of key topics.

This book was specifically designed for multiple audiences with varying levels of knowledge, and each chapter can also stand alone as its own text. Any healthcare provider who treats adolescents (especially adolescents with allergic conditions) will learn a comprehensive approach not available elsewhere that will help prepare patients for independent living. In addition, adolescents themselves may learn about their own conditions and ways to improve their self-management. Parents, caregivers, school personnel, and family members will find these chapters useful as well.

Thank you for taking the time to read this book. If even one life is positively impacted by our work, then this undertaking will be deemed a success.

David R. Stukus
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Contents

1	The Allergy Epidemic	1
	Kathleen Grisanti and Mitchell H. Grayson	
2	Adolescent Brain Development and Implications for Adolescents with Allergies	15
	Amy Hahn and Jessica L. Hoehn	
3	How Can We Best Communicate with Adolescents?	31
	R. Claire Roden and Elise D. Berlan	
4	The Many Faces of Nonadherence in Adolescents	43
	Michael R. Gionfriddo	
5	Allergic Rhinitis	55
	Margaret Redmond	
6	Allergic Rhinitis Pertaining to Adolescents	81
	Mervat Nassef and Marc L. Rubin	
7	Asthma: A Heterogeneous and Challenging Chronic Condition	95
	David R. Stukus and William C. Anderson III	
8	Managing Adolescent Asthma: More than Just Medications	119
	William C. Anderson III	
9	Food Allergies: An Overview	137
	Jialing Jiang, Lauren M. Kao, Ozge N. Aktas, and Ruchi S. Gupta	
10	Food Allergies and the Teenager	153
	Nancy S. Rotter and Michael Pistiner	
11	Atopic Dermatitis: Overview	169
	Benjamin T. Prince and Rekha Raveendran	
12	Atopic Dermatitis Pertaining to Adolescents	187
	Rekha Raveendran and Benjamin T. Prince	

13 Other Allergic Conditions: Venom Hypersensitivity, Drug Allergy, Chronic Urticaria/Angioedema, and Primary Immune Deficiency.	203
Brian Schroer	
14 What Now? Practical Steps for Adolescents with Allergies and Asthma to Manage Their Healthcare Independently.	223
Marc L. Rubin and Mervat Nassef	
15 A Practical Approach for Clinicians to Prepare Adolescents for Independent Living.	231
Brian Schroer	
Index.	239

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Chapter 1

The Allergy Epidemic



Kathleen Grisanti and Mitchell H. Grayson

Introduction

Allergic disease encompasses a wide variety of illnesses, including, but not limited to, atopic dermatitis, food allergy, asthma, and allergic rhinoconjunctivitis; together these diseases afflict millions of people worldwide [1, 2]. The economic impact of allergic diseases is significant, costing millions of dollars in lost work productivity [1]. At an individual level, those afflicted can have decreased quality of life [3], predisposition to sinus and skin infections [4], disordered sleep [3], poor concentration at work and school, and increased healthcare utilization [3]. Two of these allergic diseases, asthma and food allergy (and resulting anaphylaxis), have the greatest risk for fatal outcomes, and the adolescent population is most at risk [4]. In addition to an increased risk of mortality, individuals with uncontrolled asthma are more likely to be unemployed; however, if they are gainfully employed, they are more likely to have lost productivity due to sick days and activity limitations at work [5]. There are ways to avoid these dire outcomes—optimal asthma control can be achieved with current therapies (see Chaps. 7 and 8 for in-depth discussion) and, in food allergy (Chaps. 9 and 10), recognizing

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and avoiding the offending allergens, as well as using epinephrine early during anaphylaxis. The fact that the medical community has the treatments and knowledge of how to prevent most of these poor outcomes underscores the importance of transferring that knowledge to patients and empowering them—specifically adolescents—in the management of asthma and other atopic conditions, so that as adults, they are unhindered by their disease. Given the current allergy epidemic—notable for the rapid rise in atopic diseases worldwide over the last 50 years—it is imperative that patients have the tools to successfully manage their atopic illnesses.

History of Atopic Disease and Prevalence Studies

We may be in the midst of an epidemic of allergic disease, but allergic diseases are not new and have been in existence for thousands of years. The first possible report of an allergic disease appeared in 2641 B.C. in ancient Egypt. Hieroglyphs decorating the tomb of Pharaoh Menes detail his death shortly after a wasp sting, raising suspicions for anaphylaxis due to venom hypersensitivity. Ancient biographical notes written by the Roman historian Suetonius during early days of the Roman Empire detailed various physical aspects and maladies of the first Roman Emperors. From these notes, it seems that Emperor Augustus (Julius Cesar's great nephew and the first Roman emperor) was afflicted with the atopic triad of asthma, atopic dermatitis, and seasonal allergic rhinitis. Two of Emperor Augustus' male relatives also had symptoms consistent with atopic disease with perennial rhinoconjunctivitis and allergy to horses. This likely represents the first documentation supporting what is a common characteristic of atopy today—the genetic predisposition to develop allergic disease [6].

While it seems allergic diseases have been around for thousands of years, the beginning of the recent surge in allergic disease appears to have begun in the late 1700s and early 1800s. In the late 1800s and early 1900s, hay and rose fever (i.e., allergic rhinoconjunctivitis) began to garner recognition. In the 1960s, asthma was not considered a common pediatric illness, but by the 1970s a noticeable increase in prevalence had occurred [7]. Today asthma is the most common noncommunicable pediatric illness [1]. Another ripple in the allergy epidemic occurred in the late 1990s with the rapid rise in food allergy prevalence [7]. Various studies support the rise in allergic disease, and below we will detail evidence supporting these various waves of allergy epidemics from population studies in both the United States and globally (see Table 1.1).

Prior to reviewing the data, it is important to understand pitfalls present in prevalence estimates from population-based surveys. The symptoms of allergic rhinitis can be indistinguishable from those of nonallergic rhinitis. The determination of allergic rhinitis is based on positive allergy testing (either skin or serum) and demonstrating that allergic sensitization correlates with clinical history. Both evidence of allergic sensitization and supporting history are needed to make an accurate diagnosis—and not all studies are designed to determine this important distinction [2]. While population surveys might overestimate the prevalence of allergic rhinitis by including patients with nonallergic rhinitis or patients with a positive skin or blood test but without a correlated clinical history, allergist diagnosed allergic rhinitis

Table 1.1 Prevalence of atopic diseases in the United States and worldwide

	United States			Worldwide	
Atopic dermatitis [9, 14]		0–17 years old			6–7 years old 13–14 years old
	1990s	7.4%		1990s	
	2010s	12.5%		2000s	0.9–22.5% 0.2–24.6%
Allergic rhinoconjunctivitis [2, 9]		4–26%			6–7 years 13–14 years
				1990s	0.8–14.1% 1.4–39.7%
				2000s	1.8–24.4% 1–45%
Asthma [9, 12, 13, 15, 16]		6–11 years	12–17 years		6–7 years 13–14 years
	1960s	5.3%	6%		
	1970s	4.8%	6%	1990s	2.3–23.1% 2.5–37.6%
	1970–1980s	7.6%	6.5%		
		>6 years		2000s	2.5–37.6% 3.4–31.2%
	2005–2006	8.8%			
		All ages			
	1970s	3%			
	1996	5.5%			
	2008	7.8%			
Food allergy [21–23]		<18 years		Australia and the United Kingdom reported 5–10% for all foods in preschool-aged children (<i>data acquired from oral food challenge</i>)	
	1997	0.4% PN ^a	0.2% TN ^b		
	2008	1.4% PN ^a	1.1% TN ^b		
	2007	3.9% reported for all foods		China reported 7%	

^aPN peanut allergy

^bTN tree nut allergy

likely underestimates prevalence, as not all people with allergic rhinitis seek out or have access to an allergist. Asthma studies suffer from these same issues. Therefore, population surveys may well overestimate prevalence, but they remain our best assessment for the overall burden of allergic diseases.

Allergic Rhinitis

The current prevalence of allergic rhinitis has been reported to be 4–26% in the United States [2], with an estimated 10–30% of the population affected worldwide [8]. The International Study of Asthma and Allergies in Childhood (ISAAC) was undertaken to establish the prevalence of allergic diseases worldwide and specifically focused on asthma, allergic rhinoconjunctivitis, and eczema in the pediatric population. The ISAAC study design relied on patient and parent symptom questionnaires to determine prevalence of disease. There are three phases of the ISAAC multi-country, cross-sectional surveys. The initial phase, ISAAC Phase One, gathered data from a total of 700,000 children across 56 different

countries to establish an initial prevalence of asthma, allergic rhinoconjunctivitis, and atopic dermatitis. ISAAC Phase Two attempted to delve into further detail, attempting to identify specific drivers of atopic disease. ISAAC Phase Three recreated Phase One after 5–10 years in an attempt to determine if prevalence was indeed rising as suspected [9].

During ISAAC Phase One, which took place from the early to mid-1990s, the prevalence of allergic rhinitis in children 6–7 years old was found to range from 0.8 to 14.9%, while in children 13–14 years old, the prevalence was 1.4–39.7%. Five years after Phase One, the Phase Three study, spanning from the late 1990s to the mid-2000s, demonstrated that the prevalence rates of allergic rhinitis had increased for both age groups: in children 6–7 years old, prevalence increased to 1.8–24.4%, and in children 13–14 years old, rates increased to 1.0–45%. This increase in prevalence of allergic rhinitis was especially marked in the younger age group [9]. This trend likely stems from a combination of predisposing genetic factors in addition to environmental influences, which are discussed later in this chapter.

Asthma

The prevalence of asthma has risen both in the United States and worldwide. Estimates are that around 300 million people globally [1, 10, 11] (4.3% of the population) are afflicted with asthma. Prevalence rates vary based on age, country of origin, sex, race, and socioeconomic status. Within the United States, the Health Examination Survey (HES) collected national data on asthma prevalence from the 1960s (1963–1969), and the National Health and Nutrition Examination Surveys (NHANES) I and II collected data from the early 1970s (1971–1974) and the late 1970s–1980 (1976–1980), respectively. In children aged 6–11 years, the prevalence of asthma actually declined slightly from 1963 to 1974, with the prevalence of asthma in HES II (1963–1965) being reported as 5.3%, but by NHANES I (1971–1974) it had dropped to 4.8%. However, the change by 1976–1980 was dramatic, as the prevalence of asthma for 6 to 11-year-olds in NHANES II data was 7.6%. A less dramatic effect was seen in adolescents aged 12–17 years, with asthma being steady in both HES III and NHANES I at 6%, increasing only slightly to 6.5% by NHANES II (1976–1980) [12]. Subsequent NHANES studies from 2005 to 2006 found the prevalence of asthma for persons greater than 6 years of age to be 8.8%. This study also collected serum IgE to determine the association between total IgE and prevalence of asthma. Not surprisingly, the mean total IgE was higher in those with asthma [13]. Data collected by the Centers for Disease Control and Prevention (CDC) as part of the National Health Interview Survey (NHIS) also support increased asthma prevalence occurring since the early 1970s. In 1970, the prevalence of asthma in the United States, according to the NHIS, was 3%, which then increased to 5.5% in 1996 and 7.8% by 2008. The greatest increase in asthma prevalence was noted in black and urban children and is likely related to environmental exposures unique to the inner city, such as increased crowding and exposure to indoor allergens such as dust mites, cockroach [14], and mouse [15, 16].

The global prevalence for asthma in the pediatric and adolescent population was assessed in ISAAC Phase One and Three in a manner similar to that done for allergic rhinoconjunctivitis. Depending upon the country, ISAAC Phase One (early to mid-1990s) found prevalence rates of asthma in 6–7-year-old children ranging from 2.3 to 32.1%, while in children 13–14 years old the prevalence ranged from 2.5 to 37.6%. Five to ten years later, Phase Three (late 1990s to the mid-2000s) data were obtained and the prevalence rates for asthma had increased in both age groups—but only marginally. Children 6–7 years old demonstrated a modestly increased asthma prevalence of 2.5–37.6%, while children 13–14 years old had rates that remained relatively stable (or modestly decreased) ranging from 3.4 to 31.2% [9]. These data and the data from the US studies suggest that the greatest increase in asthma prevalence occurred from the early 1970s until the 1990s, but has been relatively steady since. Thus, the modest differences seen in the ISAAC studies are likely due to their comparison of prevalence between the early and late 1990s.

Atopic Dermatitis

Data from the US 2012 NHIS study demonstrated that atopic dermatitis (AD) prevalence peaks in early childhood and then declines during adolescence—staying relatively steady throughout adulthood [17, 18]. The NHIS found that in the United States, prevalence rates for AD in children (aged 0–17 years) increased from 7.4 to 12.5% from the late 1990s to the early 2010s [14]. This increase appears to be unequally distributed among races/ethnicities as non-Hispanic, black children had higher prevalence of AD than non-Hispanic, white, or Hispanic children. This discrepancy was apparent even after controlling for socioeconomic status [14]. Furthermore, there is a varying geographical distribution of atopic dermatitis within the United States, with children living in urban areas more affected than those in less urban environments [17].

Based on ISAAC Phase Three, the global prevalence of atopic dermatitis depends upon the country surveyed. For example, in India, atopic dermatitis prevalence for 13 to 14-year-olds was 0.9%, while the same age group in Ecuador had a prevalence of atopic dermatitis of 22.5%. For 6–7-year-olds in China, the prevalence was 0.2%, while in Colombia, it was as high as 24.6%. In comparison to ISAAC Phase One (obtained from the early to mid-1990s), the prevalence of AD appears to have increased in children 6–7 years of age and 13–14 years of age, primarily among those in more Westernized, developed countries rather than less developed, poorer countries [9].

Food Allergy

In the 1980s, food allergies were relatively rare and not felt to be a major public concern [7]. However, 30 years later, there are peanut-free schools and widespread allergy labeling on prepackaged foods. Food allergy is deemed the newest wave in

the allergy epidemic, and data support this assertion. Most food allergy studies have been performed in Westernized countries—the United States, Canada, the United Kingdom, and Australia—and data on the prevalence of food allergy outside of these Westernized countries are lacking.

Estimates of food allergy prevalence are plagued by pitfalls similar to those mentioned previously [19]. Population surveys or serum-specific food allergen IgE testing is known to overestimate prevalence, whereas relying on a diagnosis by an allergist through a combination of history and confirmatory serum or skin testing might underestimate prevalence. It is critical to remember that the “gold standard” for diagnosing food allergy is a double blind, placebo controlled, oral food challenge, something that is resource intensive and not practical for most clinical practices. Specialists usually rely upon suggestive history in a patient with evidence of allergic sensitization to a suspected trigger. Practitioners must be mindful that allergic sensitization alone is insufficient to diagnose food allergy, as skin and blood tests often give false-positive results (i.e., they demonstrate sensitization in someone who actually does not have an allergy to the food). Most large-scale studies rely on patient reports or serum IgE testing to determine prevalence and, therefore, overestimate the true prevalence of food allergies [20].

In the United States, sequential population surveys undertaken in 1997, 2002, and again in 2008 attempted to determine the prevalence of self-reported peanut and tree nut allergy. The researchers found that over 1% of the US population self-reported allergy to peanut, tree nut, or both. The overall prevalence rates for these specific food allergies for all ages combined did not seem to vary significantly from 1997 to 2008. However, when looking at children younger than 18 years of age, the prevalence of (parental/guardian) self-reported food allergy to either tree nut or peanut increased over threefold to fivefold from 1997 to 2008. This translated to an increase in prevalence of peanut allergy in this age group from 0.4% in 1997 to 1.4% in 2008, while the prevalence of tree nut allergy increased from 0.2% in 1997 to 1.1% in 2008 [21]. These data suggest that in the US pediatric population, peanut and tree nut allergy prevalence has dramatically risen from the late 1990s to the late 2000s.

A similar meta-analysis specifically focused on the pediatric population in the United States assessed cross-sectional data acquired from the early 1990s to the mid-2000s from multiple surveys (NHIS, NHANES, the National Hospital Ambulatory Medical Care Survey (NHAMCS), the National Ambulatory Medical Care Survey (NAMCS), and the National Hospital Discharge Survey (NHDS)) to estimate and identify trends in food allergy prevalence. Based on these multiple studies, the authors determined that in the United States, prevalence of reported food allergy in the pediatric population increased by 18% from 1997 to 2007, with 3.9% of the pediatric population reporting a food allergy in 2007. In addition to increases in patient-reported food allergy, the NAMCS and NHAMCS studies found food allergy-related ambulatory care visits nearly tripled from the 1990s to the early 2000s. Not surprisingly, hospital discharges with food allergy or anaphylaxis as a diagnosis code also increased from the late 1990s to the mid-2000s [22]. These studies demonstrate that not only are patient reports of food allergy increasing, but

the diagnosis of food allergy (at least by coding) by healthcare professionals also has increased.

Mirroring data from the United States, rates of peanut allergy in children have been reported to be around 1% or higher (and likely rising) in Australia, Canada, and the United Kingdom. In Australia and the United Kingdom, oral food challenge-based investigations reveal that food allergy prevalence is 5–10% in preschool-aged children; China has reported a similar rate with 7% prevalence [23]. The HealthNuts study based in Melbourne, Australia, reported oral challenge-proven food allergy to be present in over 10% of 12-month-old children, but the actual prevalence varied based upon food allergen—8.8% had egg allergy, 3% had peanut allergy, and 0.8% had sesame allergy. This study also estimated cow's milk allergy prevalence at 2.7%, but the allergy was not confirmed with oral food challenge—only by the presence of a suggestive history and positive skin prick testing [24]. This study supports higher food allergy rates in young children, as has been shown in the other studies. Prevalence of various food allergens varies by country of residence (which likely is due to both genetics and environmental exposures) [19].

The most common food allergen worldwide is cow's milk, followed by egg [25]. The third most common food allergen, however, varies based upon age, geographic region, and dietary patterns. In the United States, peanut allergy is the third most common food allergy, while in Japan wheat is third [26]. While cow's milk and egg are the most common food allergies, they are usually outgrown by school age. In contrast, food allergy to peanut and tree nut is not commonly outgrown, and the majority of those affected tend to be afflicted for life. Furthermore, unlike cow's milk and egg, baking peanut appears to make the protein more allergenic [27]. Therefore, when discussing the prevalence of food allergy, it is clear that risk varies according to type of food and geographic location.

An important development in the understanding of increased peanut allergy prevalence comes from results of the Learning Early About Peanut (LEAP) study. LEAP investigators observed that Jewish children living in the United Kingdom had significantly higher rates of peanut allergy (almost ten times higher) than Jewish children (presumably of similar genetic background) living in Israel [28]. They also noted that peanut products were introduced to Israeli children at a younger age (around 7 months) compared to children living in the United Kingdom (usually after 1 year of age). From these observations, they designed the first randomized interventional study to determine if avoidance or consumption of peanut early in life could prevent development of peanut allergy. The infants recruited for the study were between 4 and 11 months of age and had a history of atopy with either severe eczema, egg allergy, or both. Subjects underwent initial skin prick testing and oral food challenge to peanut and were then assigned to either consumption (instructions to consume 2 g three times weekly) or avoidance of peanut. They continued to adhere to either consumption or avoidance until age 5 years, at which time the presence of allergy to peanut was reassessed by food challenge. The results were remarkable, demonstrating that early introduction and regular consumption of peanut had a 70–86% relative reduction in the development of a peanut allergy in a high-risk cohort of children [28]. This protective effect appeared to be sustained, as children

who regularly consumed peanut from infancy to age 5 years did not have any increase in peanut allergy prevalence even after avoiding peanuts for a year [29].

Previous to the LEAP study, it was unclear which strategy—early exposure or avoidance—was superior in preventing the development of food allergy. Clinical guidelines and recommendations in the late 1990s and early 2000s supported avoidance; however, based upon the LEAP study, we now know and think these guidelines may have paradoxically increased the prevalence of food allergy. By the late 2000s, the recommendation to avoid certain allergenic foods early in life was retracted [28]. The LEAP study, published in 2015, finally provides strong evidence for early introduction as a preventative strategy for peanut allergy. Whether this protective effect from early and ongoing introduction applies to other foods remains to be determined.

Environment Versus Genetics

While it is clear that the prevalence of allergic disease is increasing, it is unclear what is driving this change. As mentioned previously, for peanut allergy, it may relate to increased exposure, but for environmental allergens, this seems less likely. Clearly there is a strong genetic component to atopic disease—the risk of atopy in a child with one atopic parent is around 30–40%, while with two atopic parents, this increases to nearly 80% [30]. Genome-wide association studies have highlighted a few genetic loci that seem to correlate with the presence of atopic disease [31, 32]. However, the rapid rate at which atopic diseases have increased cannot be explained solely by genetic inheritance. In fact, the rapid rise in these diseases strongly supports a role for an environmental influence driving the epidemic.

Evidence supporting a role for the environment comes from studies of the prevalence of allergic disease in immigrants and children of recent immigrants. Foreign-born children living in the United States have lower odds of atopic disease—including asthma, atopic dermatitis, allergic rhinoconjunctivitis, and food allergy—than children born in the United States. However, the prevalence of atopic disease in foreign-born children quickly rises after residing in the United States for longer than 10 years [33, 34]. It is unclear what specific changes in the environment are driving the increase in prevalence, although it has been proposed that exposures to specific infections, hygiene practices, or diet might be to blame.

Additional evidence for environmental influence in the development of allergy comes from a US study comparing environmental exposures, immune profiles, and the microbiome with asthma prevalence in Amish versus Hutterite farm children. Both populations have similar genetic backgrounds and lifestyles, living in farming communities in the Midwest (Amish in Indiana and Hutterites in South Dakota) with large family sizes, high rates of vaccination, high-fat diets, low rates of obesity, breastfeeding as infants, minimal exposure to pollution and tobacco smoke, and decreased exposure to indoor pets. However, there are some distinct differences—the Amish follow traditional farming practices, whereas the Hutterites have transitioned to industrialized farming. Amish children had much lower rates of asthma

and allergic sensitization compared to Hutterite children. There were significant differences in the gastrointestinal microbiome and environmental exposure to endotoxin between the two groups, with higher endotoxin levels found in Amish homes. Using a mouse model, the authors demonstrated that house dust from Amish (but not Hutterite) homes helped dampen the development of allergic airway disease. These data strongly suggest that variations in the environment can be either protective or detrimental in the development of allergic sensitization and asthma [35].

Hypotheses for Atopic Disease Development

While it is clear the prevalence of allergic diseases is increasing and this has a strong connection to genetics and the environment, it is much less well understood why allergic diseases exist in the first place. Several hypotheses have been put forward, which include the hygiene hypothesis, skin barrier disruption, microbiome dysbiosis, and the viral hypothesis (see Table 1.2). These will be discussed individually below, but it is quite likely that a combination of all of these potential mechanisms is actually underlying the atopic epidemic.

The observation that pre-hygiene societies have low prevalence of atopy versus rapidly rising atopy in post-hygiene, Westernized societies has given rise to the *hygiene hypothesis*. The hygiene hypothesis purports that the Th2, pro-allergic immune response initially developed as a defense against helminths and parasites. As living conditions changed after the advent of hygienic practices—purifying water, wearing shoes, antimicrobial treatment—there was a decrease in the exposure to bacterial and parasitic disease. Without constant stimulation from infections, the immune system began reacting to previously innocuous, environmental antigens [36, 37]. Support for this hypothesis comes from the fact that pre-hygiene societies do not seem to exhibit allergic disease while, as mentioned, post-hygiene societies have increasing prevalence of atopic disease.

Table 1.2 Hypotheses postulated to account for the allergy epidemic

<i>Hygiene hypothesis</i>
• Reduced exposure to bacteria, parasites, and helminths in the modernized world has led to the immune system skewing toward development of atopy [36, 37]
<i>Barrier regulation hypothesis</i>
• Disruptions in epithelial and mucosal barriers permit allergens access into deeper layers of tissue where they cause irritation, resulting in the host immune system skewing toward allergic inflammation [4, 36–38]
<i>Microbiome dysbiosis hypothesis</i>
• Changes in the normal bacterial flora residing at the epithelial or mucosal surfaces of the host skew the immune system toward development of atopy [10, 40–42]
<i>Viral hypothesis</i>
• Infections with respiratory viruses early in life predispose children to develop asthma and, after infancy, exacerbate asthma [43–45]

There appears to be a critical period during infancy and early childhood when the immune system can either develop tolerance or skew toward a Th2 (pro-atopic) response to antigens. The atopic march refers to the progressive development of allergic diseases—starting with atopic dermatitis, followed by development of allergic rhinoconjunctivitis, and finally, asthma [38]. Given that atopic dermatitis is a skin disease, and has been associated with abnormal skin barrier, it has been postulated that the underlying disruption of the skin barrier has allowed atopic disease to develop and flourish.

The *barrier regulation* hypothesis suggests that perturbations in the epithelial and mucosal barriers permit allergens into areas of the body where they previously were not encountered, causing irritation and subsequent allergic sensitization. Epithelial and mucosal barriers normally exhibit a tolerant, non-inflammatory immune environment. However, if the barrier is disrupted, the attempted repair will activate the Th2 pathway, skewing any immune response toward atopy. There are a few studies and observations that support this hypothesis. The allergic march is one observation that suggests sensitization via the epidermis precedes the progression of allergy and diseases involving the respiratory tract. Similarly, with food allergy, sensitization to food antigens can occur via permeable skin, as seen with eczema and filaggrin loss of function mutations [4, 36]. Another example of disrupted epithelial barrier leading to allergic disease is the recently identified delayed anaphylaxis to mammalian meat. This is a disease where subjects develop anaphylaxis hours after eating mammalian meat and are found to have IgE against galactose- α -1,3-galactose (α -Gal), a sugar that is found in certain ticks. Subjects become sensitized to α -Gal when bitten by the ticks. Thus, the tick bite bypasses the normal intact skin barrier, allowing for development of an atopic (IgE-mediated) response to the sugar [37].

A special type of barrier dysfunction may be thought to underlie the response to pollution. Levels of pollution exposure have been correlated with both development and exacerbation of atopic dermatitis, allergic rhinitis, and asthma. Initially this connection was noted through epidemiologic and birth cohort studies, but with further investigation using mouse models and human peripheral blood monocyte studies, it was shown that pollution—and more precisely, diesel exhaust particles—results in epithelial stress and skews lymphocytes to a Th2/Th17 response [38, 39]. Clearly, mucosal and epithelial barriers are important components of the immune system and play an important role in determining tolerance versus allergic sensitization and disease.

The *microbiome hypothesis* suggests that changes in the microbiome influence the host's barrier immune response and either can be protective against atopic disease or encourage development of atopy. The observations that delivery via cesarean section, living in an urban environment, formula feeding, and exposure to antibiotics early in life correlate with increased atopy led to the hypothesis that perturbations of the microbiome (dysbiosis) might underlie the development of atopy. Studies assessing the microflora in the stool of infants suggest that there is a certain bacterial milieu in infants destined to develop allergic asthma. This effect of the gastrointestinal microbiome was limited to a short time frame—the presence of dysbiosis at 3 months of age, but not at 1 year of age, was associated with the development of asthma [10]. The presence of different microbial organisms may not directly impart an increased risk of atopic disease, as metabolic products of the

microbiome can play an important role. The so-called metabolome is the combined metabolic products of the microbiome and has been examined with respect to development of atopy. In particular, a reduction in the production of short chain fatty acids (SCFA) seems to increase risk of atopy, while an increase in production of SCFA correlates with a protective effect [10, 40–42].

Viral infections have been implicated in the development and exacerbation of atopic disease—most specifically with asthma—hence the *viral hypothesis*. The intimate relationship between severe respiratory syncytial viral (RSV) infections in early infancy and persistent asthma was first described in the 1970s. Subsequent studies demonstrated that anti-RSV IgE was produced as part of the anti-viral immune response and the level of anti-RSV IgE correlated with the risk of wheezing. Further evidence for a possible Th2 response against RSV was the fact that eosinophilia at the onset of RSV infection also positively predicted the persistence of wheezing. However, the cytokine profile during acute RSV bronchiolitis consists primarily of IFN γ , a Th1 cell product, as opposed to IL-4, IL-13, and IL-5, which are normally released by Th2 cells and are typical of the atopic response. Even with this difference in the primary cytokines produced, a study in the mid-1990s showed that infants admitted for RSV bronchiolitis were more likely to develop asthma and aeroallergen sensitization by 3 years of age compared to those infants who had RSV infections that did not require admission. The mechanism(s) tying severe RSV respiratory tract infection to atopic disease is not known, and is an area of ongoing research. It is not known, for instance, whether viral infections drive development of atopy or simply uncover a predisposition for atopy that may associate with a more symptomatic response to the virus. As mentioned, this is an area of continued research, and hopefully future studies will better clarify this relationship [43–46].

Exposure to an increasing burden of allergenic proteins could be fueling the allergy epidemic. Noting outbreaks of allergy to ladybug in cases of infestation, Platts-Mills suggested that high levels of allergen exposure could drive sensitization and allergic disease. Perhaps sensitization to certain environmental allergens is also related to increased exposure. Changing landscapes during urbanization of the United States have created a niche for ragweed, which has become rampant in areas where it previously would not have been able to flourish. Indoor allergens—dust mites and pet dander—have also become important contributing factors to allergic disease, as humans have increased time spent indoors and subsequently become exposed to higher levels of these perennial allergens [37]. It is unlikely that increased exposure alone explains the allergy epidemic, but it could be a contributing factor.

Conclusion

In summary, allergic diseases impact millions of people worldwide with significant personal and economic impact for patients, families, and their communities both locally and globally. The prevalence of allergic diseases, including atopic dermatitis, asthma, allergic rhinoconjunctivitis, and food allergy, has risen drastically over the past 50 years and has made once infrequent illnesses commonplace. It is still

unclear why this has occurred, but there are some important aspects that are clear: a genetic predisposition to atopy with environmental influences—and, for some atopic diseases like food allergy, a critical window in infancy where disease modulation can occur. As a society, we must continue to explore mechanisms and modulators of atopic disease, working toward prevention and/or disease modification. In the meantime, providers will continue to empower their patients and families, working with them to control these chronic diseases. The transition of care as patients move from childhood to adolescence into adulthood can be difficult as the patient takes on more responsibility for their healthcare. Nonetheless, this transition is critical and provides a great opportunity to prepare the adolescent patient for successful lifelong disease management.

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Chapter 2

Adolescent Brain Development and Implications for Adolescents with Allergies



Amy Hahn and Jessica L. Hoehn

Introduction

In this chapter, we first briefly summarize brain development and its impact/implications for adolescents with allergies. We then discuss some key areas of psychosocial development literature that are relevant for adolescents with allergies, including emotions and psychopathology in adolescents, social functioning and quality of life, and autonomy development and its relation to illness management.

The Adolescent Brain (Normative Adolescent Brain Development)

There is extensive literature regarding neurodevelopmental changes in adolescence; changes in intellectual functioning, cognition, and affective regulation from childhood to adolescence are well documented. In the past few decades, advances in neuroimaging and other technologies have enabled researchers to link observed developmental changes in behavioral, intellectual/cognitive, and affective functioning to changes in brain structures and processes. In this section, we summarize important concepts and highlight some relevant findings from this large and extensive cohort of literature regarding adolescent brain development (Fig. 2.1).

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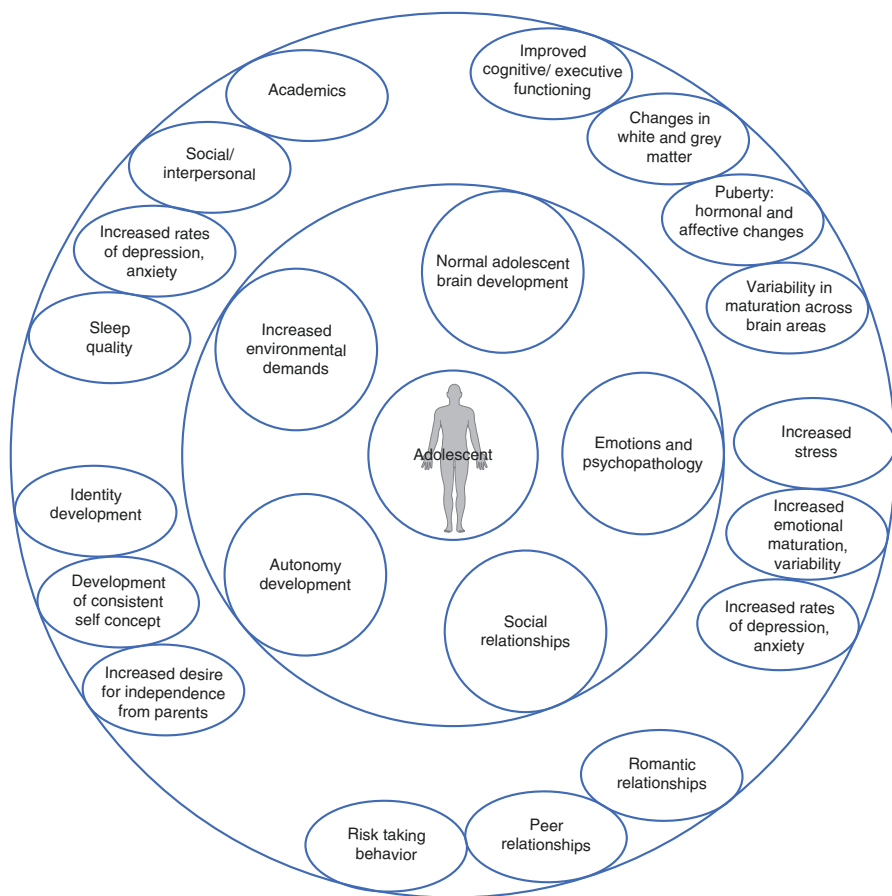


Fig. 2.1 Themes impacting normal adolescent development

The following subsections are not meant to present an exhaustive review of neurodevelopmental and neuroimaging literature, but rather a summary of certain key findings. Some relevant concepts from literature regarding the adolescent brain are covered.

Changes in Cognition and Executive Functioning

One of the hallmarks of adolescent brain development is improvement in cognitive functioning. As children continue to mature throughout adolescence into early adulthood, they show significant improvement in abstract thinking, mental flexibility, self-direction, self-regulation, attention, working memory, and affect regulation [1, 2]. It is generally agreed upon that cognitive development in adolescence can be attributed to not one singular process but a host of cognitive abilities, i.e., *executive*

functions: separate processes that develop in tandem in the brain and integrate to produce improvements in abstract thinking, cognitive performance, self-regulation, etc. [3]. This conceptualization of cognitive development is in contrast to previous views of cognitive development, which emphasized identification of one potential underlying mechanism that could be attributed to development of consciousness and/or global cognitive improvements [4]. Based on recent imaging studies and other studies of neurocognitive development, there is currently no single unifying accepted theory of adolescent development (i.e., no longer current support for Piaget, Erickson, etc.) [2–4].

Multiple neuroimaging studies and studies of neuropsychological performance have emphasized the complex interworking processes involved in cognitive development/executive functioning. Individuals in early and late adolescence show improvement in reasoning, processing speed, working memory, and attention [1, 3, 5]. Functional neuroimaging studies have shown that these “executive functioning” processes are housed in the prefrontal cortex, though evidence has shown that connections between brain areas also play a significant role [6]. Executive functioning and thus cognitive abilities in general appear to improve throughout adolescence due to a complex integration of structural changes to the prefrontal cortex, increased rapid connectivity of nerves through increased myelination, and synaptic pruning across multiple brain areas but especially in the prefrontal cortex [7].

Structural Changes Occur Within the Brain During Adolescence, Including Changes in White and Gray Matter

Neuroimaging studies have consistently shown a general increase in white matter and decrease in gray matter from childhood to adolescence. Brain volume generally (and white matter specifically) increases in adolescence and young adulthood in contrast to childhood [6, 8]. With increases in white matter, there is evidence of corresponding decreases in gray matter volume. Findings from the Philadelphia Neurodevelopmental Cohort (PND), a large-scale study of brain maturation and cognitive development in typically developing individuals [9], have shown that gray matter volume appears to increase through childhood, plateau in late childhood/early adolescence, and then decrease through adolescence and young adulthood [6, 8]. While gray matter volume decreases, density tends to increase, and much of the decreases in gray matter are attributed to (a) growth in white matter and (b) synaptic pruning. Several studies have demonstrated sex differences in gray matter density and volume, as well as more generalized sex differences in the rates of development of different brain areas [6, 8]. These sex differences in brain maturation map onto differences in neurocognitive performance improvement based upon sex; males show faster rates of maturation in areas of the brain relating to spatial reasoning and processing speed, while females show faster maturation in attention and social cognition [6]. The brain as a whole undergoes increased myelination throughout early adolescence, which leads to improved communication between brain structures and systems [7].

Continued Brain Development as Individuals Age into Early Adulthood

Adolescence is characterized as a period of continued change and development for individuals, with changes in hormones, cognitive/intellectual abilities, and affective regulation. Historically, neurodevelopmental researchers believed that early adolescence was the most relevant time for adolescent brain development, given that the prefrontal cortex undergoes significant growth and structural changes during early adolescence [10]. However, neuroimaging and neurodevelopmental research in recent decades have shown that the brain continues to develop and change throughout the adolescent period and well into early adulthood, with the general consensus being that some brain functions (such as the executive functions) are not fully developed until well into young adulthood [3, 7]. The prefrontal cortex and superior temporal gyrus have been found to be the last areas to fully mature [11]. This delay in the full maturation of executive functioning has important implications for how adolescents self-regulate, as discussed further below.

There Is Significant Variability in Maturation of Different Brain Areas and Across Individuals

In general, development in adolescence can be understood as a balance of maturing processes in cognition, affect, and behavior [3]. Areas of the brain generally mature at different rates, which has implications for understanding adolescent behavior and adolescent psychopathology. There is also evidence of significant within-individual variability in which lobes, systems, connections, and other brain structures mature, with some individuals more variable than others [6]. Individuals with higher within-individual variability may be at increased risk for psychopathology, as parts of their brains may be functioning at higher levels than other parts or areas [6].

Puberty Induces Hormonal and Affective Changes, Which Have Important Implications for Adolescent Brain Processing of Risks Versus Rewards

Due to hormonal changes from puberty, individuals in early adolescence tend to experience increased emotional arousal and increased experience of affect [3]. They also tend to feel increased motivation toward sensation-seeking and orientation toward rewards. Adolescents' increased autonomy and improved cognitive functioning also tend to expose adolescents to more stressors and life challenges, as they become more independent. However, because executive and regulatory processes (primarily housed in the prefrontal areas, as well as connecting structures between

brain areas) do not tend to fully develop until late adolescence or early adulthood, adolescents often experience increased emotion and behavioral impulses, without fully developed abilities to regulate these experiences.

This increased activity in affect has also been shown to have an impact on adolescents' decision-making. Compared to children and adults, affect plays a larger role in adolescent decision-making, with adolescents more likely to follow a "gut feeling" regarding a decision rather than cognitively evaluating a decision [3]. This may play a role in adolescents engaging in more risky behaviors, particularly when consequences are long term (e.g., medical adherence). Processes and brain structures for regulating affect, and understanding long-term consequences, continue to develop throughout late adolescence but are often not fully developed when adolescents start managing their medical needs. These differing rates of brain maturation for various structures may put adolescents at increased risk for developing psychopathology [12] and are detailed below with discussion regarding adolescent psychopathology and allergies.

Emotions and Psychopathology in Adolescents

Adolescence is a period of time marked by puberty, increased desire and effort toward independence from parents, and evolving emotional maturation. Emotional functioning is important to consider in the context of adolescence given hormonal changes, in addition to increased social, interpersonal, and academic stress. In general, the onset of puberty contributes to increased autonomy, conflict with parents, and developing cognitive abilities [2]. Moodiness is also an often cited marker of adolescence, though hormonal changes are only partially contributory and socio-environmental stressors additionally contribute to increased negative affect.

In addition to normative emotional development and functioning, it is important to consider the impact of psychological diagnoses during adolescence. According to epidemiological research, the average prevalence of any psychiatric disorder for adolescents (ages 12–19) is 21.8% [13]. In a review of studies between 1996 and 2011, specific occurrence of diagnoses in adolescents includes an average of 12.1% meeting criteria for substance abuse or dependence, 10.7% for anxiety disorders, 6.1% for depressive disorders, and 3–4% for behavior disorders (i.e., conduct disorder, oppositional defiant disorder, or ADHD).

As children transition into adolescents, rates of depression increase, with higher rates of depression in adolescent females [2]. Additionally, studies indicate that rates of drug abuse and some anxiety disorders (panic disorder and agoraphobia) also increase from childhood into adolescence. Conversely, rates of ADHD and separation anxiety decrease in adolescence. Studies demonstrated mixed results for generalized anxiety, as one study described an increase in prevalence for females only as they enter adolescence [14], while other studies demonstrated an overall decrease for both males and females [15].

Allergies and Psychopathology

It is important to consider normative adolescent emotional development and rates of psychological diagnoses in the context of chronic illness. Studies have researched the comorbidities of allergies and psychological diagnoses in children, adolescents, and adults and in general have suggested links between allergy and symptoms of anxiety, depression, ADHD, and sleep disruption. For example, one study in adults with allergies (food and/or nonfood) found associations with both anxiety and depression diagnoses [16].

Through the use of a large community-based longitudinal study, researchers have been able to highlight the occurrence of both psychopathology symptoms and diagnoses in children (ages 10–16) with and without food allergy [17]. These researchers found that, compared to participants without food allergy, participants with food allergy on average had one more symptom of any psychopathology. Additionally, this research indicated relationships between a food allergy diagnosis and separation anxiety, generalized anxiety, ADHD, and anorexia nervosa. Furthermore, over time, food allergy predicted increased symptoms of generalized anxiety and depressive symptoms. However, it is important to note that there was no difference between those with food allergy and those without in terms of occurrence of mental health diagnoses. Thus, researchers found heightened levels of symptoms but not confirmed diagnoses. In interpreting these results and similar findings in other studies, authors have posited that perhaps heightened occurrence of certain symptoms may be reflective of youth adapting to life with a food allergy, rather than meeting criteria for certain psychiatric diagnoses.

In general, research has shown higher rates of anxiety in individuals with medical diagnoses (e.g., [18]). In allergies, research has suggested linkage between allergies and anxiety, with theories to provide some rationale for these relationships. A review of the literature on asthma and allergies in children and adolescents highlighted that across studies, a relationship between allergies/asthma and anxiety exists, particularly panic disorder [19]. Furthermore, in a 2006 review of the literature, Friedman and Morris [20] summarized findings that point toward an increased occurrence of anxiety in children/adolescents with allergies, including allergic rhinitis, asthma, food allergies, and non-specified allergies.

Various theories about these relationships have been posited, including commentary on a potential bidirectional relationship between anxiety (specifically, panic disorder) and allergies due to the somatic symptoms involved [21], with both biological and environmental factors contributing. Biological theories speculate that anxiety and allergies have common structural/neurochemical processes, including autonomic nervous system activity, and have additionally been hypothesized to be genetically linked. Cognitive-behavioral theories suggest that classical conditioning can help explain the link between allergies and anxiety, in that the unconditioned experience of an allergic reaction creates a conditioned fear of these symptoms. Additional theories posit learning theory, in that parents model anxiety for children

in response to allergy symptoms and in turn children learn and develop anxiety in the context of their allergic disease.

In regard to allergies, perhaps most commonly researched has been the association between food allergies and anxiety and/or other symptoms of psychopathology. This is likely due to the potentially life-threatening nature of some food allergy diagnoses and the need for hypervigilance with eating, which lend to certain characteristics of an anxiety diagnosis. It is possible that some level of anxiety is adaptive and even beneficial, to aid an adolescent in their efforts at constant monitoring and vigilance in their responsibilities; however, one can also argue that anxiety can significantly interfere with daily life and have a negative impact on the adolescents' socio-emotional functioning. Fox and Warner [22] found a relationship between social anxiety and food allergy, only in male youth, when compared to males without food allergies. Additionally, these researchers found a correlation between social anxiety and parental worry and control, suggesting a possible influence of parental behavior and child anxiety.

Studies have looked at the occurrence of food allergy and symptoms of anxiety, depression, and general reports of distress in children and adolescents. One study found an increased risk of anxiety in adolescents with food allergy [23]. However, other studies have suggested that children and adolescents with food allergies function in the average range in regard to psychological distress. Perhaps surprisingly, LeBovidge and colleagues [24] reported no significant differences in anxiety and depressive symptoms in youth with food allergies (ages 8–17 years) when compared to a normative sample; in fact, the youth with food allergy reported better functioning for depressive, anxiety, and social stress symptoms. However, anxious coping and separation/panic were higher in the food allergy youth. It is possible that youth with food allergies may display symptoms of anxiety in order to adapt to the demands of their disease. Furthermore, results also indicated that self-report of more negative attitude toward food allergy was related to increased depressive symptoms, anxiety symptoms, and social stress. Thus, perhaps one can posit that attitude toward food allergy may have a more significant impact on emotional functioning than the disease itself. Similarly, in a study of college-aged young adults ages [18–22] with and without food allergy, no differences were found in anxiety, depression, autonomy, or parent overprotection between the groups [25]. Differences instead were found when the food allergy group was broken down into two groups: having experienced an anaphylactic reaction or not. Young adults who reported prior anaphylaxis described more worry, increased perception of disease severity, and greater maternal overprotection. Thus, disease indicators likely contribute to an increased likelihood of distress symptoms, over and above simply having an allergy diagnosis alone.

Some research has suggested a possible link between allergy and ADHD symptoms. Specifically, when comparing youth with ADHD to those without, results indicated a significantly increased amount of allergic sensitization to skin prick test and increased prevalence of allergic rhinitis in those with ADHD [26, 27]. Further research is needed to determine reasons for this increased risk.

Allergies and Sleep

Perhaps a contributing factor to the allergy-ADHD relationship may be due to sleep concerns that have been linked to allergy. Due to increased allergic symptoms at night, sleep can be disrupted for these individuals. Furthermore, poor adherence to treatment and/or more severe disease may exacerbate sleep issues. In children and adolescents with allergic rhinitis, a large percent report a significant impact of disease on sleep, including the impact of symptoms on sleep onset and maintenance. Further, these sleep concerns have been reported to impact daytime sleepiness and overall quality of life [28]. Compared to healthy peers, undergraduates with allergies and with allergies + asthma described poorer sleep quality and poorer health-related quality of life. The undergraduates with allergies and allergies + asthma had a greater number of sleep disturbances and an increased use of sleep medication. Poor sleep quality was related to lower health-related quality of life [29]. The relationship between sleep disruption and allergic rhinitis has been documented into adulthood, with patients with moderate to severe allergic rhinitis reporting higher rates of insomnia compared to healthy peers [30]. Additionally heightened was the allergic rhinitis patients' experience of snoring compared to peers, as well as reported daytime fatigue. In summary, allergy negatively impacts sleep quality, which in turn may impact daytime sleepiness and fatigue and overall functioning, including their perceived overall quality of life.

Social Functioning and Quality of Life

Adolescent development involves a complex interaction of genetics and family, peer, and community environments. To understand the social functioning of adolescents, one must consider their relationships with parents and peers, in addition to the impact of psychosocial stressors on their overall functioning and quality of life. Additionally important is the focus on development of self-concept during adolescence [2]. For the adolescent with allergies, their self-concept includes their medical diagnosis and needs; this self-concept may be influenced by perceived quality of life and in turn impact their social interactions and relationships.

Relationship with Parents

Adolescence often includes increased conflict with parents, with one potential theory attributing this to the youth's desire for individualization. With increased conflict comes a decline in close relatedness and less time spent together [2]. Until adolescence, a parent is generally responsible for a child's disease management and understanding. With an increased desire and need for autonomy, adolescence marks

the beginning of varying stages of transition of disease responsibilities [31]. Depending on the family, one can ascertain that this transition may or may not be marked with anxiety, stress, and conflict. Regardless, emotional support from individuals in one's social network has been identified as the most common source of support for adults with allergies and/or asthma, particularly from family [32]. Thus family support, though changing across developmental stages, is central and important.

Relationships with Peers and Social Environments

In addition to shifting relationships with parents, adolescence includes increased time spent with peers [2]. Friendships in adolescence are characterized in general by trust, loyalty, and intimacy. Adolescents with allergies must determine ways to cope with their diagnosis while also navigating peer social environments. In a study of adults with allergies and/or asthma, the most common coping strategies to manage their disease include avoiding specific environments, avoiding thinking about their condition (i.e., "denial"), acceptance, and seeking health care [32]. Thus, adults report use of both adaptive and nonadaptive coping strategies to manage their disease, which can have significant impact on their social involvement as well as overall stress. Though only speculation, one can assume that adolescents using avoidant coping strategies (similar to their adult counterparts) may miss out on social activities and become isolated from peers. Additionally, adolescents have reported experiences of lack of understanding from others and/or others dismissing their need for strict avoidance, which likely contributes to feelings of isolation [33]. Adolescents have reported a desire for their friends to know more about their allergy and perceive benefit from this social support, though in one study many indicated that they had not informed friends about their medical condition [34].

Peer Influence/Risk-Taking

Adolescent relationships also include peer influence, which can impact both prosocial and risk-taking behaviors. Most adolescents may "experiment" with problematic behavior, but most do not continue to engage in these behaviors to an intense or dangerous extent [2]. In general, socially responsible decision-making has been found to be more common in young adults as compared to adolescents, likely due to development and psychosocial maturity [35]. Of concern for the adolescent with food allergy is the high stake of engaging in experimentation, i.e., a potentially fatal reaction in circumstances where they may mismanage their allergy. The highest risk of death in the food allergy population is in adolescents [36], which suggests the serious implications of risk-taking in this group. In one qualitative study, adolescents denied significant concern about anaphylaxis, despite having a past

anaphylactic reaction; the authors purported that this was likely due to the adolescents not remembering the reaction [37]. While lacking worry about anaphylaxis may aid in minimizing anxiety, it likely contributes to an adolescents' minimization of risk.

Research is mixed about the perceived burden of carrying an epinephrine autoinjector, indicating both lack of burden reported by adolescents and qualitative interviews noting occasional forgetfulness as well as reported annoyance [37, 38]. In one study, only 61% of adolescents reported they always carried their autoinjector, with varying adherence depending on circumstances (e.g., youth reported almost always bringing it when they travel, but only 53% carry it when wearing tight clothing and 43% when participating in sports [34]). Furthermore, more than half of the adolescents interviewed reported an incident in which they intentionally ate a potentially allergen-containing food. Adolescents determined to be "high risk" based on these factors described feeling different because of their food allergy and reported less concern about it. Thus, the influence of peers, increased likelihood to engage in risk-taking, and desire to "fit in" all contribute to an adolescent's allergy experience and management.

Quality of Life and Allergy

Quality of life (QOL) is a construct often measured to describe level of functioning for individuals and/or groups across various domains, including physical/health, social, and emotional. Health-related quality of life (HRQOL) refers to those aspects of functioning pertaining to health and medical conditions. In food allergies, QOL and HRQOL have been quantified by both generic and disease-specific measures in order to more specifically understand the impact of food allergy as compared to other diseases (using generic measures) and through the use of questions unique to the food allergy experience (using disease-specific measures [39]). Food allergy requires vigilance in monitoring all food intake and preparedness in case of accidental ingestion; as such, it may impact an adolescent's social, emotional, and school-related functioning. While an adolescent with food allergy may not experience daily symptoms as a result of their diagnosis, the regimen, preparedness, and monitoring involved certainly can place significant burden on QOL.

Over the past decade, HRQOL measures specific to food allergies have been developed and validated for children, adolescents, adults, and parents [40]. Parents have described the burden of food allergies to limit their abilities to engage in family activities, in addition to having an emotional impact on them as a parent and a lower overall perception of health/wellness of their child [41]. HRQOL studies have demonstrated food allergies to impact functioning across several domains, including social (e.g., attending restaurants, traveling, and spending time at others' houses), emotional (e.g., worry, frustration, sadness if missing out on activities), and general physical health [42]. Caregivers have also highlighted their child's food allergies to impact meal preparation, school attendance, decision to home school, and general

stress levels [43]. According to parents, findings have consistently demonstrated the impact of food allergy to be exacerbated when the child has multiple food allergies (>2); findings have been inconsistent as to whether associated atopic disease contributes added burden [42, 43].

Parents and families certainly are affected by a child's food allergy across domains. As a child enters adolescence, the individual and family likely remain affected but in different ways. Adolescents become more independent in their social activities and gain increasing responsibilities for their disease management compared to childhood. Thus, adolescent-specific HRQOL measures have been developed with the goal of targeting this subset to identify the unique impact of food allergy at this stage of development. Research has indicated better quality of life in teenagers with food allergy who have not experienced anaphylaxis, compared to those who have; similarly, those who perceive their risk of death as low have better QOL scores than those who perceive risk of death as high [38]. When compared to adolescents with allergic rhinitis, asthma, or atopic dermatitis, adolescents with food allergy reported worse QOL. Specific concerns for adolescents appear different than parent or child reports and include social activity limitation, food choice limitation, concerns about being a burden to others, and concern about lack of education about food allergy at school [38]. Additionally, teens did not endorse burden of carrying an epinephrine autoinjector nor their parents being overly attentive to their allergies. Parents have reported worry related to transitioning allergy responsibility (including monitoring for allergens and responding to reactions) to their teenagers [37].

The impact of allergy on quality of life has also been demonstrated in nonfood allergy populations, though to a lesser extent. For example, in a large community-based sample, young adults with allergic rhinitis described their disease to impact social and emotional quality of life; those participants with comorbid asthma reported an additional impact to physical functioning [44]. A review of the literature cites symptomatology of allergic rhinitis as a burden in itself, in addition to disrupted sleep and the related consequences of poor sleep, including daytime fatigue and difficulties with activities of daily living. Further, lack of diagnosis and/or inadequate treatment may add an additional burden to those with allergic rhinitis [45].

Adolescent Autonomy and Illness Management

Adolescence is a crucial period for autonomy, self-concept, and identity formation. Along with improvements in cognition and abstract thinking, adolescence is a time in which individuals develop more abstract self-concepts and a stable sense of self. When compared to children, adolescents make fewer social comparisons and begin to define themselves according to their self-beliefs and behaviors [2, 3]. Self-concept becomes more consistent as adolescent individuals age. By late adolescence and early adulthood, individuals typically have a more defined sense of self and a consistent perception of their own personalities [3]. Thus, self-concept,

autonomy, and self-management are crucial characteristics of adolescent development, and these processes are vulnerable to impact from allergies and other medical conditions.

Adolescents managing chronic conditions such as allergy (food allergy or allergic rhinitis) often experience difficulties related to autonomy and self-management of their illness (Table 2.1). As noted above, development of autonomy is a crucial process in adolescence, and deficits in autonomy have been linked with various internalizing and externalizing difficulties [46, 47]. However, effective illness management for allergies, as well as other medical conditions, often necessitates greater parental involvement than adolescents would otherwise prefer or require [48]. For example, parents of children with food allergy may need to be more involved in children’s food intake and increase their monitoring of children’s activities in order to protect children from accidental exposure to allergens. Research has shown that parents of children with food allergies may be more likely to be overly involved even in activities that do not involve medical care or illness management [49]. This could negatively impact autonomy development into adolescence. For example, Polloni et al. [50] examined self-concepts of children and adolescents with food allergies along with healthy controls and found that adolescents with food allergy were more likely to have “problematic” self-concept

Table 2.1 Potential risk-taking behaviors of adolescents with allergies across typical environments

Environment	Possible risk-taking behavior
Dining at restaurants	• Neglecting to inform waitstaff of allergy • Not having epinephrine available • Intentional ingestion of allergic food
Going to parties and/or out with friends	• Not having epinephrine available • Neglecting to inform friends of allergy • Exposing self to allergens (e.g., pets)
Dating	• Neglecting to inform partner of allergy or treatment in case of accidental exposure
Pet ownership	• Negative impact on sleep quality
Grocery shopping	• Neglecting to read labels
School attendance	• Neglecting to inform school personnel of allergy • Not having epinephrine or albuterol available • Exposure to food allergens at lunch • Exposure to environmental allergens (e.g., pet dander, mold)
Sports participation	• Not having albuterol or other medications available • Exposure to environmental allergens (e.g., grass)
Travel	• Not having epinephrine or other medications available • Dining at unfamiliar places and neglecting to inform waitstaff of allergy • Exposure to allergens via travel (e.g., planes) • Neglecting to bring safe foods
Time spent away from parents	• Lack of knowledge/confidence in managing reaction • Not having epinephrine or other medications available

beliefs. They were more likely to view themselves as less competent, more likely to have negative views of themselves and their abilities, and more likely to have negative self-concepts about themselves as a family member.

However, normative processes in adolescent autonomy development—such as increasing independence and self-management—likely put adolescents at greater risk for difficulties with adherence to allergy management and self-management of medical care in general. Developmental concerns play a role in adolescents' adherence to medical regimens in adolescents with allergic conditions. For example, as previously discussed, successful self-management of food allergies involves avoidance of the identified allergen, as well as ability to correctly utilize epinephrine autoinjectors and other interventions for accidental allergen exposure. Studies of adolescents with food allergies have shown that many adolescents do not carry their epinephrine autoinjectors, and many (more than half for one study by Monks et al. [51]) do not know how to treat an allergic reaction [51, 52]. Jones and colleagues [53] found adolescents in their sample were generally not fully adherent in carrying epinephrine autoinjectors. Researchers have also found teens and young adults are likely to intentionally consume foods that they may be allergic to [54, 55]. Of the individuals who die due to anaphylaxis from exposure to food allergens, most are adolescents or young adults, with these deaths attributed to adolescents not having brought/easily available access to their epinephrine autoinjectors [56, 57].

Some allergy researchers have begun measuring facilitators and barriers to adherence in adolescents, in order to help adolescents overcome these difficulties in adherence. For example, Jones et al. [53] found that increased social support via food allergy support groups, perception of fewer barriers to disease management, greater perceived severity of food allergy, and possession of an anaphylaxis management plan (from physicians/medical team) were all associated with better adherence for adolescents. Some allergy researchers have also begun to create measures to measure barriers to adherence in adolescents with food allergies. Herbert et al. [55] developed a measure of facilitators and barriers to food allergy management for adolescents. Preliminary results indicate the measure has reliability and some predictive validity, with individuals who are more adherent more likely to report more facilitators, while less adherent individuals identify more barriers.

Conclusion and Implications

Adolescence is a period of time characterized by neurodevelopmental and psychosocial changes. This developmental stage includes increased occurrence of mental health diagnoses, an increase in psychosocial stressors, changes in social network and influences, and desire for autonomy. In working with adolescents, a biopsychosocial perspective is of paramount importance in understanding the dynamic influences contributing to their behaviors. Specifically, while an adolescent may present as cognitively and developmentally mature, providers should recognize that

neurological, emotional, and social growth continues into adulthood. Thus, our work with adolescents is best when we offer a balanced perspective of respecting their desire for autonomy and increased responsibility while also recognizing they are not quite adults. Understanding and valuing these multiple components of influence can help providers most appropriately align with adolescents with allergies.

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Chapter 3

How Can We Best Communicate with Adolescents?



R. Claire Roden and Elise D. Berlan

Introduction

Pediatric patients with normal development require a transition in care from a parent-focused model of care to an adolescent-focused model at some point during their teenage years and beyond that to an adult model of care around age 18 years. There are two major challenges to the physician-patient relationship during this period of time: one, how to effectively communicate with the adolescent patient, and two, how to transition them to the adult provider who will ultimately provide care when the teen has reached adulthood. In this chapter, we will explore effective communication strategies for talking with adolescents and their families, as well as the elements of an effective transition to an adult-style model of care.

How to Effectively Communicate with Adolescent Patients and Their Families

Successful communication with adolescent patients requires a style distinct from what might be useful for communicating either with younger children and their families or with adult patients. This is largely due to the developmental tasks of adolescence: it is both normal for teenagers to become more independent as they age [1], and in order to have successful transition of care, the patient must develop

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a sense of ownership over their health¹ [2]. Adolescent patients benefit from time alone with their physician, with most professional organizations recommending some time devoted to confidential conversation alone between the physician and the teenage patient [3]. Important considerations for communication with adolescent patients include (1) cognizance of the adolescent mindset during conversation with a healthcare provider, (2) importance of speaking directly with the adolescent patient, (3) importance of confidential conversation with the adolescent patient, and (4) being aware of common communication pitfalls.

The Adolescent Mindset

Two important concepts for a strong relationship with adolescent patients include collaborative communication and patient-centered care. On the surface, these two ideas seem self-explanatory; however, in the context of adolescence, when the patient is extremely self-conscious and experiencing self-awareness for the first time as a normal developmental milestone, these two approaches are both essential and challenging to adopt.

Collaborative communication is a practice that “emphasizes the relationship between people, viewing interpersonal communication and relationships as inexorably entwined [4].” In this case, the relationship is between the adolescent patient and the healthcare provider. While relationship-based communication may seem unusual, even inappropriate, to some physicians, there are data to show that an emotional connection between a patient and provider leads to improved health outcomes in teenage patients [2]. Younger teenagers, in particular, are more likely to be sensitive to the inherent power differential between the physician and the patient [5]. These younger patients tend to be more likely to reveal pertinent information to their physician if the physician is cognizant and respectful of this relationship dynamic [5], and they tend to value a warmer, more open relationship with their physician [6].

Direct Communication

An important illustration of this is the feeling of the adolescent being “left out” of their own care, which is a recurring theme in research in communication styles between adolescent patients and physicians. In a qualitative study of interviews with medically complex adolescents, one young woman summed up this sentiment as “I go to see [the doctor], but I’m not sure why ‘cos mum talks about things.” Another young woman with cystic fibrosis noted that “some doctors still think that dad or mum is more important than me, and they have to talk to them instead of me.

¹Please see Chap. 2 of this textbook for a more comprehensive discussion of adolescent psychosocial development.

But it's no good talking to them. I'm the one with the cough" [5]. These patients' feeling that they are not the focuses of their own care highlights a major sticking point in interactions between teenagers and physicians: the importance of thorough communication between the physician and patient, as well as the importance of private conversation.

Confidential Communication

There are several reasons for physicians of any specialty to talk to adolescent patients alone. For the parent, this skill can help lay the foundation for collaborative communication as the teenage patient ages. The practice of talking to teenage patients in confidence is associated with increased engagement with the healthcare system and patient ownership over illness process, the patient revealing more information and seeking more counseling from a provider [5] and ultimately a more successful transition from pediatric to adult care [7].

Several studies place the ideal age to begin speaking to teens alone, or to at the very least begin addressing patients themselves instead of their parents, at around ages 13–14 [6, 8]. During this period of middle adolescence, teenage patients generally start to do more information gathering on their own during visits with the physician, with parents taking more of a supportive role [6]. Teenage patients also generally start to have more conversations aimed at exploring their relationship with their provider around this time period, whereas their parents tend to have previously established this when the patient was a younger child [8]. It is understandable that in what may be a longstanding relationship between the parent-child dyad and the physician, the parent established a relationship dynamic with the provider well before the patient is in a developmentally appropriate stage to do so. As autonomy is one of the major milestones of adolescence, at some point during a prolonged physician-patient relationship, one might view it as essential that the physician seek a way to promote the adolescent's self-determination in a healthcare setting, in particular through talking to the patient in confidence [2].

The importance of a confidential interview with the adolescent patient purely for practical, information-gathering purposes cannot be overstated. Most physicians have probably encountered, at some point in their training, a visit with a teenage patient where the history and focus of a visit changes entirely with the parents absent from the room. There is surprisingly little research into this practice, and most studies of adolescent communication with physicians are conducted with a parent present for the entire history. That said, one of the rare studies that does address this notes the importance for information gathering goes both ways: not only are teenagers less likely to be entirely forthcoming with more obvious things, such as drug and alcohol use, they are also less likely to ask questions about their future health needs with a parent present. This inhibition occurs not just when parents are around, but patients feel less comfortable revealing information when more people (i.e., medical trainees) are present in the exam room [5].

How to Talk to Teens Alone

The practice of inviting parents to step out of the room can be daunting for a physician who is not already in the habit of doing so. The authors of this chapter suggest informing the family at the start of a visit that the patient can expect some time alone with the provider during the course of the appointment. A possible script after introductions might be, “At some point during this visit, I typically spend some time talking to my patients one-on-one, but before that I would like to talk to both you and your mother/father. I’ll let you know when the time has come.” In visits with an 11- or 12-year-old patient, informing the family that starting around age 13 or 14 the patient will spend some time alone with the physician can be helpful for preparing everyone for upcoming changes in communication techniques. The authors also suggest reviewing state and local laws regarding confidentiality in interviews between parents, minor patients, and a healthcare provider. Laws regarding minor patient confidentiality and parental notification may vary by state. For example, while all states and the District of Columbia allow minors to consent for treatment and testing for sexually transmitted infections, fewer than half of states have no restrictions on the ability of minors to consent to contraceptive services [9]. Laws regarding “mature minors,” or persons who are not legal adults but who may consent to their own healthcare, also vary from state to state [9]. This variability in state law as it applies to children necessitates that clinicians be aware of what services they can and cannot provide to teenage patients who present for care without parents and what limits the confidentiality that they can offer to adolescents.

Confidential conversation is a fundamental part of collaborative communication, which itself is essential for patient-centered care. Patient-centered care is a communication technique characterized by two domains: one, the ability to elicit patient beliefs about health and healthcare and two, the ability to facilitate patient control over illness. Patient-centered care as a whole is associated with improved patient satisfaction, and its second domain in particular is associated with improved health-related outcomes [10].

Respect and Communication

A central idea to this model of care is the concept of respect. Respect can be a nebulous idea, especially as it pertains to the patient-physician relationship. It can be defined as highly valuing patient autonomy or the practice of “unconditionally recognizing, accepting, and valuing patients as persons” [11]. In studies of respect, as in studies of “liking,” there is significant correlation between both the patient’s and physician’s perception of mutual respect and increased completeness of information sharing between both [11]. To that end, physicians who self-identify as having a patient-centered style of communication usually do. In studies designed to measure the amount and quality of physician and patient speech, these physicians tend to have speech that displays a lot of support, information sharing, and partnership-building qualities [12].

On a less formal note, the authors recall a pearl from their general pediatrics training. An attending pediatrician once remarked that “If you find yourself feeling a certain kind of way with a patient or family, they are almost certainly feeling that way about you, too.” There is extensive literature to support this sentiment [4, 12].

Common Communication Missteps

There are certain communication pitfalls to be careful to avoid when caring for adolescent patients. Some of the more pertinent ones include (1) heuristics, (2) unconscious biases, and (3) condition-centered speech (see Table 3.1).

Heuristics are the “habits of thought” that can both guide conversational form and structure as well as form the basis of bias. These habits can include deciding how likely a certain outcome is based on how easy it is to visualize, the practice of considering risks first before benefits (or vice versa), and the habit of avoiding uncomfortable or painful thoughts [4]. While heuristics are quite literally the foundation of most communication between any two humans, these thought habits can also interfere with clear and appropriate communication with adolescent patients. For example, sexuality and sexual practices in the context of chronic illness are a very uncomfortable topic for many adults as well as most teens, but addressing this

Table 3.1 Summary of common communication pitfalls

Communication error	Description	Examples	Why this matters
Heuristics	Habits of thought [4]	Deciding that an outcome is likely because it can be easily imagined; avoiding painful or uncomfortable thoughts; considering risks before benefits in decision-making	May lead to inappropriate or incomplete counseling, may cause inappropriate hope or anxiety related to disease outcomes or natural history, may cause the provider to obtain incomplete histories, can form the basis of unconscious biases
Unconscious bias	Thoughts or feelings about a particular group or topic, in particular based on emotion instead of facts	Non-black physicians are more likely to perceive black patients as dissatisfied with care [12]; children of college graduates are more likely to converse with physicians than children whose parents did not attend college [8]	Contributes to ineffective care, hampers process of transition of care, can reinforce preexisting power dynamics, can unintentionally project a lack of respect
Condition-centered speech	Focusing conversation on the patient’s illness [5]	The use of jargon or medical terminology, little discussion of quality of life, little discussion of ease of access to care	Erases the patient’s lived experience, disempowering, may contribute to poor adherence

concern—in private, of course—directly and in a nonjudgmental manner can be important for providing complete, patient-centered care to an adolescent who might otherwise be paralyzed with discomfort surrounding a topic where they both want information and are too nervous to ask for it [5]. The need to acknowledge potentially harmful or biased heuristics that a physician might have is essential for providing good care to teenagers, who are in a developmental stage of making their own “habits of thought.”

This ties in with the concepts of respect and power dynamics: providers are obliged to examine their practices for habits that might unintentionally convey a lack of respect for their teenage patient or that might reinforce the already-existing power differential between teen and adult and patient and physician. Heuristics can, as previously discussed, form the basis of bias. Most humans have some unconscious biases, and these can inhibit high-quality care. Specifically, in terms of communication research, non-black physicians tend to perceive black patients as less satisfied with their care and are more likely to have a mutually contentious relationship [12]. Another example is that children of college graduates tend to have significantly more relationship-building conversation with their physicians than their peers whose parents did not attend college [8] and may contribute to less effective transition to adult care. Both of these biases harm doctor-patient relationship.

Finally, an important cause of ineffective communication is illness-centered, instead of patient-centered, speech. This is the practice of focusing conversation on questions from the provider to the patient (or their family) with an emphasis on illness symptoms and less on quality of life, with less time devoted to questions from the patient. This type of speech may also involve the use of jargon or medical terminology. Patients with chronic illness are both particularly likely to be the subject of illness-centered speech and also particularly likely to find it disempowering. One young woman in a qualitative study noted that when her doctor spoke to her or her family in this way, she felt that “he’s more interested in what’s happening inside me than what I’m going to ask” [5]. This type of communication can include focusing questions only on physical symptoms and adherence, as opposed to also inquiring after the impact of disease on the patient’s life as a whole. An example of this may be asking a diabetic patient questions about blood sugar management without discussing the impact the school day has on eating and activity.

Why Does Communication Matter to Adolescent Transition?

The goal of practicing patient-centered care and collaborative communication with teenage patients should be to improve health outcomes, improve adolescent engagement with the healthcare system, and facilitate self-management as the patient approaches adulthood. For the teenage patient, “adherence” and “self-management” may be thought of as two distinct concepts, both of which should be addressed prior to transition [13]. These two concepts are often considered interchangeable, but

viewing them as separate domains can clarify social or structural areas that impede a smooth transition to adult care.

“Self-management” is the set of behaviors that a patient exhibits, regardless of their positive or negative values, with respect to their healthcare management. This is influenced by individual, family, healthcare system, and community-based factors [13]. For example, the behavior of going to a pharmacy to pick up a filled prescription requires action on the part of both the individual and their family; it requires a healthcare system where filling appropriate prescriptions is both uncomplicated and affordable, and it requires the community-based factor of the presence of a pharmacy that the patient can access.

Adherence is the degree to which behaviors of self-management are medically recommended [13]. An example of the distinction between adherence and self-management may be the practice of intentional non-immunization: patients that choose this path are actively making a healthcare management decision based in their own value system, which is influenced by individual, family, community, and healthcare system-based factors, but their decision is generally not medically recommended and therefore not considered “adherent.” Ideally, behaviors of self-management reflect adherence to medical recommendations, and maximizing this overlap can be achieved with effective communication.

In discussing transition of care, it is useful to consider a model of how adolescents make decisions within the context of their families. The discussion regarding what transition is and how it happens should ideally be discussed with the patient and family before any intervention actually takes place, and a framework for decision-making within the context of a patient-parent dyad (or triad) should be in place prior to these discussions. There are two general models for decision-making: the “in-control agent” and “relational autonomy” [14] (see Fig. 3.1).

The “in-control agent” model of decision-making has two foundations: one, that patient autonomy is to be respected above all else and that the party making decisions is always using a rational thought process in the best interest of whoever the decision affects [14]. This model of decision-making suggests that outside parties (such as physicians) and emotions should not exert undue influence on the rational capacities of a patient or their decision-making surrogate. As a result, physicians and other healthcare providers may have a limited role in guiding decision-making: they may, for example, present available options without making a specific recommendation for course of treatment.

The “relational autonomy” model places patients within the context of all the other relationships in their lives when making decisions. For example, this model may acknowledge that an adolescent looks to outside parties—like their friends, family, or physician—when making complicated decisions [14]. Ultimately, this model for decision-making is more of a team-based approach, and allows the physician, if requested to do so, to offer more explicit guidance than the in-control agent model. With relational autonomy, emotions and relationships are not necessarily the weaknesses and barriers that they may be to the in-control agent, who is presumed to act in a rational fashion even when doing so is virtually impossible.

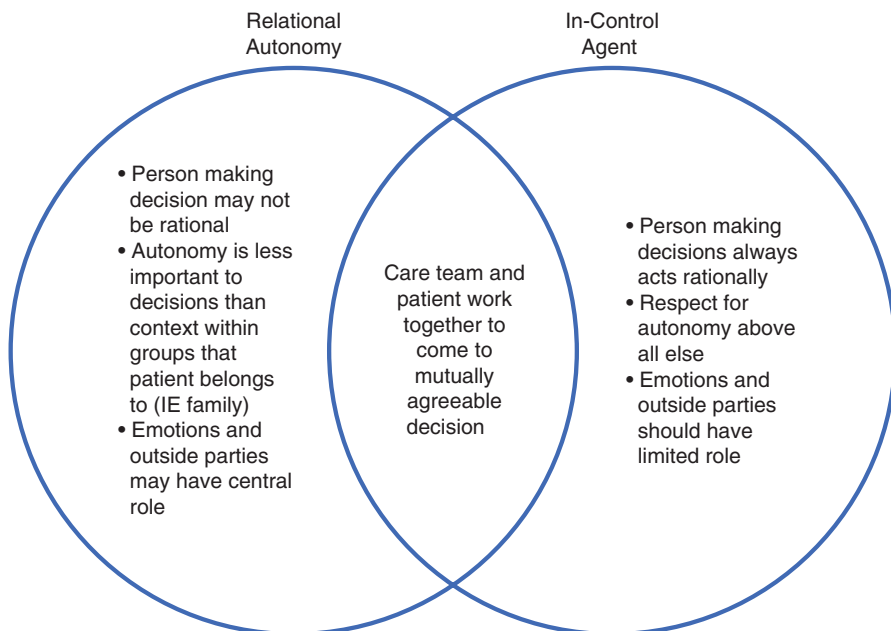


Fig. 3.1 Schematic of relational autonomy and in-control agent decision-making models

Within the context of transition from pediatric to adult care, the authors suggest that a relational autonomy approach to communication may be more appropriate than an in-control agent approach, as conversations about transition ideally take place over the course of several years [3, 15] and within the context of the family transitioning from primary to secondary decision-makers as the adolescent moves through normal development. This approach allows the family to look to the patient, as well as the transition team, for guidance in decisions when then patient is younger, and allows for a smoother change as the decision-making party evolves from the family to the patient.

How to Effectively Transition Care for Adolescent Patients and Their Families

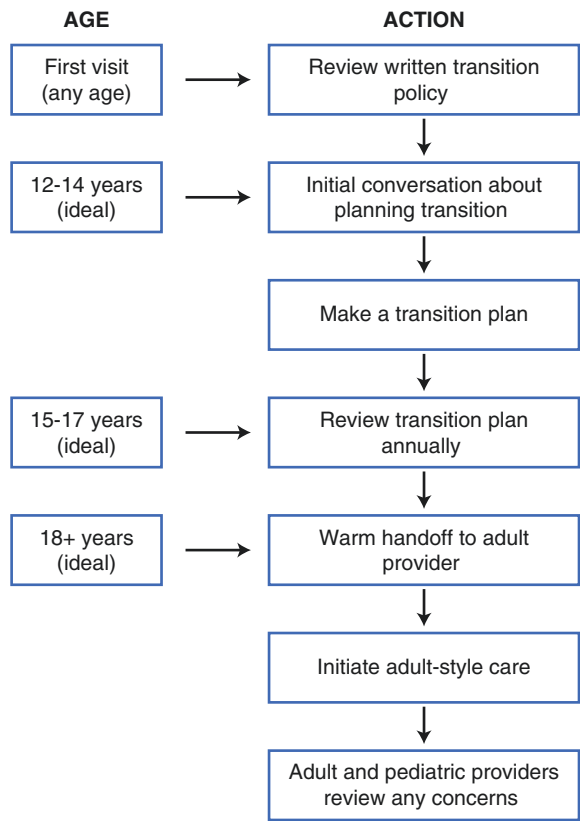
“Transition” or “transition of care” refers to the process of graduating a patient from a pediatric model of either specialty or primary care to an adult model. The process should also ideally involve a spoken or written communication between the pediatric and planned adult providers. In many instances this happens at age 18, or the age of majority, though this cut-off may be institution-dependent. This transition in style of care should occur regardless of the primary training of the physician in question, should they be a pediatrician, family medicine physician, internist, or

internist-pediatrician, as the right to developmentally appropriate care is essential for all patients. For example, a patient may see the same internal medicine-pediatrics-trained allergist from age 6 to well into adulthood. Even if the patient does not change providers at age 18, the provider should “transition” the patient to adult-style care within the same office when the patient has reached the age of majority. Patients with chronic healthcare needs require a more complex healthcare transition plan [3, 16, 17].

The importance of a purposeful, planned transition of care is difficult to overstate. Most transitions tend to resemble “a drift away from pediatric care rather than a clearly planned and executed handoff,” [3] with several systemic barriers in place that greatly reduce the chances of a transition going smoothly. These barriers can include financial and time constraints, anxiety, lack of appropriate training, hospital protocols and policies, and restrictions from third-party payers than may impede appropriate access to care for patients and families in the process of transitioning from pediatric to adult care [3, 16]. While it is crucial to acknowledge these numerous obstacles, it is more important to recognize the known medical complications of a poorly executed transition, which can include increased hospitalizations, decreased adherence and self-management of care regimens, and loss to follow-up [15]. Because of the clear risks of incomplete or poorly planned transition, all physicians who provide care to pediatric patients should have a transition policy in place and should adhere to it.

There are several models of transition of care, with numerous widely available charts and graphs demonstrating various algorithms for transition of care. Detailed discussion of a specific such algorithm is beyond the scope of this chapter. Excellent, detailed examples are available from GotTransition.org [17] and the American Academy of Pediatrics (AAP) [3], among others. The goal of this section is to discuss features and recommendations for planned transitions to maximize the chance of smooth transfer of care from the pediatric to adult medical worlds, based upon guidelines from multiple groups (see Fig. 3.2). One of the most universally recommended interventions regarding transition of care from a pediatric to an adult model is that discussion of transition should begin well before it actually takes place. This is recommended by the AAP, the American Academy of Family Physicians (AAFP), the American College of Physicians (ACP) [3], the Society for Adolescent Health and Medicine (SAHM) [16], and the European Academy of Paediatrics (EAP) [15], among others. The EAP suggests that discussions about transition should begin around ages 13–14 years old, at the latest a year before transition is to occur and not before puberty has taken place [15]. The AAP recommends age 12–13 for similar reasons [3]. As previously discussed, the period of middle adolescence is extremely important for developing a communication style that reflects the growing independence of the adolescent and can assist with the patient taking ownership over their healthcare needs [6]. In general, providers for medically complex patients tend to prefer to transition based upon age, comorbidities, and pregnancy [18]. Regardless of these preferences, a successful and smooth transition will not occur without appropriate patient ownership of medical conditions, as previously discussed [3, 15]

Fig. 3.2 Schematic of general plan of care for transition



As discussion about transition should begin at a relatively young age, these conversations should remain an important, ongoing part of healthcare and should ideally take place during dedicated appointments [3, 4]. Collaborative decision-making and relational autonomy models of thought become increasingly important as transition approaches, and providers should strive to restate goals of care and reconfirm all decisions at the end of each appointment [4].

The parties to be involved in conversations surrounding transition of care vary based upon clinic setting, illness chronicity, and availability of specialty staff. The AAP and SAHM both recommend having a staff member who specializes specifically in coordinating and planning transition of care [3, 16]. This provider does not necessarily need to be a physician and could be a social worker, advanced practice nurse, physician assistant, or other patient care coordinator. Some families may prefer to have a new face handle their transition of care instead of their habitual physician, as this may paradoxically ease some of the more emotional aspects of transition and improve concerns that their physician is “rejecting” or “abandoning” them [19].

The content of these conversations should vary based upon the teenager’s developmental stage and specific healthcare needs. All pediatric offices should have a specific, written, transition policy that should be made available to all patients at the

start of conversations about transition of care, and it should include plans and timelines for when various transition milestones should occur [3]. These transition plans should include information about what to expect in the adult healthcare world. As the adolescent ages, it will be important to specifically address how laws impacting the physician-patient-parent triad change when the patient attains the age of majority. In particular, information regarding assent and adult-style consent to treatment, confidentiality, privacy, and sharing of health information (including the Health Insurance Portability and Accountability and Family Educational rights and Privacy Acts) should be made available to the patient and parent [7]. All families should also be given information about guardianship, advance directives, and healthcare proxies, though families with complex healthcare needs may require this information earlier or more in-depth in their transition [3, 15–17].

Conclusion

As we have discussed throughout this chapter, communication and transition of care for adolescent patients are very complex and rich topics. There is no one single way to appropriately communicate with patients and families, but awareness of the specific communication needs of teenagers as they relate to adolescent development and the changing role of the parent in healthcare can help improve the relationship with the physician and ultimately lead to a smoother transition of care. Transition of care itself is often characterized by a period of drifting away from the pediatric world and fumbling into the adult world and can be a time of increased risk of poor health outcomes, even for generally uncomplicated youth. A strong foundation in clear communication techniques and planning for transition of care can ultimately help assist the adolescent in becoming the happy, healthy, functional adult that all pediatric providers want their patients to become.

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Chapter 4

The Many Faces of Nonadherence in Adolescents



Michael R. Gionfriddo

Introduction

Allergic diseases, such as allergic rhinitis, asthma, and eczema, affect millions of adolescents [1–4]. These conditions cause significant morbidity and mortality. For example, it is estimated that uncontrolled asthma was associated with nearly 14 million missed school days in the United States in 2013 [5]. Many treatments exist which can help manage the symptoms of these diseases and prevent acute exacerbations. Unfortunately, many adolescents have trouble integrating these treatments into their daily lives. As a result of nonadherence, adolescents put themselves at risk of poor outcomes ranging from poorly controlled chronic symptoms to death. For example, children and adolescents who have asthma and lower levels of adherence to controller medications have higher risk of asthma exacerbation [6]. There are many factors which contribute to adolescents' medication taking behavior. Understanding the many faces of nonadherence can help healthcare professionals, parents, and adolescents develop strategies to successfully integrate treatment into their daily lives, thereby reducing their risk of adverse outcomes and improving their quality of life.

This chapter will review the complex nature of multiple different factors which can all contribute to nonadherence among adolescents with allergic diseases (see Table 4.1). The examples used throughout this chapter will focus on asthma, as this is the allergic condition with the most robust literature and understanding of factors associated with nonadherence. However, many of the principles discussed herein can be applied to other allergic diseases such as allergic rhinitis, atopic dermatitis, and food allergies. The approaches described to address nonadherence in the adolescent patient with asthma can be extrapolated to these other conditions as well.

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Table 4.1 Multiple factors involved in nonadherence

Drug factors	Nondrug factors
Improper use of devices (inhalers)	Lack of instruction regarding proper use
Cost of medication	Concern about side effects
Difficult dosing (multiple times/day)	Dissatisfaction with health care professionals
Side effects	Poor supervision, training, or follow-up
Dislike of medication	Anger/denial about condition
Limited access to pharmacy	Underestimation of disease severity
	Forgetfulness

Clinical Vignettes

Asthma

Susan is a 15-year-old girl. Susan is very competitive and likes to play soccer. Susan also has mild asthma. To manage her asthma, she is prescribed a daily low-dose controller medicine as well as a rescue inhaler. Her asthma is triggered by exercise as well as by seasonal allergies. Her mother reminds her to take her medication, and she is usually good about managing her asthma. Recently, she moved to a new school and has told her mother that “she’s not a kid anymore and doesn’t need to be babied.”

Food Allergies

James is a 13-year-old boy. James likes to hike and play baseball. James is also allergic to peanuts, but he doesn’t like to talk about it. As a precaution James is supposed to carry his epinephrine auto-injector with him at all times. Unfortunately, the auto-injector is very expensive. In addition, James is often “on the go” and frequently forgets to carry his auto-injector with him. Fortunately, James does not have to use it very often. He also finds it difficult to speak up in groups and is reluctant to “announce” that he has a food allergy when going out to restaurants with friends or his baseball team.

Allergic Rhinitis

Mary is an 18-year-old girl. In the spring, Mary graduated from high school and over the summer moved to a new town to start college. Mary has a roommate Beth who has a cat. Recently, Mary was diagnosed with allergic rhinitis. To manage her symptoms, Mary was prescribed a nasal spray. Mary dislikes using the nasal spray and often self-treats with an over-the-counter antihistamine. The antihistamine, however, often makes her drowsy, so she often goes without and experiences symptoms as a result. Beth also lets her cat go throughout their apartment, including on Mary’s bed.

Factors Which Affect Adolescents’ Treatment Adherence Behavior

An adolescent’s ability to adhere to treatment is challenging and often not dependent upon any specific factor, but ultimately the result of many different factors contributing to one another (see Fig. 4.1). These factors include the adolescent’s

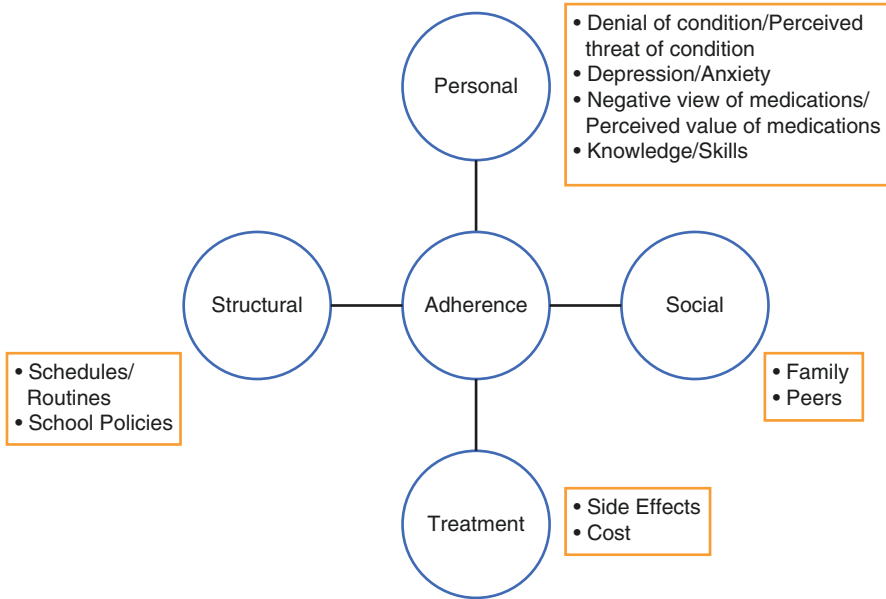


Fig. 4.1 Factors affecting adherence in the adolescent with an allergic disease

self-perception, their condition, the treatments prescribed to manage their condition, and their understanding of others' (e.g., family, friends, community, society) perceptions. In addition to their personal perceptions, the knowledge or skills of the adolescent contribute to their ability to adhere, as does their ability to make treatment part of their routine and integrate it into their busy schedules. Intrinsic factors related to the condition or the treatment, such as a medication's propensity for causing undesirable effects, also affect adolescents' decision-making. Finally, factors external to the adolescent, such as school policies, affect adolescents' abilities to adhere to their prescribed treatment regimens.

Personal Factors

Denial and Depression

The manner in which an adolescent views their self, their illness, and their place in the world may affect their ability to adhere to medications. Allergic diseases, while often diagnosed by a healthcare provider, are experienced first by the adolescent. The meaning or etiology the adolescent applies to these symptoms may not match those of the medical establishment. The adolescent may deny that they have the disease. For some, this may be due to differing illness narratives, where the adolescent attributes their symptoms to a different illness [7]. In asthma, for example, parental illness models which differ from those of the medical establishment may contribute to nonadherence [8, 9].

Adolescents may also deny they have the illness altogether [10, 11]. This has been found in studies of adults with asthma, where issues such as stigma and negative perceptions of the illness contributed to denial [10]. The negative connotations associated with the label of “asthma” made it such that individuals did not want to accept it as part of their identity. These feelings affected behavior, with those who denied or distanced themselves from asthma unlikely to adhere to medication use because to some, taking the medication would be synonymous with accepting that they have asthma. This finding has been confirmed among adolescents [12–15]. As one adolescent stated in a focus group: “It’s like, trying to escape from it. Like, maybe if I don’t have to take the medicine it’ll go away, or like if I take the medicine then I’m like accepting the fact that I have this” [14].

Adolescents may also have views of medications which do not promote adherence. A general dislike of medications is common [11]. Some adolescents with asthma may also hold these views, which contributes to nonadherence [15, 16]. As one adolescent stated: “I don’t think it’s [taking medications] a good idea and it’s really degrading like taking pills all the time... It like makes you feel ill, it’s a reminder sitting there saying you’re ill and it’s not nice, it puts you down taking pills” [15].

In addition to adolescents’ views of their illness and treatments, their views regarding themselves and their place in the world may affect their ability to manage their treatment regimens. Specifically, depression and anxiety have been linked to lower levels of medication adherence, including in asthma [17–20]. This link has been explored in adolescents with asthma; however, the relationship between asthma, depression, anxiety, and adherence is still unclear [21–23]. While further work needs to be done to clarify this relationship, clinicians treating adolescents with asthma should monitor for symptoms of depression and anxiety and manage appropriately, as depression and anxiety have been independently associated, although not consistently, with worse asthma control and more exacerbations [20, 23–25].

Perceived Threat of Condition

Many adolescents explore their independence through taking risks, including non-adherence to treatment for their allergic disease [21]. Contributing to this risk-taking behavior is a sense that the disease is not a threat. For example, among a sample of adolescents with food allergies, those who perceived their allergy to be more severe were more likely to be adherent to self-care behaviors, such as carrying their auto-injector with them (OR = 1.24 95% CI 1.01–1.52) [26]. Another study of young adults with asthma found that the most common reason for nonadherence was lack of perceived need, driven mostly by a feeling that they felt well without using the medication [27]. Similarly, qualitative studies have found that some adolescents link the severity of asthma with the necessity for using medications [14, 28–30]. For example, one adolescent discussed how her asthma wasn’t as bad as others, and as a result she doesn’t need to take her medication: “I think people have it [asthma] a

lot worse than me and it's like I just like don't need it [corticosteroid inhaler] sometimes and I can go, I can go a few days without it..." [28].

For some adolescents, the threat of the disease wanes over time. In these situations, nonadherence may transition from an unintentional (i.e., forgetting) to a more active or intentional process as they experiment with whether or not they need the medications [12, 13, 28, 31]. In some cases, the adolescent stops taking their medicine altogether, but in other cases, this process of experimentation reinforces the need to take their medicine. For example, one adolescent stated: "When I first started it was OK but then I forgot a couple of times, and then I couldn't be bothered to do it, to try and remember. I thought, 'oh no, it's not worth it, I'm alright, you know, I don't need it.' But I've found out since I've been taking it that's it's really helped me..." [31].

Perceived Value of Treatment

While for some adolescents, the threat of the disease can affect adherence, for others a contributor to nonadherence is uncertainty around the effectiveness or value of the treatment. If adolescents believe that the treatment is ineffective, they are less likely to adhere to the medication [12, 32–36]. For example, in one study, one adolescent described how he felt his inhalers worked so he took them, while he felt his other medicines did not work so he often forgot to take them: "I don't usually forget to take my inhalers cos I know that they help, I can't really feel the tablets helping so I usually forget to take them" [32].

Knowledge and Skills

Knowledge contributes to how an adolescent views their disease and treatment. Many adolescents often have misconceptions that may contribute to nonadherence. While there is some inconsistency [37], the literature appears to support a link between knowledge and adherence [22, 37, 38]. A reason for this inconsistency may be due to whether the parent of the adolescent was questioned about knowledge, as well as the shared responsibility for asthma management that occurs between adolescents and their caregivers. The difficulty in measuring knowledge likely also contributes to this discrepancy [39]. However, there is evidence that adolescents may have knowledge of asthma and yet fail to act on that knowledge [40, 41]. In these situations, other barriers, such as forgetfulness, may affect an adolescent's ability to adhere to medication [12, 36].

One example of how knowledge can contribute to nonadherence is a lack of understanding surrounding the differences between preventer or controller medications such as inhaled corticosteroids and reliever medications such as short-acting β -agonists [14, 32]. Such confusion may prove harmful for adolescents as they fail to gain the full benefit of controller medications, such as inhaled corticosteroids, if they use them on only an as-needed basis when they have symptoms [14, 42]. While

this strategy in particular can be an effective treatment strategy for some specific patients [43], using controller medications on an as-needed basis is a common form of nonadherence.

Another example of a common misunderstanding that may influence medication adherence in asthma is the belief that, rather than being a chronic illness, asthma is something which is acute and episodic, exemplified by the phrase “no symptoms, no asthma” [44], or something that could be “outgrown” [14, 40, 45]. This belief tends to minimize the importance of controller medications to help prevent symptoms of asthma, which can then lead to reliance or overuse of reliever medication [31]. For some, this was an intentional behavior, as one boy stated: “I’ll take it [medication] when I feel symptoms” [9]. Yet, for others, symptoms served as a reminder to take medications, and therefore a lack of symptoms led to forgetting to take the medication [46].

An important component of adherence is not only taking the medication but taking it correctly [47]. Incorrect use of medication can include taking it more or less often than prescribed, using doses different from what was prescribed, and, with asthma in particular, incorrect inhaler technique. Many adolescents with asthma struggle with incorrect inhaler technique [48, 49], which has been associated with higher rates of hospitalizations and lower rates of asthma control [49, 50]. While several interventions have been tested to improve asthma inhaler technique, it is currently unclear which approach is best, especially among adolescents [51]. Regardless, clinicians should assess inhaler technique regularly and educate adolescents on the appropriate technique, along with the opportunity to practice in the office setting with a trainer device (or their own inhaler). Adolescents should be encouraged to communicate with their clinician if they are not confident or have questions regarding their inhaler technique [52].

Social Factors

Family

Family has an important influence on adolescents’ medication taking behavior. This influence can either positively or negatively affect medication adherence. Parental illness beliefs were highlighted above as a potential factor influencing adolescents’ adherence [8, 9], but other factors can also affect adherence, such as parental beliefs about medications [53, 54].

Adolescence is a time of transition where the adolescent grows increasingly independent, including in the management of their health. However, adolescents often continue to rely on their parents for support in managing their health during this transition [55]. While one study found no difference in adherence based upon level of family support [56], several studies have highlighted the importance parental support can play in promoting adherence. For example, adolescents often rely on their parents to remind them to take their medication [9, 12, 32, 35, 36, 55, 57, 58]. As one adolescent stated: “I take them by myself but my mom has to remind me

otherwise I don't do it" [32]. For some adolescents these reminders were annoying but still useful: "... [My mother reminding me] gets annoying, but it helps because I don't forget..." [35]. This strategy, however, can also be counterproductive as the adolescent attempts to assert their independence. In a few studies, adolescents reported that they lied about medication use [32, 55]. Sometimes this is done out of laziness. As one adolescent stated: "Sometimes, most of the time my mum says, 'have you took it' and I just can't be bothered to go and take it but I say I have so she don't get worried, well I can't really be bothered if I am walking to the kitchen, so I just tell her I have" [32]. Other times, it is about asserting independence: "It's rather annoying my mother asking me daily if I've taken my Flixotide. What's that got to do with her? I don't want get mixed up in her problems either. I'll take it when I feel symptoms" [9].

As the adolescent transitions toward independence, more responsibility is placed upon them for managing their disease. During this transition, however, the management of the disease may suffer as tasks previously delegated to the parent are taken on by the adolescent [40, 59]. For example, monitoring the amount of medication and requesting a refill when necessary [40], or adhering to medication: "My mother used to be like you know you got to do your inhaler, use the machine before you go out and so she would prevent it from happening, but now I just wait for it to happen..." [59]. During this transitional period, care must be given to both support the adolescent and at the same time allow them to take on more responsibility. The amount of support given should be gauged on an individual level and based upon factors such as willingness to accept responsibility, maturity, and knowledge of asthma and asthma medications and not based upon age. Clinicians and parents should also recognize that the adolescent's need for support may fluctuate based upon their situation, as well as over time. For example, during particularly busy or stressful times, or if the adolescent begins to suffer from anxiety or depression, additional support may need to be given to maintain adherence and disease control.

Peers

Like family, peers can also either have a positive or negative influence on adolescents' adherence behavior. While peers can be supportive and promote adherence behavior [13, 33, 60, 61], they can also have the opposite effect [56]. Additionally, perceived or actual stigmatization of the adolescent with an allergic disease by their peers may negatively affect adherence. Many adolescents desire to be viewed as "normal," and having the allergic condition sets them apart, which can lead them to be labeled as "abnormal," either by themselves or others [30, 34, 62]. In conditions such as asthma, use of medication in public may also set them apart. While not universal [14, 31, 33, 63], many adolescents with asthma report being embarrassed to take their inhalers in public, and as a result they either hide to take their medicine or avoid taking it in public altogether [13, 34, 58, 60, 64–67]. As one adolescent stated: "It was very embarrassing for me to take my inhaler. People know about asthma, and yet they treat you weird. I used to hide myself taking my inhaler because I hated it when people looked at me. I felt offended, I felt ashamed" [66].

Treatment-Related Factors

Side Effects

Side effects related to treatments for allergic diseases can negatively affect medication adherence. Inhaled corticosteroids, a common treatment for asthma, have been associated with a variety of side effects, including dysphonia (difficulty speaking), infection (especially oral infection such as oral candidiasis), cough, osteoporosis, cataracts, and impaired growth [52]. Some adolescents may also experience weight gain if they require oral systemic corticosteroids [52, 64]. For some, side effects may be so bothersome or severe that they discontinue therapy [12, 32, 33, 59, 64, 66, 68]. As one adolescent stated: “When I’m reaping all the side effects and I was just thinking, you know, nuts to this, look at me I’m a mess and asthma is ok I’m just not gonna take them for a while to see what happens” [32].

The main treatment for the immediate relief of asthma symptoms, short-acting β -agonists, is also associated with side effects. The most common side effects include tremor and tachycardia [52]. Adolescents sometimes also report anxiety or feeling “hyper,” which may contribute to nonadherence [34]. In addition to the abovementioned side effects, some adolescents were concerned about becoming dependent or addicted to the medication [29, 33], while others complained that the inhalers have a bad taste and this contributed to their decisions to be nonadherent [29, 33, 46, 59, 63].

Cost

The treatments for allergic diseases can often be expensive. While many adolescents do not directly pay for their medications, they can be sensitive to the pressures that cost may place upon their family. This can sometimes lead to adolescents rationing their medication to avoid having to refill the medication as frequently [14, 58]. Other adolescents and their families can simply not afford the medication or face other barriers to accessing the medication (e.g., transportation) [14, 45, 66]. Clinicians should explore the extent to which cost is a concern for the adolescent and their family, and when possible, prescribe less expensive alternatives. In situations where this is not possible, focusing on non-pharmacologic approaches to manage the disease (e.g., breathing exercises in asthma), or connecting the adolescent and their family with resources which may help cover the cost of the prescriptions, may help to facilitate adherence.

Structural Factors

Schedules and Routines

Adolescents often have busy schedules. Some adolescents can incorporate disease management into their routines, which facilitates adherence [12, 13, 63], while others cannot. Even among adolescents who incorporate disease management into their routines, when their routines get disrupted, nonadherence may result. For example, if the

adolescent is running late for school, they may end up forgetting their medication in their haste to catch the bus, or prioritize getting to school over taking their medication, especially if it is perceived as being time consuming [14, 16, 32, 34, 46, 57, 60, 63]. As one adolescent stated: “Sometimes I forget... Because like when I’m getting ready for school, I have to try and get my breakfast and my stuff packed and my bag down by the door and get dressed and all that stuff, so I hardly have time for puffers” [46].

School Policies

In qualitative studies of adolescents with asthma, several adolescents described situations where school policies were not conducive to adhering to their medications [59, 69, 70]. For example, adolescents may not be allowed to carry their medication with them and may have to either keep it in their locker or keep it stored in the nurse’s or administrator’s office. In these situations, adolescents may experience distressing symptoms without access to relief, as one adolescent recalled: “I was in PE and having trouble breathing and [the teacher] said ‘Well, we’re almost done so just wait a minute,’ and she wouldn’t let me go inside to get my inhaler” [70]. Clinicians and parents should understand local school policies as it relates to medication to ensure that adolescents have timely access to medication to facilitate both optimal medication adherence as well as the least amount of symptoms or distress possible.

Conclusion

Nonadherence in adolescents with allergic diseases is not a simple behavior. There are many factors which contribute to nonadherence in the adolescent. Many times, nonadherence is unintentional, such as when the adolescent forgets to take the medication, which has a variety of causes, but could also be intentional due to factors such as dislike of medicine, not believing the disease is a threat, or not finding the medication to be effective. Understanding adolescents’ reasons for nonadherence, either intentional or unintentional, is a helpful first step to tailor strategies to help overcome barriers to adherence and facilitate integration of the treatment into the adolescent’s daily life.

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Chapter 5

Allergic Rhinitis



Margaret Redmond

Background

Allergic rhinitis, historically referred to as “hay fever” or “pollinosis,” is one of a group of atopic diseases that result from the production of immunoglobulin E (IgE) antibodies to specific proteins found in environmental exposures such as pollen or dander. Rhinitis is defined as the presence of at least one of the following symptoms: nasal congestion, rhinorrhea, sneezing, and itching [1]. Rhinorrhea can be either anterior or posterior. Symptoms involving the eyes, ears, and throat are often associated with allergic rhinitis. Rhinitis is broadly classified as allergic or nonallergic, the full scope of nonallergic rhinitis will not be explored in this chapter, but a brief overview is provided in Table 5.1.

The International Study of Asthma and Allergies in Childhood published a series of studies demonstrating the prevalence of allergic rhinitis increased from 1992 to 2006. Global prevalence was between 1 and 45% with higher prevalence in industrialized countries and in adolescents compared to school age children [2]. In the National Health Interview Survey of 2015 administered by the Centers for Disease Control in the United States, 8.4% of persons less than 18 years of age or 6.1 million people reported “hay fever” in the last 12 months [3].

Rhinitis is not life-threatening but has been shown to have significant effect on quality of life. Adolescents with allergic rhinitis have been found to have a decrease in school performance, lower exam scores, and increased sleep disturbance [4, 5]. One study that looked at exam performance found that adolescents with symptomatic allergic rhinitis were 40% more likely to have a grade drop in exam performance

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Table 5.1 Types of rhinitis

<i>Allergic rhinitis</i>	
Intermittent/seasonal	IgE mediated to outdoor allergens present only for a portion of the year
Persistent/perennial	IgE mediated to indoor allergens present year round
Occupational	IgE mediated to proteins present through work exposure
Local	Absence of systemic IgE production, but reaction occurs with nasal provocation tests
<i>Nonallergic rhinitis</i>	
Infectious	Recurrent viral infection will typically cause a waxing and waning history of chronic congestion and rhinorrhea
Vasomotor	Typically triggered by irritant exposures such as cold air, strong scents, or temperature changes
Gustatory	Episodic, thin rhinorrhea triggered by hot or spicy foods
Occupational	Non-IgE mediated to chemical sensitizers present through work exposure
Hormonal	Triggered by either menses or pregnancy
Drug-induced	Either a side effect (oral contraceptives, antihypertensives) or rebound following overuse (nasal decongestant sprays)
Atrophic	Progressive atrophy of nasal mucosa occurs in older adults
Secondary to systemic disorder	Systemic diseases can be associated with rhinitis, but not typically in isolation (sarcoidosis, cystic fibrosis, granulomatosis with polyangiitis)

from between the practice and official exam and those reporting use of a sedating antihistamine on the day of exam were 70% more likely to have a grade drop [4]. This impairment illustrates the importance of appropriately treating allergic rhinitis symptoms. It was recently shown that adolescents who responded to allergic rhinitis treatment had significantly improved quality of life compared to those who did not [6].

In order to have allergic rhinitis, patients must first be sensitized to specific allergens. Sensitization occurs when antigen is taken up by antigen-presenting cells (APCs) in the tissue and then presented to CD4 naïve T cells in the presence of IL-4 and IL-13 which predispose to the formation of a Th2-type helper T cell [7]. These cells are inhibited by IL-10-secreting regulatory T cells, but there is evidence that certain Treg populations are less effective in patients with allergy [8]. Th2 cells secrete more IL-4 and IL-13, which along with co-stimulation of B cells promotes the class switching of B cells to produce IgE. Allergic reactions involve an early-phase reaction mediated by the cross-linking of IgE bound to IgE receptors on the mast cell, which results in release of preformed mediators, most notably histamine. These mediators lead to vasodilation, bronchospasm, and mucus production. The late-phase reactions are mediated by the recruitment of other immune cells and the production of TNF- α and GM-CSF [7].

Allergic rhinitis is defined by the presence of IgE antibody to proteins present in the environment (aeroallergens) and development of symptoms with exposure to the aeroallergen. A patient can be sensitized to one aeroallergen or many, but to be defined as allergic and not only sensitized, symptoms must be present with exposure. Classification of allergic rhinitis can be described using intermittent (<4 weeks)

and persistent (>4 days a week and >4 weeks duration) or seasonal (present for a portion of the year) and perennial (present year round) [1, 9]. Severity of allergic rhinitis is termed mild if there is normal sleep and no impact on daily activities, work, or leisure. Moderate/severe severity is designated when one of the following is present: abnormal sleep; impairment of daily activities, work, school, or leisure; or troublesome symptoms [9]. It is also important to note that allergic and nonallergic rhinitides are not mutually exclusive. It is possible for patients with IgE-mediated symptoms to also have symptoms triggered by typical nonallergic irritants like cold air or weather changes, a phenomenon termed mixed rhinitis [1].

Clinical Vignette

A 17-year-old female presents with a history of chronic nasal congestion. She reports that she had year-round nasal congestion for the last 3 years. She denies any sneezing or ocular symptoms. She reports that she is worse in the spring and fall. She denies any worsening symptoms around pets; she has no pets in the home. She initially attempted cetirizine 10 mg once daily but did not have improvement in her symptoms. She then was switched to fexofenadine 180 mg once daily without improvement. On exam she is found to have infraorbital vasoedema bilaterally (shiners) and erythematous, edematous nasal turbinates bilaterally. She is nervous about skin prick testing and would prefer to not have testing today. Her mother voices willingness to purchase dust mite encasements, remove the carpet in the home, and install an HEPA filter.

While allergic rhinitis is not life-threatening, this case illustrates why an accurate diagnosis is so important in directing proper treatment. Skin prick testing may reveal that she is not sensitized to any environmental allergens and that symptoms are being caused by nonallergic rhinitis. Patients with nonallergic rhinitis do not benefit from oral antihistamines, but if in the case of an inaccurate diagnosis, providers and patients may continue to pursue unhelpful forms of treatment. Allergen avoidance is an important component in the successful management of allergic rhinitis but does not provide any benefit for nonallergic rhinitis. Without an accurate diagnosis, well-intentioned parents may make significant changes in lifestyle with the removal of pets from the home, home renovation with removal of carpets, or installation of filtration symptoms that cause significant stress and expense, all without symptom benefit.

Diagnosis

The patient history and physical exam are always the most important components in establishing a diagnosis of allergic rhinitis. Factors in the history and physical exam should direct the choice of it and what diagnostic testing to pursue. In order to consider a diagnosis of rhinitis, patients must report symptoms of nasal congestion, anterior and/or posterior rhinorrhea, sneezing, or itching [1]. Allergic conjunctivitis

occurs in at least 50% of patients with allergic rhinitis and 40% of the US population [1, 10]. Symptoms can include ocular redness, itching, and watering. There is evidence that conjunctivitis symptoms are underreported, as a recent study found that while only 55% of patients self-reported ocular symptoms, when asked specifically about the presence of specific ocular symptoms, 95% of patients with allergic rhinitis had presence of allergic conjunctivitis [11]. Headache, cough, and impairment in sense of smell can also be associated with rhinitis. In allergic rhinitis, symptoms should be bilateral, but the severity of nasal congestion may rotate between left and right sides due to the underlying nasal cycle wherein the nasal airways have alternating congestion and decongestion [12]. If a patient reports that symptoms of congestion, drainage, or fullness are present only unilaterally, this should raise suspicion that an anatomic abnormality or foreign body may be contributing to symptoms. Risk factors that can be identified from history include a family history of atopy, with increased risk if both parents are atopic [1, 13, 14].

The timing and duration of symptoms also play an important role in identifying allergic rhinitis. While timing varies depending upon geographic location, in North America, tree pollen is released in the spring, grass pollen in the summer, and weed pollen in the fall. The effect of climate change on aeroallergens is twofold. Plants exposed to elevated levels of carbon dioxide produce more pollen, and pollen seasons are being lengthened by warmer weather [15]. If the first frost does not occur until December or January, it is very possible for historically autumnal weed pollen allergens to persist into the winter months. Another factor that can distinguish between allergic and nonallergic rhinitis is a history of symptoms triggered by the change of season (classically nonallergic) versus worsening as the pollen season continues. The priming effect associated with allergic rhinitis leads to a decrease in the amount of allergen needed to trigger symptoms after prolonged exposure to the allergen, thus resulting in worsening symptoms as the pollen season progresses and a subsequent delay in symptom relief after the end of pollen season [16, 17].

The presence of physical exam findings that are classically considered allergic, i.e., the allergic salute and allergic shiners, is not predictive of allergic rhinitis, *per se*, but can be present in any child with chronic rhinitis symptoms. The transverse crease across the nose is a physical change secondary to repeated rubbing of the nose, regardless of cause. Infraorbital vasoedema (shiners) is caused by an accumulation of fluid in the vasculature of the orbicularis oculi muscle and the overlying thin eyelid skin, and any cause of nasal congestion can cause this fluid retention [18]. Similarly, while pale, edematous nasal turbinates are more often seen in allergic rhinitis and erythematous nasal mucosa in nonallergic rhinitis, these exam findings alone are not sufficient to make a diagnosis.

The presence of specific IgE antibody toward aeroallergens determines sensitization. These antibodies can be detected by either skin prick or *in vitro* testing. While a serum total IgE > 100 IU/mL prior to age 6 is associated with increased risk of allergic rhinitis, there is not a role for obtaining total serum IgE in the diagnosis of allergic rhinitis [19]. Skin prick testing generally is preferred over serum IgE testing as it provides improved sensitivity, but if a patient has severe eczema, has dermatographism, or is unable to discontinue antihistamine medications due to symptom severity, serum IgE testing is an acceptable alternative [1]. Skin prick testing has

been shown to be clinically reliable with sensitivity between 85 and 87% [20, 21]. The immune system is not static, and sensitization can change over time. A study following a large population in Denmark over 20 years showed that sensitization peaked in adolescence but that sensitized individuals can become desensitized. Of the population who had skin prick testing conducted four times over 20 years, 34% developed new sensitization and 22% became desensitized [22]. Intradermal testing has been shown to be more sensitive than skin prick testing, but less specific, as some of that improved sensitivity seems to be related to an irritant effect [23]. Intradermal testing can provide diagnostic benefit if you have a patient with a very clear history of symptoms with a specific exposure but negative skin prick testing and especially if the identification of specific allergies will impact treatment. Because of increased risk of systemic reaction with intradermal testing, skin prick testing should always be done prior to intradermal testing [24]. Specific organ provocation testing is the gold standard in research settings but is very rarely part of routine clinical practice for a variety of practical reasons.

Clinical Vignette

A 12-year-old male presents with year-round symptoms of nasal congestion, sneezing, and itchy nose. He has a history of previous testing that revealed sensitization to tree pollen, weed pollen, and dog. Symptoms were previously mild, and he preferred to treat with fexofenadine 180 mg once daily. He notes that the medication helps when he remembers to take it. He played baseball for the first time this year and reports that his symptoms were much worse in the spring. He also notes that he often is particularly stuffy in the morning. These symptoms have been present for years, but he did not feel that they were bothersome until this baseball season. In your discussion with him, he admits that he does not always shower after baseball practices and games as he is so tired when he gets home, but he always showers in the mornings. On exam he is noted to have infraorbital vasoedema bilaterally along with pale, edematous nasal turbinates bilaterally.

When seeing this patient in the office, it would be appropriate to discuss if he would be willing to pursue further medical management. This patient is very much opposed to “having something in his nose.” There are still avoidance recommendations that may help this patient have decreased symptoms during his worst season.

Treatment: Lifestyle Modifications and Environmental Controls

Allergen avoidance is the first-line therapy available to patients with allergic rhinitis and conjunctivitis. It is important to remember that recommendations for avoidance measures vary by allergen and may differ. In regard to pollen, the goal is to restrict these aeroallergens from enclosed spaces where patients spend the bulk of their

time. Open windows and whole house attic fans increase pollen counts inside the home, and use of air conditioners with the outdoor air vents closed significantly decreases pollen counts in the home [25]. It is also recommended for patients to keep the windows up in the car while traveling. Patients should be instructed to avoid being outside during the time of the day when the pollen count is highest, especially if their disease is severe. Generally, tree and grass pollen is highest in the early morning and later evening, while ragweed pollen peaks at midday [26]. However, multiple meteorological factors including wind speed, wind direction, humidity, and recent rainfall contribute to pollen counts and make it difficult to predict when pollen counts will be elevated [27]. Physical barriers like nasal filters and occlusive sunglasses have shown symptom benefit in a research setting but are not currently recommended or practical for daily use [28, 29]. While it is not feasible to completely avoid pollen exposure, a few general recommendations can help. These include keeping windows shut in the home and in the car during the pollen season, avoiding being outside during the high pollen times of the day if possible, changing clothes when coming in from being outdoors, and rinsing off both hair and body after being outside, especially before going to bed to keep pollen out of the bedding.

Fungi (mold spores), in contrast to pollens, are present in both outdoor and indoor environments and are absent outdoors only when snow cover is present. While a recent rainfall is generally beneficial for lowering tree, grass, and weed pollen levels, many fungi thrive in wet conditions. In fact, recent thunderstorms are associated with high levels of fungal spore release [30]. Fungi are not a homogeneous group, some prefer damp conditions, and others release spores on dry windy days [31, 32]. Because of this significant variability, patients who are sensitized to fungus with severe disease should avoid activities that disrupt the soil or decaying plant matter (digging, raking, mowing, etc.), or if these activities are necessary, a face mask should be worn during these activities [33]. Patients with fungal sensitivities should also be diligent about cleaning and changing the filters of their air conditioners as mold can grow in these moist environments. Regarding indoor mold growth, patients should be encouraged to swiftly remediate sources of moisture within the home like flooding or leaking pipes. If mold is visible, it should be cleaned with dilute bleach and detergent on nonporous surfaces, and porous surfaces may need to be replaced following control of moisture source [1]. There are no available data on the effect that remediating moisture problems in public buildings has on allergic rhinitis, but a 2015 Cochrane review looking at asthma symptoms showed low-quality evidence that pupil's visits to the physician for upper respiratory illness decreased following school remediation [34].

While avoidance of outdoor pollen can help limit symptoms, the impact of allergen avoidance for perennial allergens is less clear. It is much more difficult to avoid perennial allergens. Dog and cat allergens are present in the community and in homes, even without a pet in home [35, 36]. It is important to communicate to well-meaning families that there is no evidence to support that dogs that do not shed are in anyway less allergenic than other dogs. A 2012 study that looked at dogs that were marketed as "hypoallergenic" had higher levels of the primary dog allergen

Can f 1 than control animals [37]. Families considering bringing a pet into the home of an allergic child or adolescents looking to get their own pet should be counseled to spend a significant amount of time in close contact with the animal prior to bringing into the home to monitor for symptom development. Families are reluctant to remove an animal from the home, and studies in rhinitis are not available, but patients with asthma had improvement in symptoms and medication usage 1 year after pet removal from the home [38]. It can take up to 6 months for pet allergen levels to significantly decrease after pet removal from a home. There is evidence that for cat, washing the cat twice a week can reduce the level of cat allergen in the home and that direct washing or wiping of the walls can reduce cat allergen in the home [39, 40]. HEPA filters are effective in dramatically reducing levels of cat allergen in a home; however, when studied, this had little impact on rhinitis symptoms [41]. It is important to note that studies are mixed in regard to the effect of continued pet exposure in children with allergic rhinitis on the development of asthma with pet allergens as a trigger [42]. Recommendations for decreasing pet allergen exposure if the pet is to remain in the home include excluding the animal from the bedroom at all times, washing hands after handling the pet, vacuuming regularly with a HEPA filter, washing the pet twice weekly, and using HEPA filters in the bedroom [42].

Mouse, rat, and cockroach are common allergens in urban homes and schools. Mouse and rat urine is the primary allergen source. An integrated approach involving filling holes and cracks in homes, cleaning, vacuuming, traps, and pesticides to manage rodent exposure has been shown to decrease mouse allergen levels [43]. Fecal material of cockroach is the source of allergenic proteins. Patients are often not aware of their exposure to cockroach, but there is an increase in the odds of cockroach allergen being present in a home when water leaks or visible cracks in the walls of the home are present [44]. An integrated approach has also been shown to be effective in significantly decreasing cockroach allergen levels and having clinical benefit for asthma, but extermination alone is not effective in decreasing allergen levels [45, 46].

Approximately 80% of homes and 85% of day care centers have detectable dust mite [47]. Dust mites are not found in areas of the United States with low ambient humidity, and newer homes typically have lower dust mite levels [48]. Dust mite avoidance recommendations include reducing humidity in the home to below 50%, HEPA vacuuming, and use of acaricides on carpets that cannot be removed, use of encasements on mattresses and pillows, and frequent washing of bedding [1]. Bedding must be washed in hot water, with the most effective temperature for removal at 60 °C (140 °F) [49]. Dust mite avoidance is commonly recommended as part of a comprehensive allergy management strategy. These guidelines have been more rigorously studied in asthma than allergic rhinitis. In children with asthma, comprehensive dust mite avoidance in combination with tobacco avoidance and regular assessment was effective, but single method dust mite avoidance strategies were not effective [45, 50]. The Allergic Rhinitis and its Impact on Asthma (ARIA) and Global Initiative for Asthma (GINA) guidelines no longer recommend single intervention dust mite avoidance for patients; however, the ARIA guidelines do suggest a multifaceted approach for inner city patients with asthma [9, 51]. There are

fewer studies evaluating the efficacy of dust mite avoidance in allergic rhinitis, but a Cochrane systematic review published in 2012 concluded that there was no evidence to support isolated use of bed covers; however, there was a trend toward interventions which significantly reduced mite load, providing some symptom relief [52]. Interventions for dust mite avoidance can be both expensive and time-consuming, and this may not be equal to the benefit gained for some patients. There is also some concern in the field that resources are possibly diverted from more effective therapies if multipronged dust mite interventions are recommended without strong evidence. However, most practitioners still make this recommendation for allergic rhinitis patients as it is a non-pharmacologic strategy with benefit [53].

Clinical Vignette

A 16-year-old male presents for follow-up for allergic rhinitis. He previously had skin prick testing 1 year ago with sensitization to tree pollen, grass pollen, and cat. He was previously well controlled on loratadine 10 mg once daily and budesonide nasal spray two sprays in each nostril once daily. His mother reports that his symptoms seem to be worsening. She notes that he seems to be congested most days and sneezes throughout the day. He reports that his symptoms are not bothering him. When medication adherence is discussed, he notes that he is using his intranasal steroid every day as prescribed. On exam he is noted to have pale, edematous nasal turbinates with mucoid stranding noted bilaterally.

Before adding an additional medication to control symptoms, it is important to ask about medication adherence. In considering additional treatment options, it is important to offer options that fit best with patient goals. If this patient felt that he might be overwhelmed by adding an additional medication, it would be reasonable to begin allergen immunotherapy (discussed below). At this time, addition of an intranasal antihistamine would be the most efficacious adjunctive medication for this patient.

Treatment: Medications

Nasal Saline Irrigation

Nasal saline irrigation has been shown to provide benefit in children with allergic rhinitis with improvement in symptoms of rhinorrhea, nasal congestion, and sleep quality [54]. These benefits are additive to intranasal corticosteroid treatment, with studies showing that the benefit in symptom control with nasal irrigation plus corticosteroid improves symptoms and allows for corticosteroid dose to be decreased with continuing symptom improvement [55, 56]. It is important to use saline irrigation prior to the delivery of intranasal medications so that the medications are not flushed out. Nasal saline irrigation involves the use of a device, either squeeze bottle

or gravity driven to deliver at least 200 mL of saline to each side of the nasal passages once or twice daily as needed. These products are available over the counter and often require the patient to mix saline packets with water at home. It is important to instruct your patients to use distilled, sterilized, or cooled boiled water due to rare case reports of primary amebic meningoencephalitis from contaminated water sources [57]. It is also recommended that devices be cleaned regularly and replaced every 3 months. The sensation of nasal saline irrigation is initially slightly strange but should not be painful. For a patient with more mild symptoms or who prefers to avoid medications, nasal irrigation can provide benefit.

Oral Antihistamines

All H1 antihistamines can be effective in treating allergic rhinitis symptoms of itch, rhinorrhea, and sneeze, with limited impact on nasal congestion [58]. First-generation oral antihistamines are not recommended for the treatment of allergic rhinitis, especially in children and adolescents, given the adverse side effect profile of these medications [59]. As these medications cross the blood-brain barrier, first-generation antihistamines have been shown to impact learning and working memory in children [60, 61]. First-generation antihistamines also have increased rates of anticholinergic effects like dry mouth and dry eyes. There are other atopic conditions where the primary treatment goal is itch control and the benefit of H1 antihistamines may outweigh the risk, but for allergic rhinitis, numerous more efficacious medications with improved safety profiles exist. Second-generation antihistamines (Table 5.2) have less sedation, although up to 14% of patients experience sedation with cetirizine. Sedation is significantly less likely with loratadine, fexofenadine, desloratadine, and levocetirizine [62–64]. Use of second-generation antihistamines as primary treatment of allergic rhinitis is suitable for patients with very mild, intermittent symptoms but is more often used as adjunctive therapy to better control itch.

Intranasal Corticosteroids

For patients with more than mild symptoms, intranasal corticosteroids (Table 5.3) have long been shown to be the most effective treatment option [57, 65]. The largest difference compared with other medications is in treatment of nasal congestion, a symptom that antihistamines are known to not impact. Meta-analysis data confirm that intranasal corticosteroids perform better in controlling rhinorrhea, nasal itching, sneezing, and quality of life compared to oral antihistamines [66]. There are multiple intranasal corticosteroid medications available, with some available in the United States over the counter (fluticasone, budesonide, triamcinolone). Some intranasal preparations are water based, others are alcohol based, and newer options deliver aerosolized puffs from dry powder instead of a liquid spray. In comparison

Table 5.2 Second-generation oral antihistamines

Drug name	Approved age	Formulations	Dosage	Considerations
Cetirizine	6 months	Oral solution, 5 mg/5 mL Tablet, 10 mg Chewable tablet, 5 or 10 mg Oral disintegrating tablet, 10 mg	6–12 mo: 2.5 mg once daily 12 mo–5 years: 2.5 mg once daily, can be increased to 2.5 mg twice daily/5 mg once daily ≥6 years: 5 or 10 mg once daily	– Pregnancy category B – Causes sedation in approximately 13% of patients – Contraindicated in patients with renal impairment
Loratadine	2 years	Oral solution, 5 mg/5 mL Tablet, 10 mg Chewable tablet, 5 mg Oral disintegrating tablet, 5 mg	2–5 years: 5 mg once daily ≥6 years: 5 mg twice daily or 10 mg once daily	– Pregnancy category B – Causes sedation in approximately 8% of patients – No dosage adjustments in renal/hepatic impairment
Fexofenadine	6 months	Oral solution, 30 mg/5 mL Tablet, 30 mg, 60 or 180 mg Oral disintegrating tablet, 30 mg	6 mo–2 years: 15 mg twice daily 2–11 years: 30 mg twice daily ≥12 years: 60 mg twice daily, 180 mg once daily	– Pregnancy category C – Lower rates of sedation (1–3%) – Dose adjustment required for renal impairment
Levocetirizine	6 months	Oral solution, 2.5 mg/5 mL Tablet, 5 mg	6 mo–5 years: 1.25 mg once daily 6–11 years: 2.5 mg once daily ≥12 years: 5 mg once daily	– Active metabolite of cetirizine – Pregnancy category B – Contraindicated in renal impairment
Desloratadine	6 months	Oral syrup: 0.5 mg/mL Tablet, 5 mg Oral disintegrating tablet, 2.5 mg, 5 mg	6–11 mo: 1 mg once daily 12 mo–5 years: 1.25 mg once daily 6–11 years: 2.5 mg once daily ≥12 years: 5 mg once daily	– Active metabolite of loratadine – Pregnancy category C – May need dose adjustment in renal and hepatic impairment

studies, the efficacy of different corticosteroid medications appears to be equivalent [67, 68]. In fact, in a non-blinded study, patients reported similar symptom improvement with use of intranasal corticosteroid as with oral corticosteroids [69]. The onset of action of intranasal steroids is within hours, but maximal effect is typically not seen for several days. For this reason, starting treatment prior to allergen exposure provides better symptom control than starting treatment after exposure [70]. If a patient has seasonal symptoms, it is recommended that they begin consistent daily

Table 5.3 Intranasal medications

Drug name	Approved age	Formulations	Dosage	Considerations
<i>Intranasal steroids</i>				
Fluticasone	Furoate 2 years Propionate 4 years	Nasal liquid, as furoate:27.5 mcg/spray As propionate: 50 mcg/spray	2–11 years: 1 spray per nostril once daily can be increased to 2 sprays once daily to control symptoms ≥12 years: 2 sprays per nostril once daily can be decreased to 1 spray once daily for maintenance therapy	– Pregnancy category C – Systemic bioavailability is less than 2%
Mometasone	2 years	Nasal liquid, 50 mcg/spray	2–11 years: 1 spray per nostril once daily ≥12 years: 2 sprays per nostril once daily	– Pregnancy category C – Systemic bioavailability is less than 0.1%
Budesonide	6 years	Nasal liquid, 32 mcg/spray	6–11 years: 1 spray per nostril once daily ≥12 years: 2 sprays per nostril once daily	– Pregnancy category B – 10–50% systemic bioavailability – Use with caution in patients with cataracts
Ciclesonide	6 years	Nasal liquid, 50 mcg/spray Nasal aerosol, 37 mcg/spray	50 mcg/spray: 2 sprays per nostril once daily, all ages 37 mcg/spray: 1 spray per nostril once daily, all ages	– Pregnancy category C – Systemic bioavailability is less than 0.1% – No hepatic dose adjustment
Beclomethasone	4 years (aerosol) 6 years (liquid)	Nasal liquid, 42 mcg/spray Nasal Aerosol, 40 mcg/actuation, 80 mcg/actuation	Liquid: 6–11 years: 1 spray in each nostril twice daily ≥12 years: 1 or 2 sprays in each nostril twice daily Aerosol: 4–11: 1 spray in each nostril once daily ≥12 years: 2 sprays in each nostril once daily	– Pregnancy category C – 10–50% systemic bioavailability
Flunisolide	6 years	Nasal liquid, 25 mcg/spray	6–14 years: 1 spray per nostril three times daily or 2 sprays in each nostril twice daily ≥15 years: 2 sprays per nostril twice daily or 2 sprays per nostril three times daily	– Pregnancy category C – 10–50% systemic bioavailability

(continued)

Table 5.3 (continued)

Drug name	Approved age	Formulations	Dosage	Considerations
Triamcinolone	2 years	Nasal liquid, 55 mcg/spray	2–5 years: 1 spray per nostril once daily 6–11 years: 1–2 sprays per nostril once daily ≥12 years: 1 spray per nostril once daily	– Pregnancy category C – 10–50% systemic bioavailability
<i>Intranasal antihistamines</i>				
Azelastine	6 months	Nasal liquid, 0.1% or 0.15% solution	6 months–5 years (0.1% liquid): 1 spray per nostril twice daily 6–11 years (0.1% or 0.15%): 1 spray per nostril once daily ≥12 years: 1–2 sprays twice daily	– Pregnancy category C – Bitter taste reported by 20% of patients – Onset of action 15–30 min
Olopatadine	6 years	Nasal liquid, 0.6%	6–11 years: 1 spray per nostril twice daily ≥12 years: 2 sprays per nostril twice daily	– Pregnancy category C – Bitter taste – Onset of action 30 min
<i>Assorted</i>				
Cromolyn sodium	2 years	Nasal liquid, 5.2 mg/spray	2 years +: 1 spray per nostril 3–4 times a day	– Pregnancy category B
Ipratropium bromide	5 years	Nasal liquid, 21 mcg/spray, 42 mcg/spray	5 years +: 2 sprays per nostril four times a day	– Pregnancy category B

use of intranasal steroids 2 weeks before the presumptive start of their season. Even for patients with intermittent symptoms, the use of as needed intranasal corticosteroid leads to improved symptom control compared to as needed use of oral histamines [65].

The most common side effects reported by patients being treated with intranasal corticosteroids include local nasal mucosal irritation, nose bleeds, and unpleasant drainage down the throat. When instructing patients on the correct technique for administering intranasal corticosteroids (Table 5.4), it is important to focus on angling the tip of the spray away from the nasal septum (toward the ear on the same side) and to take a gentle inhalation at time of spray. Without instruction, patients will often angle the spray medially and occlude the opposite nostril in order to increase the sniffing potential of the nostril being treated. The end results of incorrect technique are deposition of the medication in posterior oropharynx instead of the nasal mucosa, decreased efficacy, and increased likelihood of side effects. Many studies in children have not shown evidence of adrenal suppression in children receiving intranasal corticosteroids [71]. One recent study showed a decrease in the growth velocity of 0.27 cm/year in patients receiving fluticasone furoate, but no

Table 5.4 Intranasal medication technique

Step 1	Blow the nose to remove mucoid material
Step 2	Look down toward the ground
Step 3	Angle tip of nozzle up and out in the nostril (toward ear lobe of ear on the same side). Use of the opposite hand to the side of the nose can improve ease of angle
Step 4	Actuate spray while inhaling gently

evidence of adrenal suppression [72]. It is important to think about your patients in context as many patients with allergic rhinitis may have other atopic disease for which they are receiving topical corticosteroids and for whom the addition of intranasal steroid may contribute to adrenal suppression.

Intranasal Antihistamines

Intranasal antihistamines (Table 5.3) have been shown to be effective in controlling allergic rhinitis symptoms and have improved symptom control compared to oral antihistamines [73, 74]. There are two intranasal antihistamines currently available and have been shown to be equally efficacious [75]. Intranasal antihistamines have been shown to be slightly less efficacious than intranasal steroids as a single-agent therapy, but the combination of the two medications was more efficacious than either agent alone [76]. Because of this additive effect, there is a product available that delivers azelastine and fluticasone in the same product. The most common side effects with nasal antihistamines include sedation and a bitter taste following administration, which is reported in less than 10% of patients [77]. Intranasal antihistamines can be very useful in patients who continue to have symptoms with intranasal corticosteroid treatment, but because of the rapid onset of action of the medication, intranasal antihistamines are an excellent choice for a patient who prefers as-needed dosing for allergic rhinitis symptoms.

Additional Therapies

There are several over-the-counter decongestant nasal sprays available containing medications like phenylephrine, oxymetazoline, xylometazoline, and naphazoline. These medications used as single therapy for longer than 3–5 days have been shown to cause reduction in efficacy and rebound nasal congestion, a phenomenon termed rhinitis medicamentosa [78]. There is some evidence that use of intranasal corticosteroid and intranasal decongestant at the same time can avoid this adverse effect, but this is still not recommended for long-term care [79]. Cromolyn sodium is a mast cell stabilizer available as a nasal spray but has been shown to be less effective than intranasal corticosteroids [80]. It also requires four times daily dosing which is

impractical for most children and adolescents. Ipratropium bromide is most typically used in patients who have significant rhinorrhea that is resistant to other therapies; it is generally less effective than intranasal corticosteroids [81]. Montelukast is a leukotriene receptor antagonist approved for allergic rhinitis. Montelukast has been shown to be less effective than corticosteroid nasal sprays in the control of allergic rhinitis symptoms but may have some additive effect when combined with oral second-generation antihistamine [82]. There is no indication for use of montelukast as first-line therapy for allergic rhinitis, but if your patient is unable to tolerate a nasal spray, there may be a role for second-line therapy.

Ophthalmologic Medications

Use of intranasal corticosteroids has been shown to improve conjunctivitis symptoms as well as rhinitis symptoms [83], but some patients require additional therapy. The most effective additional therapies for ocular symptoms are topical medications with antihistamine and mast cell stabilization properties. There are many of these products currently available that are approved for use in patients down to age 2 (olopatadine 0.1%, alcaftadine 0.25%, bepotastine 1.5%, and epinastine 0.05%). These medications are typically dosed one drop per eye twice daily with an onset of action within minutes. There are also treatments that have mast cell stabilization properties alone (cromolyn sodium 4%, nedocromil 2%, and lodoxamide 0.1%). Mast cell stabilizers require 1–2 weeks of treatment before clinical benefit is apparent and even then are less effective than the combination of antihistamine and mast cell stabilizer [84]. Several over-the-counter products include an antihistamine and a vasoconstrictor, but these medications are not appropriate for long-term use as when stopped, these medications can cause a rebound hyperemia [85].

Clinical Vignette

A 14-year-old female presents to the office for follow-up of allergic rhinitis. She last had skin prick testing for environmental allergens 3 years previously. At that time she was found to be sensitized to tree pollens, grass pollens, weed pollens, and cat. She has never had a cat in her home. At initial diagnosis she was placed on cetirizine 10 mg once daily and fluticasone nasal spray one spray in each nostril once daily. She initially had marked improvement with complete control of symptoms of nasal congestion, sneezing, and itchy eyes. At her recent follow-up, she reported that symptoms were no longer well controlled, but she had not stopped her cetirizine prior to that appointment. She denied any missed dosing of medications or change in her avoidance strategies. Her fluticasone nasal spray dose was increased to two sprays once daily, and she was started on azelastine two sprays twice daily. She followed up 1 month later with improvement in symptoms with the addition of azelastine but also reported sedation impairing her ability to focus at school.

Assuming she is an otherwise healthy child, she would be an excellent candidate for subcutaneous allergen immunotherapy (SCIT). However, many adolescents are uninterested in SCIT due to the time commitment involved, aversion to needles, or lack of transportation. If she was mono-sensitized to grass, a sublingual immunotherapy (SLIT) tablet would be appropriate. Given her continued symptoms and sedation with additional medications, she agrees to pursue SCIT. Skin prick testing was repeated prior to writing the immunotherapy prescriptions, and she continued to be sensitized to tree pollen, grass pollens, weed pollens, and cat but is now additionally sensitized to dust mite. Dust mite avoidance was recommended in addition to SCIT.

Immunotherapy

Indications for treatment with specific allergen immunotherapy include uncontrolled rhinitis symptoms despite use of medications and avoidance strategies, coexisting rhinitis and asthma, rhinitis with proven sequelae, intolerance to medication due to side effects, or when there is a desire to decrease long-term medication use. There are currently two FDA-approved forms of immunotherapy available in the United States for children, subcutaneous injections (SCIT) and sublingual tablets (SLIT); sublingual drops have not been FDA approved. Allergen immunotherapy is indicated for children with allergic rhinitis sensitive to aeroallergens confirmed through either skin prick testing or serum-specific IgE elevation [86].

Currently two grass pollen sublingual tablets, one short ragweed tablet and one dust mite tablet, are FDA approved (Table 5.5). Grastek® (ALK-Abelló A/S, Hørsholm, Denmark) is a single-grass (Timothy grass) pollen tablet that relies on northern pasture grass cross-reactivity that is approved in children from 5 years of age [87]. Oralair® (Stallergenes S.A. Antony, France) contains five grass pollens (sweet vernal, orchard, perennial rye, Timothy, and Kentucky bluegrass) and is approved for use starting at 10 years of age [88]. Both tablets can be dosed co-seasonally, beginning 12–16 weeks prior to the grass season and continuing daily through the end of the grass pollen season. Ragweed SLIT (Ragwitek®, ALK-Abelló A/S, Hørsholm, Denmark) is available but is only approved for adults 18 years of age [89]. Dust mite SLIT (Odactra®, ALK-Abelló A/S, Hørsholm, Denmark) was most recently approved in March 2017, also approved for patients starting at 18 years of age [90]. Subcutaneous immunotherapy has been used with good results for well over 100 years in allergic rhinitis, with efficacy demonstrated in multiple trials for patients with multiple aeroallergen sensitization. The SLIT option is newer in the United States (used for decades in Europe) and is ideal for patients who are mono-sensitized, children with needle phobia, or patients unable to receive injections in a healthcare setting. SLIT is not appropriate for patients with severe or uncontrolled asthma, eosinophilic esophagitis, or history of severe allergic reaction. SLIT can safely be administered at home with the initial dose given in a physician's office (with 30 min of observation) and self-injectable epinephrine available at home.

Table 5.5 Sublingual immunotherapy tablets

Drug name	Approved age	Formulations	Dosage	Considerations
Grastek® (ALK-Abelló A/S, Hørsholm, Denmark)	5–65 years	Tablet, 15 mcg Timothy grass pollen	5–65 years: 1 tablet sublingually once daily starting 12 weeks prior to grass pollen season	– Timothy is cross-reactive with northern grass pollens – Contains fish gelatin – Has been approved for year-round use to create sustained effectiveness
Oralair® (Stallergenes S.A. Antony, France)	10–65 years	Tablet 100 IR (index of reactivity), 300 IR containing pollen from timothy, orchard, Kentucky blue, perennial rye, and sweet vernal grass pollens	10–18 years: 1 100 IR once daily for 1 day, 2 100 IR for 1 day, then 1 300 IR tablet sublingually daily 18–65 years: 1 300 IR tablet sublingually once daily -start 16 weeks before grass pollen season	– Contains all northern grasses – Only sublingual tablet without fish gelatin
Ragwitek® (ALK-Abelló A/S, Hørsholm, Denmark)	18–65 years	Tablet 12 Amb A 1 (primary short ragweed allergen) units	18–65 years: 1 tablet sublingually once daily starting 12 weeks prior to ragweed season	– Contains fish gelatin
Odactra® (ALK-Abelló A/S, Hørsholm, Denmark)	18–65 years	Tablet 12 standardized house dust mite allergen units	18–65 years: 1 tablet sublingually once daily, can be started at any time of the year	– Contains fish gelatin

Children have unique benefits from receiving allergen immunotherapy including improvement in control of rhinoconjunctivitis symptoms, potential to prevent the development of asthma, and reduction in risk of developing further allergic sensitization [91–95]. When comparing the two immunotherapy methods, 73% of patients receiving SCIT and 49% of patients receiving SLIT had an improvement in a standardized mean difference in symptom scores, and 57 and 32% reported a reduction in medication, respectively [96, 97]. Both SCIT and SLIT have been shown to have benefit in both the short and long term, up to over a decade after completing therapy [98, 99]. A recent review demonstrated that both SCIT and SLIT therapies are safe for children [100]. Efficacy and safety of allergen immunotherapy have been shown in children under 2 years of age, but immunotherapy has not been typically given to children under 5 years of age, except for cases of severe allergic reactions or anaphylactic venom reactions, due to concerns about limited communication from pre-school age children should adverse reaction occur [86, 101, 102].

Local reactions are common in both SCIT and SLIT. Local reactions in SCIT involve erythema, swelling, itching, and tenderness at the injection site. These reactions occur in 71% of patients, though 87% of these patients rate the reactions as not bothersome [103]. In SLIT, local reactions are typically mouth itching and swelling and occur in 46% of patients, with only 4% in one study discontinuing therapy due to reactions [104]. The risk of systemic reaction with conventional immunotherapy dose schedules is estimated to be 0.2%; risk increases to as much as 34% when using a rush immunotherapy schedule [105, 106]. Fatality with a systemic reaction following SCIT injection is possible and has been estimated at one fatality in 2.5 million injections [24, 107, 108]. Recent data indicate that this rate may be decreasing, with possible causes including better screening of patients with known risk factors like uncontrolled asthma and earlier epinephrine administration [109]. Sublingual tablets have a lower incidence of systemic reactions; however, there is still a risk of anaphylaxis (black box warning) which is why patients are prescribed epinephrine for home administration of SLIT tablets [100].

Omalizumab (monoclonal anti-IgE antibody) is not indicated for the treatment of allergic rhinitis in children or adolescents, but it has been studied as an adjunct with subcutaneous immunotherapy in patients who are otherwise unable to tolerate immunotherapy due to systemic reactions [110]. The addition of omalizumab to immunotherapy has no adverse effect on either the short-term or long-term efficacy and benefit of immunotherapy [111].

In addition to the benefits in symptom control, immunotherapy in children has been associated with a 30% reduction in total healthcare costs, inclusive of immunotherapy costs, that was evident 3 months after initiating therapy [112–115]. Immunotherapy should be considered in all children over age 5 years old with allergic rhinitis who have symptoms despite pharmacologic management, who wish to decrease their use of medications, and who have a family history of asthma but have not yet developed asthma or in children younger than 5 years old with severe symptoms that do not improve with medical management.

Clinical Vignette

A 17-year-old male presents for follow-up of allergic rhinitis. He had skin prick testing 6 months ago and was positive to dust mite, grass pollen, and dog. His symptoms were completely controlled with use of loratadine 10 mg once daily, mometasone nasal spray two sprays once daily, and dust mite avoidance. He notes that his symptoms have been steadily worsening for the last 3 months. His mother admits that there have been a lot of stressors in the family in recent months including a recent move and addition of a new puppy in the home. She notes that in the move, his dust mite encasements were lost and that the puppy is a hypoallergenic dog so she feels confident that the new puppy is not contributing. On exam, he has pale, boggy nasal mucosa with mucoid stranding noted bilaterally, and his conjunctiva is mildly injected.

When patients who have previously had control of their allergic rhinitis symptoms present with loss of control in symptoms, it is important to consider that new sensitization may have developed, exposures may have changed, medication adherence may be diminished, or symptoms have worsened. In this patient, it is less likely that new sensitization has developed given how recently he had skin testing performed. Decrease in medication adherence is very possible given the increased stress on the family with their recent move. Given his history, change in exposure is the most likely etiology behind his loss of symptom control. Dust mite encasements are part of a multifaceted approach to dust mite avoidance, and evidence has shown that no dog breed is truly hypoallergenic.

Pitfalls

Many children and adolescents with chronic nasal congestion, sneezing, and rhinorrhea become accustomed to their symptoms and will diminish significance in history. Asking other family members about their perception of symptom frequency and severity is often useful. Another common pitfall in the history is that a patient will report that they have tried a nasal corticosteroid without improvement. It is important to investigate this further as questioning will often reveal that the patient used the medication for 1 or 2 days and discontinued the medication when improvement was not noted. In studies, the onset of action of intranasal corticosteroids is between 3 and 12 h, but in practice, most patients do not notice an improvement in symptoms until closer to a week of daily use.

It can also be useful to discuss the possibility of nonallergic rhinitis to your patients prior to testing. Many patients are skeptical of negative skin prick testing after being told by well-meaning caregivers, friends, and healthcare professionals that their rhinitis symptoms must be allergies. In fact patients with nonallergic rhinitis can become frustrated after repeatedly being told to use oral antihistamines without any improvement in symptoms. Reliance on oral antihistamines in favor of intranasal corticosteroids is to the detriment of both patients with nonallergic and allergic rhinitis.

The other common pitfall in regard to intranasal corticosteroids was discussed briefly previously in the chapter but is worth mentioning again. Intranasal corticosteroids are very commonly prescribed, but many patients are not given proper instruction on how to use an intranasal steroid most effectively. The average patient given an intranasal steroid without instruction will aim the nozzle straight up the nostril, possibly angle in medially, and will have a vigorous inhalation to “really get it in there.” This is often especially true if the patient feels appreciably obstructed. However, it has been documented that strong inhalation pulls the medication into the throat and the medication does not get applied to the appropriate location. Occluding the opposite nostril aids in improving the force of the inhalation but will

not improve the deposition of the nasal corticosteroid. A recent study compared the effect of nasal decongestant compared to correct technique and found that using correct technique was more effective than using a nasal decongestant prior to poor technique, even if patients feel occluded correct technique is most beneficial [116].

The correct technique involves the following steps (Table 5.4): First, blow the nose to remove mucoid material. Second, the patient should look down toward the ground; this allows the medication itself to still be vertical and improve device function. Thirdly, angle the tip of the nozzle up and out in the nostril (roughly toward the ear on the same side); using the opposite hand to the nostril can make this positioning less awkward. And lastly, spray with a gentle inhale only.

A decrease in vigilance in allergen avoidance can also contribute to worsening symptoms. Many of the avoidance practices are cumbersome and time-consuming. It is not surprising that families may not always be diligent about washing bedding, regular vacuuming, and making sure pets around are out of the bedroom. Reviewing appropriate avoidance strategies at every visit can improve adherence in avoiding relevant allergens.

Allergic rhinitis and conjunctivitis are common chronic diseases of adolescence, and, if uncontrolled, symptoms may adversely impact quality of life. Accurate diagnosis to identify triggers is important to maximize efficacy of avoidance measures, medication selection, and therapy adjustments. There are a variety of effective therapy options that can be customized to fit with patient goals and symptoms. Regular follow-up is necessary to maintain control of symptoms, but with treatment these symptoms are typically able to be well controlled.

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Chapter 6

Allergic Rhinitis Pertaining to Adolescents



Mervat Nassef and Marc L. Rubin

Clinical Vignette (Part 1)

Adam is a 17-year-old male with a history of allergic rhinitis since 3 years of age. Initially, he would complain of itchy eyes, sneezing, and runny nose in the spring and fall. He was prescribed loratadine by his pediatrician, which improved his symptoms. Each year, his nasal and ocular symptoms became progressively worse. Loratadine was no longer effective. He would sometimes have to miss his soccer games in the spring because he was bothered by his allergies. He also developed cough and shortness of breath in the spring and when visiting family members who owned cats. He was treated with albuterol for his chest symptoms. At age 8, he developed chronic nasal congestion in the winter in addition to his seasonal allergy symptoms. His parents noticed that he began to snore frequently. His teachers reported that he seemed tired in class.

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Introduction

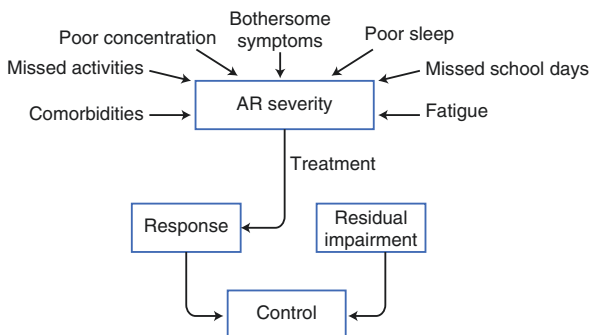
Allergic rhinitis (AR) is one of the most common chronic illnesses affecting adolescents. It can begin at any age but often presents in early childhood. As discussed in Chap. 5, AR can be subdivided into seasonal, with symptoms in spring and/or fall, and perennial, with year-round symptoms. Each of these subtypes has its own constellation of symptoms and presents unique challenges. Clinicians caring for adolescents with AR have the opportunity to help their patients and their families understand this disease and control it to avoid any negative impact.

There are a number of issues specifically related to teenagers who are affected by AR. The spring and fall allergy seasons coincide with the beginning and end of the school year, which are important time periods for teens. In the fall, they are adjusting to new classes, perhaps a new school, making new social connections, and learning new subjects. In the spring, they are taking standardized tests and final exams. It is essential to their social, emotional, and educational well-being that we help them function at their best during these important times of the year when they may be affected the most by their allergies.

Adolescence is also a time when teens transition to independence and become responsible for self-care including their health care. In order to carry out this responsibility, they must gain an understanding of their disease and its treatment. It is during the teenage years that patients with AR will leave home for the first time to go to overnight camps or to college. From a psychological perspective, an adolescent will look at the upcoming lifestyle changes as an exciting time in their life. Free from parental guidance and to set personal values, adolescents make decisions on what paths to take going forward. Unfortunately, a depth of knowledge is often missing, which decreases their ability to make informed choices. This can directly have a negative impact on their health. The new demands on their attention and schedule may cause them to neglect proper management of their allergies. This can lead to worsening symptoms and complications that are avoidable with appropriate preparation. This preparation should include an understanding of the issues that will arise both during the transition and after becoming independent, as well as how each issue can be managed. As discussed in Chap. 3, this discussion and preparation should begin well before the transition period and can be accomplished with the support of an allergist/immunologist.

Allergic rhinitis can affect many aspects of an adolescent's psychosocial and cognitive well-being. It can also lead to other medical complications such as sinusitis, worsening asthma control, and ear infections. Adolescents with AR should be assessed for these comorbid conditions as they may occur only seasonally and may be under-recognized by the patient. For example, a teen with seasonal AR may have chest tightness and a persistent cough at the peak of the pollen season. If these symptoms do not occur the rest of the year, the teen may not recognize that he/she

Fig. 6.1 Factors that can be used to assess AR severity and the level of control in adolescents



has asthma triggered by the pollen allergy and, therefore, may not receive appropriate treatment. The modified Allergic Rhinitis and its Impact on Asthma (m-ARIA) classification divides AR severity into three categories, mild, moderate, and severe, depending on the degree of impairment of four quality-of-life (QOL) parameters: sleep, daily activities/sports, work/school performance, and troublesome symptoms [1]. Adolescents with uncontrolled AR and nasal obstruction have been shown to have worse QOL than those with controlled disease [2]. In addition, female adolescents report worse QOL than males. This gender difference was not seen in younger children. Figure 6.1 summarizes the factors that influence AR severity specifically in adolescents.

Clinical Vignette (Part 2)

Adam's family sought a consultation with an allergist/immunologist. Skin testing revealed allergic sensitization to trees, grass, ragweed, dust mites, dog, and cat. The allergist recommended dustproofing his bedroom and keeping the windows closed in the spring and fall seasons to keep out the pollen. She also started him on an intranasal corticosteroid to better control his nasal congestion, changed his antihistamine to cetirizine, and started him on montelukast in the spring to control his allergic asthma. Within 2 weeks of instituting these measures, his snoring resolved, his sleep improved, and he was more alert and focused in school. His allergy symptoms were well controlled during the pollen seasons, allowing him to fully participate in his favorite sport, soccer. He was able to stop all medications in the summer between the pollen seasons. Following his allergist's advice, his mother would restart the allergy medications 1–2 weeks before the start of the season to prevent the symptoms.

Disease-Related Issues Specific to Adolescents

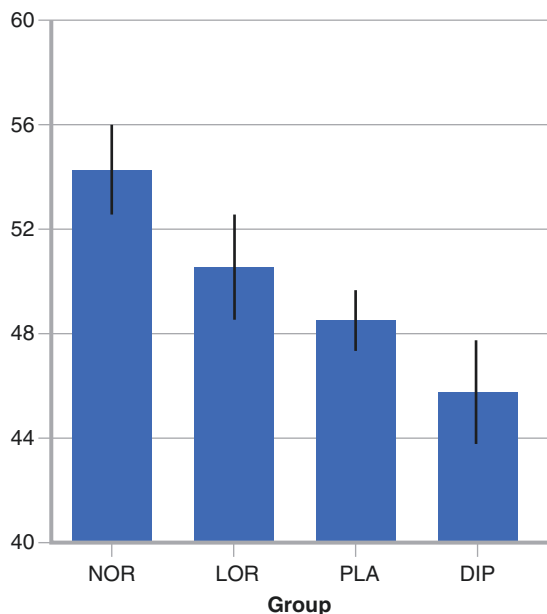
Adolescents who have had AR for years may be used to having symptoms of AR, such as chronic nasal obstruction, and not complain about them. Their perception of normal or baseline may be altered by chronic symptoms that they have become accustomed. Parents may also be desensitized to their children's symptoms if those symptoms are chronic. A parent may not recognize that his child's mouth breathing is abnormal because that is how he/she always breathe. However, even if patients and parents are not aware of the symptoms or their severity, AR can have a tremendous impact on the adolescent's activities of daily living as well as his/her quality of life [3]. Unawareness of symptoms and disease can lead to undertreatment and inadequate management of AR in adolescents and adults [4]. This finding emphasizes the need for patient and parent education followed by guidance from medical professionals.

Cognitive Issues

One of the most serious consequences of AR is its effect on cognitive performance [5]. Juniper and colleagues found that measures of impairment in the day-to-day lives of adolescents with AR were not the same as those experienced by adults [3]. Items that were specific to adolescents were (1) difficulty concentrating (doing their school work) and (2) generally not feeling well. Both of these items were important to them. In a landmark study by Vuurman, learning ability was compared between normal children and children with seasonal AR treated with placebo, a sedating antihistamine (diphenhydramine) and a non-sedating antihistamine (loratadine) [6]. Figure 6.2 from this study shows a highly significant decrease in learning performance in all treatment groups of allergic children compared to normal children. The greatest decrease in performance was in the group treated with the sedating antihistamine. In a similar study, the same author found that adolescents and young adults, age 16–25 years, with AR also had reduced learning ability compared to normal control subjects [7]. This effect was exacerbated by treatment with a sedating antihistamine and reversed by treatment with a non-sedating antihistamine/decongestant combination.

These studies have important practical implications for teens. The timing of the allergy season with the end-of-year exams puts the student with AR at a disadvantage. It is crucial for these students to effectively treat their allergies so that they can perform at their best during this important time of year. Counseling teenagers transitioning to independent living about the importance of controlling their allergies in the context of potential negative impact on school performance can be an effective approach by health-care providers. We must also help them understand that not all allergy medications have the same effects or side effects so that they can make the best treatment choices. In addition, promoting an open

Fig. 6.2 Mean ($\pm$ SE) composite learning score for every treatment group as percent of maximum. NOR=normal control, LOR=loratadine, PLA=placebo, DIP=diphenhydramine. group (Used with permission of Elsevier from Vuurman EF, van Veggel LM, Uiterwijk MM, Leutner D, O'Hanlon JF. Seasonal allergic rhinitis and antihistamine effects on children's learning. *Ann Allergy* 1993;71(2):121–26)



line of communication is helpful in case they are experiencing unwanted side effects or poor relief from their treatment.

Psychosocial Issues

The typical symptoms of AR such as frequent sneezing, nose-blowing, and sniffing can be disturbing to other students in a quiet classroom or library, leading to embarrassment by the allergy sufferer. Students with AR may feel the need to leave the classroom just to blow their nose. This can influence their concentration and learning. These symptoms can also lead to harassment or ridicule by other students affecting the allergy sufferer's emotional well-being at a time when they are more vulnerable. The (often unrecognized) psychological consequences of untreated AR include shyness, low self-esteem, depression, and anxiety [8].

Peer pressure in adolescence can be an important factor relating to AR. For example, an adolescent with dust mite allergy may agree to carpeting in the bedroom because her roommate wants it and then suffer the consequences of increased nasal congestion as a result. Adolescents with AR may find certain sports more challenging because of their seasonal allergies. Some outdoor sports such as soccer and football have seasons that coincide with pollen seasons in the spring and fall. As these seasons approach, teens who play outdoor sports must be diligent about taking their daily allergy medications to prevent and maintain control of their symptoms.

Sleep Disturbances

Sleep plays an essential role in the physical, emotional, and intellectual development of adolescents. Sleep has a restorative function and promotes learning and memory. Adolescence is marked by a significant change in sleep patterns. Up to 50% of adolescents in western countries have sleep disorders [9]. During the teenage years, bedtime is progressively more delayed on weekdays and weekends, while wake up time is later on weekends and earlier on weekdays resulting in sleep deficit on weekdays and an irregular sleep schedule. In addition to delayed sleep onset, teens also have difficulty staying asleep. As a result, most teenagers get about 7 hours of sleep per night rather than the 9 hours they actually need [10]. The reasons for this impairment in sleep include academic demands, mobile phone use, surfing the Internet, electronic gaming, watching television, and social activities. Hormonal changes during puberty may also play a role in shifting the adolescent's circadian rhythm. Gender differences have been noted with female college students reporting more sleep disturbances than male students do [11].

AR can further exacerbate sleep disturbances in adolescents. Nasal congestion is the most important symptom of AR that affects sleep [12]. The degree to which sleep is adversely affected by AR is one of the measures used to assess disease severity in the ARIA guidelines [13]. Allergy-related sleep disturbances affect 68% of patients with perennial AR and 48% of patients with seasonal AR [14]. Disturbances consist of microarousals, snoring, and obstructive sleep apnea. Interestingly, teens who have had AR since early childhood may be used to these symptoms and not complain about them. For this reason, patients with AR should be asked specifically about symptoms of sleep-disordered breathing and sleeping difficulty. Although nasal congestion is the biggest culprit implicated in AR-associated sleep disturbances, other symptoms of rhinoconjunctivitis such as sneezing, rhinorrhea, and nasal and ocular pruritus can also contribute to poor sleep quality. In addition, the inflammatory mediators that are elevated in AR, such as IL-4, IL-6, IL-1, and TNF, can directly affect sleep quality and cause daytime fatigue and flu-like symptoms [12].

The chronic sleep deficit commonly seen in adolescents and worsened by AR can have serious consequences academically, socially, and emotionally. Specific problems related to sleep deficit that have been reported include fatigue, poor concentration, memory deficit, daytime sleepiness, poor academic performance, anxiety, irritability, substance abuse (caffeine, alcohol, stimulants), impaired driving, and motor vehicle accidents [15].

Adolescent sleep is a public health issue that deserves greater attention. Physicians should educate adolescents and their parents on the importance of proper sleep hygiene as well as control of AR symptoms for physical and emotional health and academic performance. Recommendations for good sleep hygiene should include removal of all electronic media from the adolescent's bedroom, eliminating caffeine intake, consistent bedtimes, regular physical activity, and

exposure to sunlight [15]. Effective treatment for the symptoms of AR, especially nasal congestion, can improve sleep quality. According to the ARIA guidelines, intranasal corticosteroids are considered first-line treatment for patients with persistent nasal congestion [1]. Treatment with intranasal corticosteroids has been shown to improve sleep quality and reduce daytime sleepiness in patients with perennial AR [16, 17].

AR and Traffic Safety

Another public health issue that relates specifically to teens is traffic safety. It is during the teenage years that many people begin to drive. As novice drivers who often engage in risk-taking behavior, teenagers can be a danger to themselves and others on the road. According to the Centers for Disease Control and Prevention (CDC), motor vehicle accidents are the leading cause of death for teenagers in the USA [18]. The risk of a car crash is higher among 16–19-year-old drivers than any other age group. Several factors put teen drivers at risk for accidents: teens are more likely than older drivers to underestimate hazardous situations; teens are more likely than older drivers to speed; teens are less likely than older drivers to wear seat belts; at all blood alcohol levels, the risk of a motor vehicle crash is greater for teens than for older driver. The eight causes of teen crashes identified by the CDC are:

- Driver inexperience
- Driving with teen passengers
- Nighttime driving
- Not using seat belts
- Distracted driving
- Drowsy driving
- Reckless driving
- Impaired driving

AR can further impair driving ability and put teen drivers at even greater risk. Using a validated 1 h on-the-road driving test, Vuurman and colleagues evaluated the effect of AR alone, as well as AR treated with two allergy medications on driving performance and cognition [19]. In this randomized, double-blind, placebo controlled study, patients with known pollen allergy were pretreated with either fluticasone nasal spray, cetirizine, or placebo. The patients were then given nasal provocation with pollen or placebo. The left panel of Fig. 6.3 shows the mean standard deviation of lateral position (SDLP), a measure of weaving, for the entire test. More weaving was observed in the untreated pollen provocation group compared to placebo. This indicates that AR in and of itself can adversely affect driving performance. The right panel shows the SDLP while patients were driving and

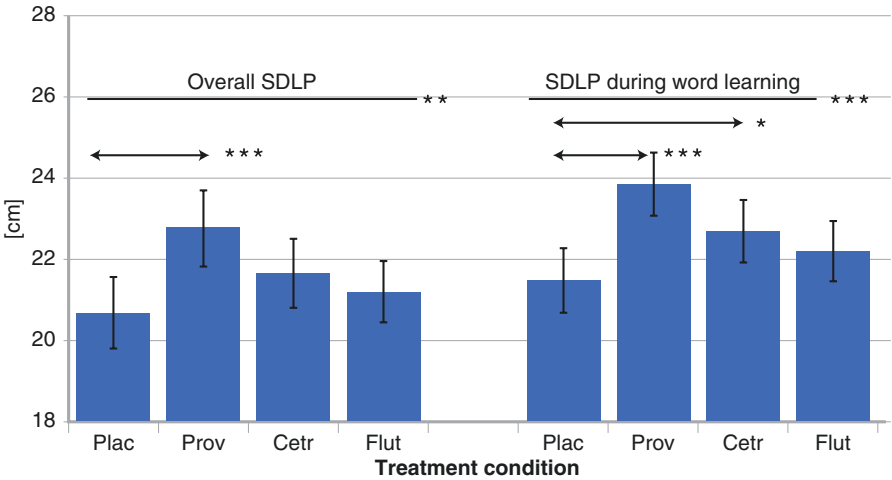
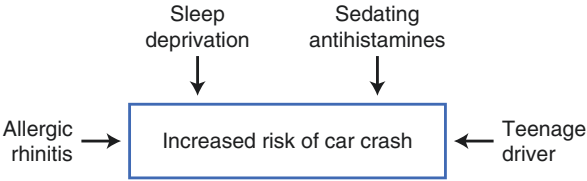


Fig. 6.3 Mean ($\pm$ SE) SDLP for all conditions of the driving test. Left panel shows SDLP for the entire test (60 min), and right panel shows SDLP during the memory test (last 15 min). Lines indicate overall significant difference between all four conditions (Omnibus test); lines with arrows indicate a significant difference ($*P < 0.05$; $**P < 0.01$; $***P < 0.001$) of a priori pairwise comparisons between placebo and the provocation conditions. Post hoc comparison between drug conditions revealed no significant difference (Used with permission of John Wiley and Sons from Vuurman EF, Vuurman LL, Lutgens I, Kremer B. Allergic rhinitis is a risk factor for traffic safety. Allergy 2014;69(7):906–12)

Fig. 6.4 Factors that increase the risk of motor vehicle accidents in adolescents with AR



simultaneously performing a verbal memory task requiring them to divide their attention between two tasks. This added stress on driving performance led to even greater impairment in driving performance in untreated pollen provocation group compared to placebo. The magnitude of this impairment was comparable to the effect of a blood alcohol level of 0.05%, which is the legal limit in many countries. This effect could be even larger if patients suffering from AR would also take other drugs that might affect their driving such as a sedating antihistamine or alcohol. The data of this study are particularly relevant to adolescents with AR, who are new drivers faced with extra cognitive demands, such as the use of in-car electronic devices or talking with passengers in the car while driving, which can put their safety at risk. Figure 6.4 summarizes factors that increase the risk of motor vehicle accidents in adolescents with AR.

Clinical Vignette (Part 3)

During his childhood years, Adam relied on his mother to give him his medications every day. As a teenager, he would sometimes be resistant to taking daily medication or would procrastinate and then forget to take them. Rather than nag him, his mother would remind him that the allergist, whose advice he valued and respected, stressed the importance of taking the medications regularly to keep the symptoms under control. This strategy reduced the tension between Adam and his mother with regard to adherence to his allergy treatment. He did not take full responsibility for taking his allergy medications until he moved to college. Prior to this move, he visited his allergist to renew his prescriptions. The allergist used this opportunity to remind Adam about how to avoid allergens in his new environment and made sure he understood what medications to take and when to take them. She also scheduled a follow-up visit during his first trip back home 3 months after the start of college.

In the first few weeks at college, Adam was busy adjusting to a new workload, making new friends and joining extracurricular activities. Because of his busy schedule, he forgot to take his allergy medication for 2 days. As this occurred during the fall allergy season, his allergy symptoms flared. He was not able to sleep and felt “sick.” The next day, he missed class and was not able to go bike riding with his friends. This incident reinforced the importance of adherence with medication. He started setting a reminder on his phone to avoid missing doses. When dividing chores with his roommate, Adam chose to take the job of cleaning the room to make sure it was done weekly and avoid arguments with his roommate.

Issues Related to Allergy Treatment

A large armamentarium of medications is available to treat allergic rhinitis. (See Chap. 5 for a thorough discussion of the various medications.) Over the past several years, many of these medications have become available over the counter allowing patients with AR to self-treat their symptoms. Adolescents who are transitioning to independent living and taking responsibility for their own health must learn how to choose from among the many allergy medications filling several isles at the pharmacy. An important principle in treating AR is to tailor the treatment to the patient’s symptoms. Adolescents with AR need to understand that not all medications available for the treatment of AR work equally well for all the symptoms. Oral antihistamines are effective for sneezing, itching, and rhinorrhea, but they have little effect on nasal congestion. An intranasal corticosteroid would be a better option if nasal congestion is significant.

Antihistamines

An awareness of the side effect profile of each medication is also necessary for the proper management of AR. Despite the availability of over-the-counter non-sedating antihistamines, it is surprising how often patients with AR self-treat with diphenhydramine, a first-generation sedating antihistamine. Sedation may not be subjectively perceived by a patient who is taking a first-generation antihistamine, which can increase risk for poor outcomes. As discussed previously, sedating antihistamines have a negative effect on learning ability [6]. Teens, particularly those starting college, must be warned about the dangers of drinking alcohol while taking antihistamines. Studies have shown that alcohol increases the psychomotor impairment of sedating antihistamines and can also interact with some of the non-sedating antihistamines [20]. In another study by Vuurman, the effects of sedating and non-sedating antihistamines on driving performance were examined, again using SDLP [21]. Figure 6.5 shows that diphenhydramine, a sedating antihistamine, significantly increased SDLP compared to the non-sedating antihistamine, desloratadine, or placebo. Diphenhydramine also slows break reaction time compared to desloratadine and placebo. These results show the importance of using allergy medications that do not cause sedation or interfere with psychomotor function. Figure 6.3 also shows that the negative effect of AR on driving performance is mitigated by medications that reduce the symptoms of AR. This ameliorating effect underscores the importance of educating adolescents who drive about the dangers of not effectively treating their AR.

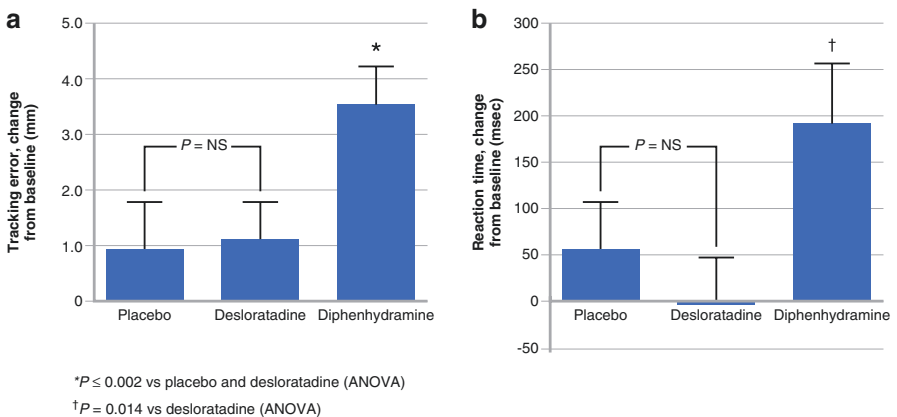


Fig. 6.5 Divided attention test results: change from baseline in (a) mean tracking error and (b) mean reaction time (Used with permission of Springer Nature from Vuurman EF, Rikken GH, Muntjewerff ND, de Halleux F, Ramaekers JG. Effects of desloratadine, diphenhydramine, and placebo on driving performance and psychomotor performance measurements. *Eur J Clin Pharmacol* 2004;60:307–13)

Decongestants

Teens should be cautioned about the stimulant effects of oral decongestants, which can lead to insomnia. Combined with the age-related and AR-related sleep disturbances discussed above, this side effect of oral decongestants can be detrimental to the teen's health and well-being.

Topical decongestant nasal sprays, widely available without prescription, can relieve nasal congestion almost instantly. However, when used regularly for more than a few days, they cause rebound congestion leading the user to apply them more frequently and become dependent on them to be able to breathe. Teens with AR must be warned about the long-term use of nasal decongestants so that they do not fall into this addiction.

Adherence

Daily use of maintenance medications such as intranasal corticosteroids is essential to establishing good control of symptoms. Adolescents may have difficulty adhering to a daily medication schedule. (See Chap. 4 for a thorough discussion of factors involved in nonadherence.) As children, they relied on their parents to remind them to take their medications. When they move away from home, they may simply forget to take their daily medications. New demands on their attention can also distract them from this important task. As they assume responsibility for managing their AR, several factors can help them maintain adherence:

1. Understanding the direct relationship between adherence with treatment and control of their disease
2. Understanding the negative consequences of poor control of AR on their school performance and QOL
3. Use of tools such as health apps or setting reminders on their phones to take medications and refill prescriptions

Clinical Vignette (Part 4)

Adam experienced another setback in his allergy symptoms when his roommate's girlfriend went home to visit her family and left her cat with them. He had agreed to this arrangement on the condition that if his allergy symptoms were not controlled with medication, the cat would have to be removed. Within a few days, Adam developed nasal congestion, frequent sneezing, and difficulty sleeping because of these symptoms. His antihistamine and intranasal steroid were not controlling his symptoms. He also developed cough and wheezing requiring albuterol treatments. He talked to his roommate about his

condition, and, without argument, his roommate quickly found another home for the cat. Adam was glad he had set the rules with his roommate from the beginning. However, it took several weeks and frequent thorough cleaning of the room for Adam to fully recover from this episode.

During his first trip back home, Adam revisited his allergist. He informed her that his allergy symptoms were bothering him during outdoor activities at school even while taking his medications regularly. He was also having flare-ups of his symptoms when visiting friends who owned pets. His allergist could see that Adam's allergies were now affecting his quality of life. She offered him the option of starting immunotherapy to reverse his environmental allergies and reduce his need for medication. After discussing this treatment option with his family and arranging with the student health service to receive the injections at school, Adam received his first injection at his allergist's office and took his allergen extract with the instructions provided by his allergist to school. Within a few months on immunotherapy, Adam's allergy symptoms improved. He was able to participate in more outdoor activities and was able to tolerate visits to houses with pets without suffering.

The Visit with the Allergist: Helping Teens with AR Manage the Challenges of Independent Living

Transitioning to independence is a monumental process in an adolescent's life. It requires preparation on many different levels. Enlisting the help of an allergist/immunologist can be invaluable in preparing the teen with AR to handle the challenges presented by his/her condition in a new environment. The allergist can play an important role in imparting the fundamental knowledge about the disease and its management, providing a "roadmap" for the safe trip ahead. This preparation may require several visits. Education is paramount, including the following key concepts:

- Recognition of AR symptoms, comorbid conditions, and complications such as asthma and sinusitis
- Proper use of medications to treat the symptoms (and what not to use)
- Discussion of when to start and stop each medication
- Environmental allergen avoidance measures in the new location
- Correct technique for using nasal sprays and nasal irrigation
- Importance of adherence with regular treatment to maintain control of symptoms
- Arrangements to continue immunotherapy administration at the new location (if already receiving)

At subsequent visits with the allergist, the adolescent should be able to demonstrate that he/she clearly understands the disease and its management and has gained the knowledge enabling them to take over and be in control. In addition, prescrip-

tion transfers to the new pharmacy should take place, and immunotherapy extracts with instructions for administration should be provided. (See Chap. 3 for more information.) An excellent tool for health-care providers processing the transition from pediatric to adult health care, without a disruption in care, is <http://www.got-transitions.org>. This tool can be used for transfer of care from any one medical facility to another. After the adolescent has settled into his/her new environment and has established a new routing, a follow-up visit should be scheduled, either with the allergist at home or with the new provider. The purpose of this visit is to ensure that the teen is successfully able to manage the allergy and address any questions or issues that have arisen in the new setting. The patient's response to treatment and residual symptoms should be assessed at this visit to determine the level of control of the disease and make adjustments in the treatment accordingly (Fig. 6.1).

Conclusion

Allergic rhinitis can present significant challenges to adolescents who are transitioning to independent living. Control of this disease is essential to the adolescent's cognitive, psychosocial, and academic well-being. With proper planning and, when indicated, with support of an allergist/immunologist, it is possible to achieve good control through education of the adolescent about the symptoms of AR, impact on activities of daily living, and treatment tailored toward symptoms. Preparation well in advance of the transition is necessary to reduce exposure to the relevant allergens in the new environment and ensure adherence to the required medications. Follow-up is also important to guide the adjustments in the management that may be necessary to maintain control.

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Chapter 7

Asthma: A Heterogeneous and Challenging Chronic Condition



David R. Stukus and William C. Anderson III

Background

Asthma is one of the most prevalent chronic pediatric health conditions, affecting approximately 9% of all children and adolescents in the United States [1]. Asthma exacerbations are a leading cause of annual emergency department (ED) visits and hospitalizations, and children with asthma are 1.5 times more likely to require any urgent healthcare utilization compared to children without asthma [2–4]. In addition, the economic impact to society is large in regard to healthcare expenditure, missed school days, and missed work due to poor asthma control and exacerbations [4]. Mortality rates among children from asthma have remained steady over the past decade (195 deaths per year, on average, from 2005 to 2015) [5]. Minority children living in urban environments are especially adversely affected by asthma, with prevalence rates 2–3 times higher than the general population and a mortality rate sevenfold higher in non-Hispanic black children than Caucasian children (10 deaths per million vs. 1.33 deaths per million) [2, 5]. Not only is asthma common, but it frequently interferes with daily functioning and quality of life. Fortunately, with proper diagnosis and management, asthma can be well controlled for the majority of children and adolescents. This chapter will discuss the challenges that line the pathway to gaining asthma control and prevention of exacerbations.

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Asthma Is a Heterogeneous Disease

Risk Factors for Development

It is well known that a family history of asthma and/or allergies is a strong risk factor for the development of asthma. However, we have yet to identify an exact genetic mutation or predetermination; several genetic loci have been correlated with increased risk for asthma development. Most experts agree that asthma, particularly among children, develops from a complex interaction of genetic predisposition (inheritance from parents) and early life, even in utero, exposures to various triggers (environment) [6]. This combination of genes and environment can lead to the development of asthma, but this combination is not the same for everyone. Some examples of early life exposures that have been correlated with increased risk for asthma development include tobacco smoke, traffic pollution, pet dander, increased use of antibiotics, low vitamin D levels, and respiratory syncytial virus infection [6]. Protective factors are strongest for infants born into a farming environment with exposure to endotoxins and bacterial diversity, which has been demonstrated through the hygiene hypothesis [7]. An evolving area of research is focused on the microbiome as a potential early life indicator, cause, and/or potential area of manipulation that may contribute to the development of asthma [8].

Underlying Mechanisms

The pathophysiology of asthma is complicated yet relatively straightforward. According to the National Heart, Lung, and Blood Institute asthma guidelines, asthma is defined as a chronic inflammatory condition of the lower airways hallmarked by recurrent and reversible episodes of bronchoconstriction [9]. These two elements of inflammation and recurrent bronchoconstriction are shared by most people with asthma, along with airway hyperresponsiveness. However, the specific causes or triggers of these pathophysiologic processes vary greatly, which have ramifications in regard to personalized and effective therapy. With long-standing disease, particularly in patients who have poor control and recurrent exacerbations, long-term irreversible changes can take place. The airways of asthmatics can undergo remodeling through angiogenesis, smooth muscle hypertrophy, and changes to the mucus-secreting goblet cells. While no cure currently exists for asthma, effective treatment can control symptoms, prevent exacerbations, and decrease risk for long-standing irreversible changes to the lower airways [9].

Inflammatory Mediators

The majority of children and adolescents with asthma have a Th₂-predominant cytokine milieu associated with their asthma [10]. This includes pro-inflammatory cytokines such as interleukin-4, interleukin-5, and interleukin-13 [11]. Interestingly,

these cytokines are also involved in the development of allergic processes. As such, roughly 60–80% of children with asthma also have environmental allergies. A subset of asthmatics have a Th₁-predominant cytokine profile, with interferon- γ noted in the lower airways of this asthmatic profile [11]. Cell types involved in the localized and systemic inflammatory response also vary, with eosinophils and mast cells predominantly involved in the Th₂ response and neutrophils responsible for Th₁ inflammation.

Characterization

Given the heterogeneity in pathophysiology and, as discussed further in this chapter, response to therapy, efforts have been made to better identify what type of asthma someone has through assessment of clinical history and/or biomarkers. This has led to the adoption of various phenotypes and endotypes to better identify specific types of asthma. A phenotype is a set of observable characteristics of an individual resulting from the interaction of their genotype with their environment. An endotype is a subtype of a condition, defined by a distinct functional or pathobiological mechanism. Phenotypes can be thought of as observable characteristics, which may offer clinically relevant information but do not necessarily offer insight into the underlying disease process. Identification of someone's asthma phenotype can group patients together for improved understanding and treatment of their asthma, allowing for potentially more targeted interventions [12]. Endotypes differ from phenotypes by describing distinct disease entities and pathophysiologic mechanisms. Identification of someone's endotype can yield very specific information about their response to treatment and has important ramifications for clinical trials and research given that asthma is not “one size fits all” but rather a collection of similar yet highly variable pathophysiologic processes [13]. See Table 7.1 for examples of various asthma phenotypes and endotypes.

Table 7.1 Examples of asthma phenotypes and endotypes

Phenotype	Endotypes
Eosinophilic	Allergic asthma, aspirin-sensitive asthma, hypereosinophilic asthma
Exacerbation prone	Allergic asthma, aspirin-sensitive asthma, preschool wheezer with risk factors, viral-exacerbated asthma
Exercise-induced	Cross-country skiers' asthma, allergic asthma, preschool wheezer with risk factors
Adult-onset	Aspirin-sensitive asthma, infection-induced asthma, hypereosinophilic asthma, neutrophilic asthma
Fixed airflow limitation	Neutrophilic asthma
Poorly steroid-responsive	Neutrophilic asthma, airflow obstruction related to obesity

Clinical Vignette

A 12-year-old boy presents for evaluation of recurrent cough and wheeze. He states that symptoms began about 4 years ago. He develops cough and wheeze with upper respiratory infections and changes in the weather. He has had four separate emergency department visits for respiratory difficulty, including once after he attended an outdoor bonfire. He has been treated with prednisone six times in the past 2 years and receives antibiotics during his upper respiratory infections/coughing episodes approximately four times a year. He has had one prior chest radiograph during an acute episode of cough/wheeze that revealed right middle lobe atelectasis, and he was diagnosed with pneumonia. In between acute episodes, he denies any coughing or wheezing. His parents report that he does not have asthma because he plays sports and runs all the time without any difficulty. He had atopic dermatitis as an infant/toddler, which has essentially resolved. He also develops itchy, watery eyes and sneezing/runny nose each spring and early summer. The family has two dogs and one cat at home and his father smokes cigarettes but “always outside.”

Physical examination reveals enlarged nasal turbinates with pale, bluish mucosa. Lung exam is normal with good aeration bilaterally and no wheezes or cough. Skin exam is clear without rash.

Spirometry is obtained which reveals normal lung function with FEV₁ 110% predicted, FVC 100% predicted, FEV₁/FVC ratio 102%, and FEF₂₅₋₇₅ 81% predicted.

Diagnosis

As with any condition, establishing a diagnosis of asthma begins with a thorough clinical history. It is important to keep in mind that asthma symptoms in children and adolescents often wax and wane over time. Most people report no baseline or chronic symptoms and only have respiratory symptoms upon exposure to their triggers. A diagnosis of asthma can only be established once a pattern of reversible and recurrent episodes of suspected bronchospasm has occurred. Most experts agree that asthma can be diagnosed after at least four separate wheezing/coughing episodes or when suspicion is high given pertinent family history or history of other comorbid conditions. There are many viral illnesses that can result in lower respiratory tract infections and wheezing in otherwise healthy individuals, i.e., rhinovirus, enterovirus, RSV, and metapneumovirus. Thus, acute wheezing without a history of prior episodes of respiratory symptoms would not be consistent with asthma.

The family history should be considered in the diagnosis of asthma. If biological parents or siblings have a history of physician-diagnosed asthma or allergic conditions such as atopic dermatitis or allergic rhinitis, then suspicion should be raised. Comorbid conditions associated with increased risk for asthma include a history of atopic dermatitis as an infant/toddler, environmental allergies, and food allergies.

Clinical history should focus on respiratory symptoms (discussed below), recurrent nature of symptoms, and how symptoms change after treatment.

The physical exam is often normal in children and adolescents with asthma, unless they are acutely symptomatic at the time of examination. A normal physical exam and lack of cough or wheeze do not exclude a diagnosis of asthma. Other signs may be present that suggest comorbid conditions associated with asthma, such as infraorbital swelling/dark circles and/or enlarged nasal turbinates with pale/bluish mucosa suggestive for allergic rhinitis and rashes consistent with atopic dermatitis.

Prior treatment should always be considered, and if no specific treatment has occurred, then a diagnostic and therapeutic trial with albuterol and/or corticosteroids can assist in making the diagnosis. Albuterol is a beta-adrenergic agonist that causes smooth muscle relaxation of the lower airways. A history of recurrent respiratory symptoms that improve (even temporarily) with albuterol use suggests bronchoconstriction and likely asthma. The effects of albuterol wane after 3–4 h and recurrence of symptoms from asthma is expected while acutely symptomatic. However, albuterol will not effectively treat cough or wheeze from other causes such as postnasal drip, sinusitis, pneumonia, or exposure to irritants (tobacco smoke, marijuana, or hookah). If a patient with recurrent respiratory symptoms has not received albuterol, this can be an excellent therapy to use on a trial basis. Patients should be instructed on when and how to use albuterol with proper technique and then asked to keep a diary of use, along with if/how symptoms changed. Within 4–6 weeks, if symptoms occur often enough, both a favorable and lack of response to albuterol can greatly assist the diagnosis. Lack of any improvement (as long as proper technique/sufficient dosing occurred) suggests causes other than asthma, whereas temporary resolution of symptoms would suggest asthma.

There are many other conditions to consider in the differential diagnosis of asthma. Consideration of these various conditions should take many variables into account, including age of onset, duration, recurrence over time, other associated symptoms, and response to therapy. See Table 7.2 for a list of other conditions to consider in the diagnostic evaluation.

Symptoms

Children and adolescents with asthma can present with a wide range of symptoms, which may occur both acutely and on a chronic basis. As mentioned previously, symptoms due to asthma should recur over time, which is a key element of the history that must be provided. For anyone with poorly controlled or severe asthma, symptoms can occur daily or throughout the day, whereas people with mild intermittent asthma may report very infrequent symptoms that only occur upon exposure to one specific trigger.

Contrary to popular belief, cough is the most common symptom among children and adolescents with asthma, not wheezing [9, 14]. Many children will not have

Table 7.2 Differential diagnosis of asthma

Infants	Toddlers	School age	Adolescents
Recurrent viral infections	Recurrent viral infections	Allergic rhinitis	Allergic rhinitis
Adenoid hypertrophy	Adenoid hypertrophy	Recurrent viral infections	Active smoking: cigarettes, marijuana, hookah
Environmental irritants (tobacco smoke)	Environmental irritants (tobacco smoke)	Environmental irritants (tobacco smoke)	Environmental irritants (tobacco smoke)
Bronchiolitis	Allergic rhinitis	Recurrent sinusitis	Recurrent sinusitis
Cystic fibrosis	Recurrent sinusitis	Vocal cord dysfunction	Vocal cord dysfunction
Foreign body	Cystic fibrosis	Adenoid hypertrophy	
Anatomic abnormality	Foreign body		
Reflux esophagitis			
Aspiration			
Tracheobronchomalacia			
Bronchopulmonary dysplasia			
Congenital heart disease			

Table 7.3 Common causes of nocturnal cough in children and adolescents

Cause	Differentiating factors
Asthma	Known or suspected history of asthma Persistent cough, wheeze Wakes from sleep Improves after albuterol
Postnasal drip (viral or allergic rhinitis, sinusitis)	Significant nasal congestion, rhinorrhea Cough productive for mucus Cough worse upon awakening in the morning Less likely to wake from sleep once asleep
Gastroesophageal reflux	Abdominal pain, belching after meals Brash taste in the posterior pharynx Eating meal/snacks within 1–2 h of bedtime
Irritant cough	Exposure to aerosolized products inside home (essential oil diffusers, scented candles, tobacco smoke, perfumes, air fresheners, cleaning agents)

audible wheezing (particularly without auscultation with a stethoscope), and lack thereof should not exclude a diagnosis of asthma. Cough can be present acutely or on a chronic basis. Post-tussive emesis, or coughing to the point of vomiting mucus or stomach contents, has been identified as a sensitive indicator of asthma. Asthma symptoms tend to worsen at night, specifically after falling asleep, or interfere with the ability to fall asleep. This can be related to the natural physiological decline in cortisol levels toward early morning, physiologic reasons such as increase in post-nasal drip when lying flat, or exposure to irritants/allergens in the bedroom. However, not all nocturnal cough is due to asthma (Table 7.3).

Children and adolescents with asthma can report a range of other symptoms including chest tightness, difficulty breathing, shortness of breath, chest discomfort, and increased work of breathing. Signs of acute asthma exacerbation and particularly of moderate-to-severe exacerbations include nasal flaring and accessory muscle use hallmarked by suprasternal and/or intercostal retractions. Retractions indicate more severe bronchoconstriction and can lead to fatigue without acute intervention; hence patients need to be aware that the presence of retractions indicates a need to use their rescue medications and seek emergency medical care immediately.

Triggers

An asthma trigger is any stimulus that provokes airway hyperresponsiveness and airflow limitation. Triggers are mostly found externally but can be internal as well. Each person with asthma has their own individual triggers, which may be one or many different things [9]. Triggers can change over time and may only provoke symptoms when a certain threshold level of exposure has occurred. Not every person with asthma shares the same triggers, but there are common triggers that frequently cause exacerbations in children and adolescents, such as viral upper respiratory infections and weather changes. Exposure to asthma triggers may provoke acute-onset exacerbations or contribute to chronic symptoms and long-standing poor asthma control [15].

It is important to identify specific triggers for anyone with asthma to assist in avoidance, if possible. Many asthma triggers are also allergens (Table 7.4), which are important to accurately identify through skin prick or serum IgE testing. Both healthcare professionals and patients may misidentify triggers, and patients may be misdiagnosed with allergies or advised to partake in costly remediation measures without confirmatory testing. Avoidance strategies vary according to the specific trigger; see Table 7.5 for some measures to avoid common triggers inside the home.

Clinical Vignette

A 13-year-old female presents for evaluation of cough and chest tightness with exercise. She is an active athlete and reports onset of symptoms approximately 15 min after she starts vigorous exercise. This occurs throughout the year and is reproducible whether she is playing basketball, playing softball, or swimming. She denies cough, wheeze, or respiratory symptoms at other times and has never experienced an exacerbation requiring ED treatment or prednisone. Thus far, she has not tried any medications and typically will drink some water and keeps exercising through her symptoms but reports that this negatively impacts her performance. She has never been diagnosed with allergic rhinitis, atopic dermatitis, or asthma.

Table 7.4 Common asthma triggers

Internal	Outdoor	Indoor
Emotions (stress, anxiety, laughter)	Pollen (tree, grass, weed, ragweed)	Pet dander (cats and dogs)
Upper respiratory infections	Mold spores	Dust mites
Gastroesophageal reflux	Weather changes	Cockroaches
Exercise	Cold, dry air	Rodents
	Hot, humid air	Tobacco smoke
	Campfires	Scented candles, incense
	Pollution (ozone action days)	Essential oil diffusers
		Wood-burning stoves
		Cleaning agents

Table 7.5 Trigger avoidance measures

Trigger	Avoidance measures
Pet dander	• Keep pets out of bedroom at all times • Wash animals twice weekly • Vacuum with HEPA filter and dust several times/week
Outdoor pollen	• Keep windows at home closed at all times • Change clothing after spending time outdoors • Wash face and hair every night before bed • Use air conditioning in home and car
Dust mites	• Place zippered encasements on all pillows, mattress, box spring • Wash all linens in hot water weekly • Remove all stuffed toys from the bed • Keep indoor humidity <50% • Avoid humidifiers in the bedroom
Tobacco smoke	• Do not allow anyone to smoke inside the home at all times • Smokers should wear separate outer layer when smoking outdoors and leave layer outside

Exercise

It is a common misconception among parents, patients, and even healthcare providers that anyone with asthma will have difficulty with exercise. Many patients are also incorrectly advised to either avoid or limit their physical activity due to asthma. Exercise can serve as a trigger in three different ways:

1. Exercise-induced bronchoconstriction: This can occur in athletes who do not otherwise have asthma but develop symptoms with exercising at high intensity or prolonged duration.
2. Patients with persistent and/or poorly controlled asthma: Exercise can serve as a trigger for patients with asthma, causing reproducible symptoms with activity.
3. Patients with mild, intermittent asthma who are experiencing exacerbation: Many children and adolescents with asthma have no problems during exercise until they become ill with an upper respiratory infection or experience symptoms

Table 7.6 Suggested treatment for exercise-induced bronchoconstriction

Perform a 10–15 min warm-up period prior to exercise
Take 2–4 puffs of albuterol with a spacer device at least 15 min prior to exercise
If symptoms occur during exercise, then they should rest and take additional 2–4 puffs of albuterol with spacer. For symptoms during exercise, patients do not need to wait 4 h in between doses
Activity should not resume until symptoms have completely resolved

from other triggers such as pollen or weather changes. This may provoke temporary symptoms with exercise.

It is important for the clinician to not assume everyone with asthma will experience difficulty with exercise and equally important to not assume that everyone who experiences respiratory difficulty with exercise has asthma [16]. The gold standard diagnostic test for establishing exercise-induced bronchoconstriction is the eucapnic voluntary hyperpnea (EVH) test [17]. Unfortunately, EVH is not readily available for most clinicians to order and can be technically demanding to perform. Briefly, EVH involves having the patient inhale a gas mixture (21% oxygen, 5% carbon dioxide, and balance nitrogen) at a high minute ventilation for 6 min. Spirometry is then performed sequentially at 0, 5, 10, and 20 min after the test. A 10% decline in forced expiratory volume at 1 s (FEV₁) is considered positive for exercise-induced bronchoconstriction.

Patients with exercise-induced bronchoconstriction typically experience symptom onset several minutes after vigorous exercise begins. Patients who report immediate respiratory difficulty at onset of exercise should be evaluated for other conditions such as vocal cord dysfunction. If someone has a history of recurrent respiratory symptoms during exercise, particularly if they already have a diagnosis of asthma, a pretreatment regimen to help prevent and reduce symptom severity and frequency should be established (Table 7.6).

Comorbid Conditions

When patients have persistent and difficult-to-control asthma, hallmarked by frequent symptoms, disruption in sleep and daily activities, and/or exacerbations, then one should consider the presence and negative impact of various comorbid conditions [18]. The upper and lower airways represent one contiguous system, and significant upper airway symptoms may contribute to poor asthma control. In a similar fashion, issues related to the upper gastrointestinal tract may affect asthma given the proximity of the esophagus with the trachea and upper airway. Likewise, any external factors that impact the physiology and necessary expansion of the lungs during breathing can impact asthma as well.

Comorbid conditions to consider in children and adolescents with asthma include chronic rhinosinusitis, nasal polyposis, allergic rhinitis, adenoid hypertrophy, vocal

cord dysfunction, anxiety and depression, obesity, obstructive sleep apnea, gastro-esophageal reflux disease, and possible underlying immune deficiency such as primary ciliary dyskinesia or common variable immune deficiency. A thorough discussion of these various conditions lies outside the scope of this chapter, but it is important for clinicians to recognize the contributory factors involved and to treat these conditions accordingly.

Diagnostic Testing

Assessment of lung function is a helpful tool in both the diagnosis and management of asthma. Spirometry is recommended for all patients with asthma, both at the time of diagnosis and at least annually thereafter, with more frequent assessment if symptoms are poorly controlled [9]. Contrary to popular belief, spirometry does not definitively determine whether someone has a diagnosis of asthma. Spirometry only offers an assessment of lung function at that one time point, which must then be interpreted within the context of the clinical history.

Asthma causes obstruction of the large and small airways. As mentioned previously in this chapter, most children and adolescents with asthma experience symptoms intermittently. This concept is very important to keep in mind when interpreting spirometry as many children and adolescents with asthma can have a completely normal lung function. A normal lung function without obstruction on spirometry does not exclude a diagnosis of asthma. Patterns of obstruction consistent with asthma can be detected on spirometry through reduced forced vital capacity (FVC), reduced forced expiratory volume in 1 s (FEV_1), reduced FVC/ FEV_1 ratio, and reduced forced expiratory flow 25–75% (FEF_{25-75}) which is a measure of small airway function [19]. Children with asthma may preserve large airway function (normal FEV_1) but have reduced small airway function (FEF_{25-75}).

Any values for FVC, FEV_1 , FVC/ FEV_1 , or FEF_{25-75} that are at least 80% predicted (based upon comparison of normal values for age, gender, height, weight, and race) are considered normal [9]. There are also criteria to establish whether bronchial hyperresponsiveness may be present. When asthma is suspected, a 12% and 200 ml improvement in FEV_1 15–20 min after the administration of 2–4 puffs of albuterol is indicative of underlying bronchial hyperreactivity [9]. This can occur even when baseline FEV_1 is normal and is often a standard element of the diagnostic assessment for asthma.

Spirometry is a technically demanding procedure and most patients, including adults, require practice and coaching. Children <5 years of age can rarely exhale with enough force to generate useful readings. Even children older than 5 often require multiple attempts over time to master this challenging test. Spirometry is best interpreted when the patient is able to forcibly exhale for at least 3 s, ideally longer. There are many technical aspects that may interfere with proper testing, including incomplete seal around the mouthpiece, short exhalation time, poor posture, and coughing during the test.

Peak flow meters are handheld, portable devices that measure peak expiratory flow rate (PEFR). Peak flow meters offer a spot assessment of one measure of lung function but are entirely dependent upon patient effort. Peak flow meters are not sufficient enough to be used in the office setting in place of spirometry or to establish a diagnosis of asthma [9].

Fractional exhaled nitric oxide (FeNO) is a noninvasive measure of eosinophilic airway inflammation [20]. FeNO is one of the first commercially available and clinically useful biomarkers that can both assess for lower airway inflammation and help determine a person's asthma phenotype. Nitric oxide is a by-product of eosinophilic metabolism, and FeNO levels are typically elevated secondary to eosinophilic (Th₂ or allergic) inflammation. When elevated, FeNO levels can help establish a diagnosis of asthma when the clinical history and/or lung function findings are suggestive. FeNO can also be monitored over time both to assess response to therapy (inhaled corticosteroids often decrease eosinophilic inflammation) and gauge readiness to step-down therapy.

The methacholine bronchial provocation test is a highly sensitive diagnostic tool that can rule out the presence of asthma when the test is interpreted as negative [21]. Methacholine challenges can be technically demanding and require serial spirometric measurements after inhalation of gradually increasing concentrations of methacholine. Methacholine is a cholinergic stimulator that induces bronchoconstriction when inhaled in sufficient concentrations by asthmatics. Patients without asthma may experience bronchoconstriction after inhalation of very high concentrations of methacholine as well; thus the parameters for proper testing utilize a cutoff point of 16 mg/mL. Patients with a 20% decline in FEV₁ after inhalation of methacholine concentrations up to 16 mg/mL are suspected to have asthma. Unfortunately, methacholine testing is not readily available for most clinicians and patients.

Due to the nonspecific nature of findings and/or unfavorable cost profile, the following tests have little utility in helping to establish the initial diagnosis of asthma: chest radiograph, chest CT scan, total serum IgE level, complete blood count with differential, and bronchoscopy with lavage.

Assessment of Severity and Control

The latest version of the NHLBI asthma guidelines (last updated in 2007) separated assessment into the domains of severity and control and divided this into three age groups: <4 years of age, 4–11 years of age, and ≥12 years of age [9]. These are both extremely similar, but the distinction is helpful in deciding if/how to adjust treatment for a new asthma diagnosis (based upon severity) or for someone who is already known to have asthma (level of control). This change reflects the difficulty in truly assessing someone's asthma severity, which represents the intrinsic nature of the disease, if they are already receiving daily controller therapy. Another way to think of this distinction is to use severity to initiate medications and to assess control to adjust therapy.

When establishing the initial diagnosis of asthma, severity should be classified according to one of four levels: intermittent, mild, moderate, or severe persistent. The components used to establish level of severity include frequency of daytime symptoms, frequency of nocturnal awakenings (not just nighttime cough), use of short-acting albuterol to treat symptoms (not including prior to or during exercise), interference with normal activity, and measures of lung function (Table 7.7). The asthma guidelines utilize all five components in the assessment of severity, but lung function measures are not a necessity. The level of severity should be decided by whichever category has the most severe designation. For example, if a patient has infrequent daytime symptoms ≤ 2 days/week (intermittent) and uses albuterol 2 days/week (intermittent) but wakes at night more than once a week but not nightly (moderate persistent), then they should be classified as having moderate persistent asthma.

Once a patient has been diagnosed with asthma, their level of control should be routinely assessed at every visit and categorized into one of three categories: well controlled, not well controlled, or very poorly controlled. This utilizes very similar components as the assessment of severity, including frequency of daytime symptoms, frequency of nocturnal awakenings, interference with normal activity, and use of short-acting albuterol to treat symptoms (not including prior to or during exercise), and also incorporates lung function testing by spirometry or use of a peak flow meter (Table 7.8). In addition, the level of asthma control can be assessed through the use of one of several validated patient questionnaires, such as the Asthma Control Test (ACT) [22], the Asthma Therapy Assessment Questionnaire (ATAQ) [23], or the Asthma Control Questionnaire (ACQ) [24].

It is important to understand how to assess and interpret the level of asthma control. This assessment only takes into account the most recent 4 weeks of symptoms, albuterol use, and interference with activity. Patient recall over extended periods of time is poor. In addition, asthma symptoms fluctuate over time and are variable based upon season of the year, recent exposures, and many other factors. Thus, the assessment of asthma control really only offers a snapshot of how a patient has been feeling over the past month. This should be considered in regard to both over- and underestimating overall asthma management and need for change in therapy. For example, patients with frequent emergency room visits over the past 6 months may report good control over the past month, which would overestimate the level of control and not reflect their recent exacerbations. Conversely, patients with an acute or recent upper respiratory infection that have increased symptoms during the past 4 weeks but who have otherwise been asymptomatic without exacerbations may underestimate their level of asthma control over the long term.

While there are pitfalls to the assessment of control over a relatively short period of time (previous 4 weeks), it still offers useful information. More importantly, routine assessment and asking these questions at healthcare visits help instill necessary self-management skills within children and adolescents and help encourage realistic

Table 7.7 Classifying asthma severity in children ≥ 12 years of age and adults

Components of severity		Classification of asthma severity (youths ≥12 years of age and adults)			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment Normal FEV ₁ /FVC • 8–19 years, 85% • 20–39 years, 80% • 40–59 years, 75% • 60–80 years, 70%	Symptoms	≤2 days/week	>2 days/ week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2×/month	3–4×/ month	>1×/week, but not nightly	Often 7×/ week
	Short-acting beta ₂ -agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/ week but not >1×/ day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV ₁ between exacerbations			
		• FEV ₁ >80% predicted	• FEV ₁ ≥80% predicted	• FEV ₁ >60% but <80% predicted	• FEV ₁ <60% predicted
		• EV ₁ /FVC normal	• FEV ₁ / FVC normal	• FEV ₁ / FVC reduced 5%	• FEV ₁ / FVC reduced >5%
	Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note)	
Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category					
Relative annual risk of exacerbations may be related to FEV ₁					

FEV₁ forced expiratory volume in 1 s, FVC forced vital capacity

Notes:

Level of severity is determined by assessment of both impairment and risk. Assess impairment domain by patient's/caregiver recall of previous 2–4 weeks and spirometry. Assign severity to the most severe category in which any feature occurs

At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma severity. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate greater underlying disease severity. For treatment purposes, patients who had ≥ 2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma

Source: National Heart, Lung, and Blood Institute, National Institutes of Health, US Department of Health and Human Services

Table 7.8 Classifying asthma control in children ≥ 12 years of age and adults

		Classification of asthma control (youths ≥ 12 years of age and adults)		
Components of control		Well controlled	Not well controlled	Very poorly controlled
<i>Impairment</i>	Symptoms	≤ 2 days/week	> 2 days/week	Throughout the day
	Nighttime awakening	$\leq 2 \times$ /month	1–3 $\times$ /week	$\geq 4 \times$ /week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting β_2 -agonist use for symptom control (not prevention of EIB)	≤ 2 days/week	> 2 days/week	Several times per day
	FEV ₁ or peak flow	$> 80\%$ predicted/ personal best	60–80% predicted/ personal best	$< 60\%$ predicted/ personal best
	Validated questionnaires			
	ATAQ ACQ ACT	0 $\leq 0.75^a$ ≥ 20	1–2 ≥ 1.5 16–19	3–4 N/A ≤ 15
<i>Risk</i>	Exacerbations	0–1/year	≥ 2 /year (see note)	
		Consider severity and interval since last exacerbation		
	Progressive loss of lung function	Evaluation requires long-term follow-up care		
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk		

EIB exercise-induced bronchoconstriction, FEV₁ forced expiratory volume in 1 s, ACT Asthma Control Test, ATAQ Asthma Therapy Assessment Questionnaire, ACQ Asthma Control Questionnaire

Notes:

The level of control is based on the most severe impairment or risk category. Assess impairment domain by patient's recall of previous 2–4 weeks and by spirometry/or peak flow measures. Symptom assessment for longer periods should reflect a global assessment, such as inquiring whether the patient's asthma is better or worse since the last visit

At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma control. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate poorer disease control. For treatment purposes, patients who had ≥ 2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have not-well-controlled asthma, even in the absence of impairment levels consistent with not-well-controlled asthma

Source: National Heart, Lung, and Blood Institute, National Institutes of Health, US Department of Health and Human Services

^aACQ values of 0.76–1.4 are indeterminate regarding well-controlled asthma

expectations in regard to asthma management. For instance, someone with well-controlled asthma should experience symptoms less than twice a week, but this allows for some symptoms to occur. Hence, striving for complete elimination of all symptoms and/or need for albuterol is not only not realistic but can potentially lead to dissatisfaction with treatment.

Stepwise Approach to Treatment

Children and adolescents with asthma warrant a multifaceted approach to treatment, which includes:

- Development of self-management skills to recognize and treat symptoms when they occur and prevent exacerbations
- Identification and avoidance of environmental factors/triggers that worsen asthma
- Control of comorbid conditions that may affect asthma
- Pharmacologic therapy

Self-Management

Children and adolescents with asthma should be active participants in their care, including in the discussion of symptoms and medical management. It is important for them to learn and understand the various ways in which asthma may present, including *their* own experience with prior symptoms. They should be educated on an age-appropriate level to help them understand that asthma is a disease of the lungs and symptoms are due to tightening of their airways. Many children and adolescents may not recognize symptoms when they occur or may ignore them as it is inconvenient to stop activity or take time for treatment. They should be encouraged to use albuterol early at the first sign of new-onset symptoms and to repeat albuterol every 3–4 h until symptoms resolve.

Albuterol should not be referred to as an *emergency medication*, but instead it should be labeled as a *reliever* medication. It helps to inform patients that they will need to use albuterol (otherwise they would not have asthma) but the goal is to not require it frequently or have severe symptoms. When taught that albuterol is an emergency medication, patients may withhold treatment until they feel they are in an emergency situation or may misinterpret this as indicating the need to seek emergency care anytime albuterol is used. This seemingly minor distinction may be a source of confusion for many adolescents, and healthcare providers can play an active role in providing proper education.

A key component of self-management is the proper use of inhalers. The proper technique and use of spacers/holding chambers should be reinforced at every office visit, including time to practice with their own inhaler or a training device with feedback from the provider. Lack of spacer usage and inappropriate inhaler technique are common factors associated with nonadherence [25]. Adolescents in particular do not routinely use spacers as they are inconvenient to carry, are frequently lost, and may be socially embarrassing due to their size/appearance. Adolescents may not understand the reason for using spacers and it helps to educate them regarding aerosol deposition [26]. One approach is to not make it about the patient at all but instead discuss the “flawed” design of the metered-dose inhalers. An example discussion: “The medication inside inhalers is in a liquid form and it takes several

inches to allow it to turn into a small particle that can enter your lungs. If you place the inhaler into your mouth without a spacer, there is not enough space for that to happen and most of the medication lands onto your tongue/throat as a liquid, which is then swallowed into your stomach. This has nothing to do with you or your technique, but is a property of the medicine. However, when you attach a spacer, it allows the medicine to turn into small particles that you can then inhale into your lungs.”

Many patients have long-standing preferences to receive their asthma medications delivered through a nebulizer, as opposed to a metered-dose inhaler (MDI) with spacer. This is often reinforced by medical providers and trips to the emergency department, where it is commonplace to set a patient with an asthma exacerbation up with repeated nebulizer treatments and then return for reassessment after a period of time. However, the delivery of medication and efficacy from a MDI are equivalent, and potentially superior, to that of a nebulizer [27]. Reinforcement of this (or avoidance of relying on nebulizers in the first place) can make self-management significantly easier. Compared with nebulizers, MDIs are faster, portable, easier to use, and as effective. Healthcare providers can provide a positive benefit to their adolescent patients with asthma by instructing them on proper MDI technique with a spacer and freeing them from requiring nebulizer treatments whenever they have symptoms. This becomes even more important when adolescents transition to independent living and are responsible for their own treatment.

Another factor that healthcare providers often negatively influence is in giving recommendations for the frequency and amount of albuterol. Guideline-based therapy suggests patients start using albuterol at the onset of symptoms with dosing of up to six puffs every 3–4 h for 24–48 h at home, as long as provisions for when to seek emergency care are reviewed with patients [9]. Many providers, school nurses, and parents are told that albuterol can only be used at a dose of two puffs every 4 h, and any use that exceeds this warrants urgent evaluation. Instead of being educated about a non-evidence based, and often non-therapeutic, minimal dosing regimen, patients should be instructed to use their albuterol early and often at the first sign of new-onset symptoms [28]. This approach can provide more patient empowerment, lead to more aggressive use of albuterol with less hesitancy, and ideally lead to fewer exacerbations. Patients should also be counseled that routine use of albuterol at higher doses/frequency is a sign of poorly controlled asthma and be given clear instructions on when to call their provider for additional recommendations [28].

Written Treatment Plans

Every patient with asthma should have a copy of a current asthma treatment plan. This plan serves as a reference sheet that details their daily medication regimen, indications for when and how to start treatment, and instructions for when to call their provider or seek emergency medical care [9, 28]. There are many variations

available to use, and most adopt the traffic light model with a green zone at the top, which includes instructions for daily medications to use when patients are asymptomatic. The red zone often appears at the bottom, and this includes instructions for when an asthma exacerbation is occurring and symptoms may be more severe. The yellow zone occupies the middle of the treatment plan and is the most important part of this document. The yellow zone should provide clear instructions on when patients should start their reliever medications and/or adjust controllers, as well as any other steps to take in an effort to prevent progression to the red zone and need for urgent healthcare utilization. The “Yellow Zone Practice Parameters” by Dinakar and colleagues offers a comprehensive review of the literature and provides extensive recommendations in regard to at-home management of asthma at the onset of symptoms [28].

Unfortunately, asthma treatment plans are underutilized and often forgotten by patients. A new approach to this is through technology and recent proliferation of mobile asthma applications for use on smartphones. There are dozens of options available for adolescents to use which incorporate the traditional paper-based asthma treatment plan into an electronic version which can be immediately accessible from any handheld mobile device [29]. Prior to recommending any specific mobile asthma application for patient use, it is strongly encouraged for healthcare providers to review the aspects of the application as there is no current regulatory process involved in monitoring the development or availability of these apps, many of which contain non-evidence-based information.

Medications

As mentioned earlier in this chapter, asthma is hallmarked by two common components: inflammation of the lower airways and recurrent bronchoconstriction. Treatment of each of these components differs greatly. Assessment of asthma severity and control can help determine whether someone has persistent or poorly controlled asthma, both of which indicate more underlying inflammation and the need for daily long-term controller medications. Short-acting bronchodilators are not effective at treating inflammation and thus anti-inflammatory medications must be used. Anti-inflammatory controller medications offer the most benefit when used daily (often twice daily) and consistently, with less efficacy when used on an inconsistent basis or only when symptoms occur.

The NHLBI asthma guidelines offer a very useful approach to both initiating and adjusting therapy (Fig. 7.1). Patients should be prescribed medications on a stepwise approach, knowing that therapy may need to be increased during times of poor control but also decreased when patients have been well controlled for 3–6 months. Medications may need to be adjusted seasonally, particularly during the autumn and winter when asthma exacerbations occur more frequently. In addition, a patient’s personal history should be used to guide their individual stepwise approach, i.e., if they historically have more symptoms in the spring, then therapy can be increased

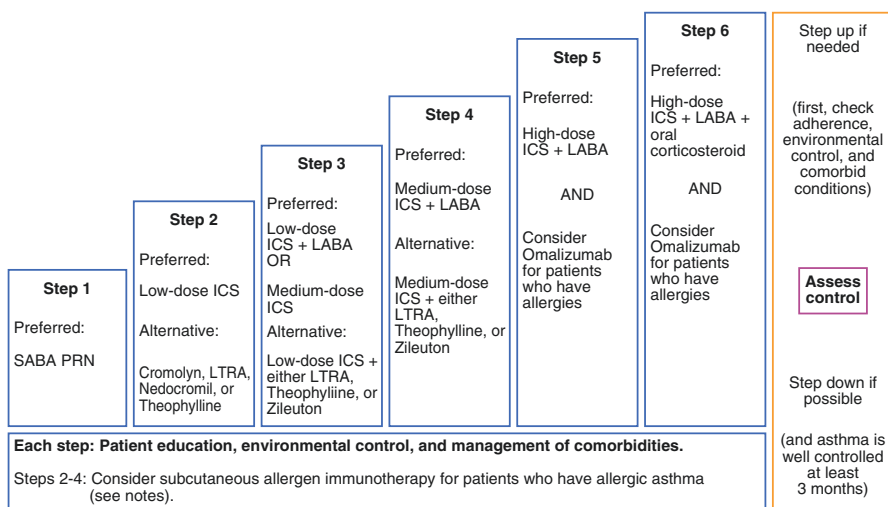


Fig. 7.1 Stepwise approach to asthma management (*Source:* National Heart, Lung, and Blood Institute, National Institutes of Health, US Department of Health and Human Services), *SABA* short acting beta-agonist, *ICS* inhaled corticosteroid, *LTRA* leukotriene receptor antagonist, *LABA* long acting beta-agonist

during that season and subsequently decreased at other times of the year. Asthma treatment should not be a static process but instead requires a thoughtful approach to adjusting medications for each patient throughout the year and over time.

Inhaled Corticosteroids

The recommended first-line therapy for anyone who warrants a controller medication is treatment with daily inhaled corticosteroids (ICS). ICS can effectively decrease lower airway inflammation for the majority of children and adolescents with asthma, particularly if they have an allergic phenotype or eosinophil-driven inflammatory process. There are multiple types of inhaled corticosteroids available to use for treatment, and each one differs according to particle size, potency, bio-availability, and dosing. Multiple clinical trials have demonstrated that the use of ICS cannot cure or change the natural course of asthma, but consistent use can effectively reduce symptoms, reduce the frequency and severity of exacerbations, and improve quality of life [30]. Hence, anyone with poorly controlled asthma or persistent symptoms should be considered for treatment with a daily ICS.

Inhaled corticosteroids can have side effects, particularly when used without spacers/holding chambers. Risk of side effects increases with increasing dose, and

high-dose ICS should never be used as monotherapy in any patients with asthma. A subset of asthmatics respond poorly to use of ICS, and there are other treatment modalities to consider prior to increasing to the highest available dosages of ICS. The most common side effects from ICS use stem from oral deposition and include sore throat, reflex cough, and oropharyngeal candidiasis. It is recommended that all patients use a spacer, rinse their mouth, and spit (not swallow) after each use of ICS, which can decrease the potential for localized side effects. Systemic absorption and negative effect on the hypothalamic-pituitary-adrenal axis is the most concerning side effect from use of ICS, but is not typically observed with proper use of low-medium-dose ICS, hence the recommendations to limit use of high doses and step-down to lowest dose when possible.

Impaired height attainment from use of ICS is a frequent concern among parents and providers. It is important to recognize that this has been studied extensively and most studies have demonstrated very similar findings: use of ICS for >12 months in children with asthma has limited impact on annual growth velocity or final adult height [31]. Studies have consistently demonstrated a potential reduction of roughly 1 cm in final adult height. This finding is important to interpret in the greater context of patients who experience frequent asthma exacerbations and require oral corticosteroids, which have a much greater risk for unfavorable side effects. This also provides additional rationale for adjusting treatment when asthma has been well controlled for a period of time and using lowest-dose ICS possible to control symptoms.

Montelukast (Leukotriene Antagonists)

Montelukast is a leukotriene antagonist that is an approved asthma treatment, available as pills, chewable tablets, and granules for small children. Montelukast is approved for use in patients with allergic asthma and exercise-induced asthma (but not as a replacement for albuterol prior to exercise). Leukotrienes are involved in the late-phase allergic response and produce Th₂ inflammation. Hence, montelukast can offer benefit in children and adolescents with allergic inflammation as the hallmark of their asthma. The NHLBI asthma guidelines do not recommend montelukast as a first-line therapy but instead recommend consideration for patients who have persistent or poorly controlled asthma despite use of low-dose ICS and require additional treatment (Fig. 7.1) [9]. Some patients may benefit from use of montelukast as monotherapy or as their first-line agent, but accurate identification of these individuals at the time of diagnosis is challenging [32]. Many patients and providers favor montelukast due to its once-daily administration, oral formulation, and concern for side effects from ICS use. However, it is important to understand the limitations in use and recommendations to use as *add-on* rather than first-line therapy.

Side effects from montelukast are less likely to occur than with ICS use, but it does carry a black box warning from the US Food and Drug Administration. The black box warning stems from reports of behavioral changes and possible suicidal ideation in patients who have received treatment with montelukast. This is recognized as a rare side effect but should be discussed with all patients prior to use, along with instruction to notify their provider should any noticeable changes occur. Most patients experience these changes relatively soon after starting treatment, within the first 30 days, and return to baseline upon discontinuation of use. Patients with a history of suicidal ideation or mental health/behavioral concerns should use montelukast with extreme caution.

Long-Acting Beta-Agonists

Salmeterol and formoterol are long-acting beta-agonists (LABAs) that offer longer-lasting bronchodilation compared with albuterol (12 h vs. 4 h). LABAs can offer improved lung function in patients with persistent obstruction due to asthma. There are three medications currently available that combine ICS with LABA and are indicated as the preferred step-up therapy for anyone with persistent or severe asthma symptoms despite use of low-dose ICS. Compared with increasing the dose of ICS, ICS/LABA combination medications offer reduced risk for side effects, improved lung function, and equal efficacy in reducing exacerbations [33].

LABAs also carry a black box warning due to potential for increased asthma morbidity and mortality, but this stems from studies that have used LABAs as monotherapy. LABAs should never be prescribed to patients with asthma without combined use with an ICS. Briefly, when used as monotherapy, LABAs will provide persistent bronchodilation and improved lung function but will not treat inflammation. This can lead to patients not appreciating an underlying increase in inflammation and worsening asthma until very late in their course. However, it is also important to note that when LABAs are combined with inhaled corticosteroids, they are not only as effective (perhaps even more so) but also just as safe as using inhaled corticosteroids alone.

Biologics

Several new targeted biologic therapies have been developed in the past few years for the treatment of severe persistent asthma [34]. These therapies utilize monoclonal antibodies to block specific cytokines and molecules involved in allergic inflammation, including immunoglobulin E (omalizumab), interleukin-5 (mepolizumab), and interleukin-4 and interleukin-13 (dupilumab). These therapies offer the first

Clinical Vignette

A 19-year-old male is a freshman in college. He has a long-standing history of asthma with exacerbations occurring each autumn. He lacks chronic cough/wheeze and exercises routinely without need for albuterol. Currently, he denies any nocturnal awakenings due to asthma. He has been prescribed several controller medications over the past few years but has never used them consistently due to his busy schedule, lack of perceived benefit, or concern for side effects. He has been to the emergency room twice during his first semester to receive oral corticosteroids for treatment of asthma exacerbations. He states that he always feels better within 2–3 days of his emergency room visits. When asked, the patient states that his asthma is well controlled and he is satisfied with his care.

glimpse into truly personalized medicine for asthma treatment. Use should be directed through a specialist who has a thorough understanding of selecting the optimal patient for each medication, dosing, and administration.

Goals of Therapy

Thus far, this chapter has addressed the heterogeneous nature of asthma, including symptoms, severity, treatment options, triggers, and self-management strategies. Goals of asthma therapy are heterogeneous as well and may differ significantly for each patient. As we shift from decades of paternalistic provider-patient relationships toward shared decision-making, it is more important than ever to include patients in the determination of goals of therapy. Healthcare providers may be concerned about preserving lung function, reducing long-term remodeling, and preventing exacerbations, but patients may be more concerned with limiting impact on their social, scholastic, and professional interactions. Patients may be willing to visit the emergency room a few times a year to receive rapid and typically effective care in exchange for not having to remember to use controller medications twice daily or limiting exposure to certain environments. Patients with frequent symptoms and nocturnal awakenings may be more concerned with poor school performance or missed work than with preventing exacerbations. Similarly, patients who are experiencing exercise limitations may list this as their primary goal, compared with other aspects of their care.

Children and adolescents should be active participants in determining their goals of therapy, which can be recorded and reviewed at every appointment. This provides valuable insight to providers, who can then discuss their patient's concerns or

raise awareness to other aspects of their care that they may not appreciate at that time. Goals should be personal and meaningful or otherwise may represent an exercise in futility. At the end of the day, patients are the ones who live with their disease day in and day out and are responsible for self-management. Having ownership of their outcome goals can provide additional motivation and increase participation in their care.

Conclusion

As this chapter concludes, it is helpful to consider each individual patient with asthma as exactly such: an individual patient who likely shares many characteristics with other asthmatics but has their own challenges and expectations for care. It is important to take the time to build an open patient-provider relationship and explore all aspects of a patient's life to provide the best care possible. It also helps to anticipate that these needs will change over time and will vary as the patient's experiences change. Flexibility and an individualized approach to therapy are often the best strategies.

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Chapter 8

Managing Adolescent Asthma: More than Just Medications



William C. Anderson III

Background

Far too often, asthma is viewed by families and providers as a condition primarily of younger children which will likely be “outgrown” with time, minimizing the expected burden of the disease in adolescents. Recent trends in asthma prevalence in the United States dispute this assumption with adolescents 11–17 years of age having the greatest prevalence of asthma at 10%, exceeding that seen in 0–4- and 5–10-year-olds [1]. The morbidity and mortality of asthma in adolescents are also no less, and at times even greater, than in the younger population. Adolescents with asthma have been found to have more frequent daytime and nighttime symptoms than younger children [2]. Their overall asthma control is poor, with 89% of adolescents having uncontrolled or partly controlled asthma per Global Initiative for Asthma (GINA) guidelines [3]. Over 80% of adolescents reported wheezing with exercise, and one-third just avoided physical activity to due to their symptoms [3]. Asthma exacerbations are equally concerning, with over half of adolescents having an asthma exacerbation in the prior year [4]. Most notably, asthma mortality ranges from two to six times higher in adolescents than elementary school-aged children [2, 5], underscoring the imperative to adequately address asthma control in this population as a potential life-saving measure.

Despite this poorer control, greater burden, and increased deaths in adolescents with asthma, they infrequently seek medical care, likely serving as a self-fulfilling contributor to these detrimental outcomes. Compared to 0–4- and 5–10-year-olds, adolescents had fewer ambulatory care visits, emergency room visits, and hospitalizations for asthma [1, 5]. In contrast to these less frequent visits to medical providers, adoles-

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cents with asthma still have higher overall health-care expenditures than their younger counterparts [6], suggesting that when care is obtained, greater resource utilization is potentially required. Adolescents with asthma less frequently use their daily controller medications compared to 6–11-year-olds, with only 15.2% of adolescents aged 12–17 years with asthma using a daily controller medication [4]. This is also reflected financially with a smaller proportion and overall amount of total health-care expenditures in adolescents going to pharmacy costs compared to younger children [6].

Beyond the physical and financial impact of asthma in adolescents, asthma also adversely affects the psychosocial aspects of adolescents' lives, which are particularly important in this developmentally critical time. In two separate surveys, adolescents with symptomatic or poorly controlled/uncontrolled asthma were found to have lower quality of life scores compared with those adolescents who never had asthma [3, 7]. Adolescents with symptomatic asthma reported significantly worse self-rated overall health, impaired physical health, and impaired mental health [7]. Notably, asthma control correlates directly with quality of life assessment, with adolescents with poorly controlled and uncontrolled asthma recording significantly lower median quality of life scores than those with controlled asthma [3]. Furthermore, those subjects with controlled or asymptomatic asthma had similar quality of life score as adolescents without asthma [3, 7], emphasizing that asthma control in adolescents can improve emotional in addition to physical well-being.

In this chapter, the impact of the distinguishing features of adolescent health on asthma management will be explored. Knowing that adolescence is a potentially perilous time in the life, health-care providers and families should explore the characteristic developmental, psychosocial, and physical attributes that separate adolescents from younger children. Only by recognizing the uniqueness of this population can care be tailored to allow adolescents with asthma to reach their best physical and emotional health and, in turn, continue this success into adulthood.

Natural History: Outgrowing, Developing, and Progressing Asthma

Clinical Vignette

Caitlin is a 13-year-old female with severe persistent asthma, allergic rhinitis to dogs and cats, and eczema. She is currently controlled on fluticasone-salmeterol 230/21 mcg two puffs with a spacer twice daily and montelukast 5 mg by mouth daily. Caitlin was diagnosed with asthma at 5 years old, and since that time, she has had four lifetime hospitalizations for asthma, including an intensive care unit admission. On spirometry, her forced expiratory volume in the first second (FEV_1) is 78% predicted, and her FEV_1 to forced vital capacity (FVC) ratio is 70%, consistent with an obstructive pattern. She still has a significant response to bronchodilator with a 13% improvement in her FEV_1 . As Caitlin enters her teens, her mother worries whether her asthma will not be outgrown as she had hoped but rather stay with Caitlin for the rest of her life.

By identifying the potential remission or progression of asthma throughout adolescence, appropriate anticipatory guidance and management strategies can be provided. In one survey, by age 19 years, 21% of children with asthma at 7–8 years of age were in remission, 41% had persistent asthma, and 38% had only periodic asthma [8]. While this underscores that the majority of subjects had either periodic or no disease in adolescence, a sizeable portion still had persistence. Persistence and severity of disease are correlated with sex, with adolescent females having greater asthma severity [9] and increased likelihood of persistence compared to males [8, 10]. In addition, persistent disease has been associated with sensitization to furred animals [8], more severe asthma [8], allergic rhinitis [11], eczema [11], maternal asthma [11], and chronic bronchitis [11]; remission has been associated with lower bronchial reactivity [10] and improved small airway lung function, specifically the forced expiratory flow at 25–75% of the FVC (FEF_{25–75%}) [10]. Similarly, new-onset wheezing and asthma can develop in adolescence, with adolescent-onset asthma accounting for 28.3% of asthma at age 18 years in a birth cohort [12]. Risk factors for the development of incident asthma in adolescence include female sex [13]; positive skin prick testing to cat, dog, or horse [13]; being first born [14]; familial stress around birth [14]; parental asthma [13]; and parental rhinitis [14].

An amassing body of evidence demonstrates that by adolescence and young adulthood, children with asthma may have a reduction in their lung growth, which may meet classification for chronic obstructive pulmonary disease (COPD) at its greatest extent. Three-fourths of participants from the Childhood Asthma Management Program (CAMP), a large prospective trial that enrolled over 1000 children aged 5–12 years, had abnormal lung function patterns in the third decade of life, with 11% meeting Global Initiative for Chronic Obstructive Lung Disease criteria for COPD [15]. This is particularly concerning as CAMP enrolled patients with only mild-to-moderate persistent asthma, suggesting that even patients without severe disease are at risk [15]. Reduced lung growth was associated with a lower baseline FEV₁, smaller bronchodilator response, increased airway responsiveness at baseline, and male sex [15]. Given these risks, efforts should be made to preserve lung function in adolescents by preventing exacerbations, counseling on smoking cessation and reducing secondhand tobacco smoke exposure, and career counseling to avoid noxious inhalations. Furthermore, providers should trend adolescents' lung functions serially to identify any potential worsening or persistent airflow obstruction.

Diagnosis: Approach and Confounders

Clinical Vignette

Jennifer is a 15-year-old female who presents with new-onset, recurrent episodes of shortness of breath, throat and chest tightness, and wheezing. Despite the use of albuterol, twice-daily inhaled fluticasone, and oral steroids, she remains symptomatic. The episodes are triggered by smoke, strong scents,

and especially exercise. Jennifer is the star of her high school soccer team, which makes her symptoms particularly stressful for her and her family. On spirometry, Jennifer was found to have blunting of her inspiratory flow loop. Given her history, direct laryngoscopy was performed that showed adduction of her vocal cords during inspiration, leading to a diagnosis of vocal cord dysfunction. Her albuterol and inhaled fluticasone were discontinued following successful symptom improvement with speech therapy.

The initial approach to the diagnosis of asthma in adolescents is similar to that seen in younger children and adults, guided by history and physical exam and supplemented by objective testing. The diagnostic process may be more difficult in teenagers as they may tend to either under- or overreport their symptoms for potential secondary gain, including wanting to not appear different from their peers, gain independence from their families, or seek additional attention [16]. Spirometry, and possibly full pulmonary function testing if warranted, with a bronchodilator response should be used to evaluate for an obstructive lung disease pattern as well as airway reversibility; see Chap. 7 for a more thorough discussion of diagnostic testing. Supplemental testing including methacholine challenge and exhaled nitric oxide measurement can be used when additional diagnostic information is needed. Furthermore, skin prick testing or ImmunoCAP testing for environmental aeroallergens may help with phenotyping patients (see Chap. 7), guiding potential treatment modalities, addressing comorbid rhinitis, identifying triggers, and assisting in predicting the natural course of the disease.

With the exception of *de novo* cases occurring in teenage years, most adolescents presenting to a provider's office with asthma will come with a previously established diagnosis of asthma. However, the provider should not take this diagnosis at face value, especially if the patient is not responding to standard therapy (Table 8.1). An alternative diagnosis should be considered if a patient remains symptomatic despite the use of albuterol and systemic steroids, confirmed medication adherence, escalating controller medication dosage, removal of any triggering exposures, and exclusion of steroid resistance. In order to avoid inappropriate and potentially detrimental treatment, any comorbid conditions should be addressed.

A diagnosis of particular concern when an adolescent patient is not responding to standard therapy is vocal cord dysfunction (VCD), also known as paradoxical vocal cord motion. VCD results from paradoxical, intermittent adduction of the vocal cords during inspiration, causing symptoms which frequently mimic asthma including dyspnea, cough, wheezing, and chest and throat tightness (Table 8.2). Often VCD and asthma occur concurrently, as a review of 1530 VCD cases in children and adolescents found that 75% of subjects with refractory asthma also had associated VCD symptoms [17]. The gold standard for the diagnosis of VCD is direct visualization of the vocal cords using laryngoscopy during spontaneous or induced symptoms [18]. Truncation of the inspiratory arm of the flow-volume

Table 8.1 Differential diagnosis of asthma in adolescents and comorbid conditions

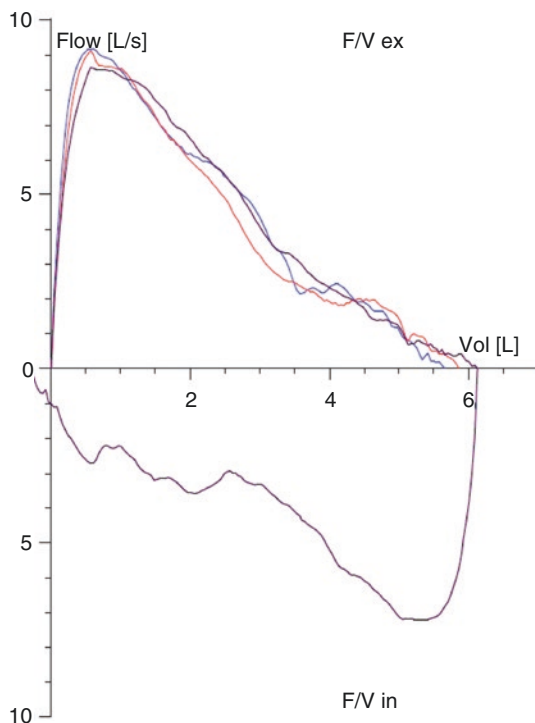
Allergic rhinitis
Anxiety
Aspiration
Chronic sinusitis
Cystic fibrosis
Deconditioning
Exercise-induced bronchoconstriction
Exercise-induced laryngeal obstruction
Gastroesophageal reflux disease
Interstitial lung disease
Malingering
Panic attacks
Primary ciliary dyskinesia
Psychogenic cough
Recurrent infection/immunodeficiency
Substance abuse including marijuana and tobacco smoking
Tumor or mass
Vocal cord dysfunction

Table 8.2 Distinguishing features of asthma versus vocal cord dysfunction

Feature	Asthma	Vocal cord dysfunction
Onset	Minutes	Seconds
Duration	Minutes to hours to days	Seconds to minutes
Dyspnea during	Expiration	Inspiration
Nocturnal symptoms	Present	Absent
Location of physical obstruction	Intrathoracic—distal airways	Extrathoracic—throat
Flow-volume loop pattern	Reduced expiratory flow	Flattened inspiratory flow
Oxygen saturation with an attack	Reduced	Normal
Effect of inhaled bronchodilator therapy	Highly effective	Ineffective/aggravating

loop with a reduction of the ratio of the maximal inspiratory flow at 50% vital capacity to maximal expiratory flow at 50% vital capacity ($MIF_{50\%}/MEF_{50\%}$) is suggestive, but not diagnostic, of VCD [18, 19] (Fig. 8.1). The development of VCD has been associated with psychological disorders including anxiety, depression, and conversion disorder, stress, rhinosinusitis, gastroesophageal reflux disease, laryngopharyngeal reflux, and inhalation of irritants [18, 19], which all should be addressed as needed during treatment. The management of VCD should involve a multidisciplinary team including asthma providers (allergists and/or pulmonologists), primary care physicians, otolaryngologists, speech therapists, and psychologists. Especially important in teenagers is empowering them to gain ownership of their VCD, through appropriate education, identification of triggers, and implementation of breathing exercises.

Fig. 8.1 Representative flow-volume loop demonstrating truncation and variability of the inspiratory arm. This flow-volume loop was obtained from a 17-year-old male patient with concurrent mild persistent asthma who presented with throat tightness associated with competitive basketball. He had resolution of his symptoms with the use of speech therapy focusing on VCD



Unique General Management Strategies

Beyond the standard goals of asthma management as outlined by the National Heart, Lung, and Blood Institute Expert Panel Report-3 (NHLBI EPR-3) guidelines to reduce symptoms, prevent exacerbations, and preserve lung function [20], additional goals of adolescent care should include minimizing school absences, encouraging physical activity, maintaining peer relationships, and empowering self-ownership of their asthma care. To meet these goals, providers may need to take a nuanced approach to adolescent care, meet them where they are, and employ management strategies that adolescents will actually adopt. Behavioral change approaches to improve asthma management can occur at the level of the adolescent, family, home, medical care, and/or community. A systematic review of such focused behavioral change tactics in adolescents, led by guidelines-based therapy, demonstrated benefit of individualized, group-based, and school-based asthma education and self-management skills training in improving asthma knowledge, quality of life, proper medication use and adherence, symptoms, and asthma control [21]. The review highlighted two areas that could be of particular focus for additional strategies: school-based programs, including observed therapy, and incorporation of technology, with provider feedback [21].

The use of technology, including websites, mobile smartphone applications (apps), and websites, can be a way to potentially engage with adolescents at a level with which they are more prone to fully interact. A recent review identified over 200 asthma-related smartphone apps available to the public, with over 50% focusing on teaching and training in techniques related to managing asthma, including providing general asthma and treatment information as well as symptom and medication tracking [22]. Limited studies to date examining smartphone apps in adolescents have demonstrated high patient engagement and satisfaction, including preference over standard paper versions of materials, such as asthma action plans [23, 24]. In one study, adolescents preferred a smartphone app for asthma which utilized medication reminders, trigger avoidance strategies, and an interactive treatment plan over other modalities for asthma education and self-management [23]. A study utilizing a smartphone app for asthma action plans demonstrated improved Asthma Control Test (ACT) scores in uncontrolled adolescent asthmatics compared to those using a paper asthma action plan [24]. Before providers and patients rush to implement the use of an app to enhance adolescents' asthma management, it should be noted that there is no accepted measure of app quality, with no approval or vetting process by the US Federal Drug Administration [22] currently in place. Therefore, providers should screen all apps before recommending them to their patients. Such screening should include a literature review for any demonstrated benefit of the app, evaluation that the medical content is correct, assessment of user-friendliness, and potential piloting with an initial limited group of patients.

Approaching Comorbid Psychosocial Conditions

Clinical Vignette

Sam is a 16-year-old male with a history of moderate persistent, poorly controlled asthma and allergic rhinitis. Up until 1 year ago when his family relocated, his asthma was well controlled on beclomethasone 80 mcg two puffs inhaled with a spacer twice daily. Since that time, Sam has had five emergency department (ED) visits for asthma and one hospitalization, all requiring oral steroids. His therapy has been escalated secondary to these hospitalizations without any improvement, prompting referral to a severe asthma clinic. During one-on-one conversations with the clinical social worker without his mother present, Sam revealed that he has had significant anxiety and depression since moving and changing schools. He has had difficulty making friends. He began smoking both tobacco and marijuana subsequently. Sam is interested in quitting to improve his asthma, but he also worries that his anxiety and depression will worsen, as he feels his drug use has helped mitigate those feelings.

Table 8.3 Psychosocial challenges in adolescent asthma management

Challenge	Unique feature in adolescent asthma	Impact on asthma management	Potential approach to care
Tobacco and substance abuse	• Increased rates of use • Increased nicotine dependence	• Worsening lung function • Increased symptoms • Increased exacerbations • Decreased controller medication use	• Confidential discussion of use • Provide quit resources • Referral to substance abuse programs if warranted
Mental health disorders	• Increased rates of anxiety and depression	• Decreased controller medication use • Increased symptom perception • Self-medication with tobacco or other drugs	• Treatment of underlying anxiety or depression • Screen for suicidality or self-harm • Referral to psychiatry
Peer relationships	• Increased rates of bullying • Fear of appearing different	• Decreased medication use • Underreporting of symptoms	• Encourage open conversations with friends regarding asthma • Refer to peer support groups • Discuss strategies to overcoming bullying

Adolescents with asthma are unique compared to younger asthmatic patients in that psychiatric conditions and behavioral choices work in synergy to impact both their adherence and subsequent asthma control outcomes. Without addressing these comorbid psychosocial conditions, medical management alone will be fruitless (Table 8.3).

Tobacco Use

Adolescents are inclined to risk-taking behaviors, including adopting tobacco smoking, with approximately 1.4 million children younger than 17 years old beginning to smoke annually [25]. While tobacco smoking has ubiquitously been found to be harmful, its respiratory effects are even more worrisome in the adolescent with asthma, causing not only increased overall wheezing episodes and exercise-induced wheeze but also a reduction in lung function, specifically the FEV₁/FVC [26]. Adolescents with asthma symptoms who smoked also reported more mentally and physically unhealthy days on quality of life questionnaires than non-smokers [7].

Despite these adverse effects, adolescents with asthma do not avoid tobacco smoking but rather actually more frequently smoke daily and smoke more cigarettes daily than their counterparts without asthma [27]. This same trend in increased use compared to their peers is also found with “alternative” forms of tobacco, including e-cigarettes [28, 29]. Of concern, adolescents with asthma had a higher prevalence

of believing that smoking e-cigarettes makes people look cool or fit and that smoking cigarettes relieves stress [29]. It is worrisome that patients at the highest risk for an exacerbation are those most likely to smoke, with nearly twice as many students who had asthma symptoms but were not using medicine smoking than pupils who had asthma without symptoms and were using medicine [27]. Recent e-cigarette use in adolescents with asthma was found to be associated with having an asthma attack in the prior year [28]. This increased rate of smoking in adolescents with asthma may be explained through increased nicotine dependence. A longitudinal study survey revealed that adolescents with asthma, including those with higher symptom severity, developed higher levels of nicotine dependence over time and made a greater number of unsuccessful smoking cessation attempts compared to those without asthma or with less severe symptoms [30].

Given the adverse effects of smoking and increased rates of nicotine dependence in adolescents with asthma, providers should inquire about tobacco use with their patients. In addition, due to similar harmful effect on lung function and asthma symptoms, providers should routinely inquire about marijuana and hookah use as well. Unfortunately, this is not being broadly implemented. Approximately two-thirds of subspecialty asthma providers reported that they infrequently inquire with their patients about substance abuse, and only 50% reported that they or their staff often verbally ask about cigarette smoking [31]. Providers should privately inquire teenagers without their parents present about tobacco smoking in all forms, including e-cigarettes, and when identified assess subject readiness to quit, counsel on the harmful effects of tobacco use especially on asthma, and confidentially provide resources and follow established guidelines to aid in smoking cessation.

Anxiety and Depression

Adolescents with asthma have an almost twofold higher prevalence of comorbid anxiety and depressive disorders compared with those without asthma [32]. The interplay between these psychiatric conditions and asthma leads to a potentially synergistic effect, with each disease contributing to the other and both leading to poorer health outcomes. A recent diagnosis of asthma, more impairment on the asthma physical health scale, and increased externalizing behaviors have been identified as risk factors for meeting criteria for anxiety and depressive disorders in adolescents with asthma [32]. Asthma control itself has an impact, with adolescents with poorly controlled asthma having higher depression, panic attacks, total anxiety, and internalizing symptoms than well-controlled asthmatics, with perceived stress being a potential driving factor [33].

Depression and anxiety in turn lead to increased risk-taking behaviors that can adversely affect asthma. Adolescents in general with more depressive symptoms have higher levels of nicotine dependence, which negatively affect successful smoking cessation; and depressive symptoms predicted a higher number of unsuccessful quit attempts, suggesting potential self-treatment of depressive symptoms [34]. These

effects of depression on cigarette use in adolescents would only compound the aforementioned effects of nicotine dependence in adolescents with asthma, exacerbating the difficulty they would have with smoking cessation. In adolescents with asthma and depression, substance use, including cigarettes, marijuana, binge drinking, and cocaine, increased [35]. As such, providers need to be conscious to screen for anxiety, depression, and other mood and psychiatric disorders in their adolescent patients, especially when treatment failure or medication nonadherence is suspected.

Peer Dynamics

Peer acceptance and social interactions are a critical aspect of adolescent development, potentially causing teenagers to minimize or avoid anything that would make them seem “different,” including the diagnosis of asthma. This social stigma can lead teenagers to deny their illness and subsequently lead to underdiagnosis, underassessment, and undertreatment [16]. High school students with asthma with current symptoms were found to have heightened social anxiety symptoms related to fear of negative evaluations and generalized discomfort in social settings compared to students without asthma and without symptoms [36]. This social anxiety in turn may prevent adolescents from taking their controller or quick-relief medications, even if medically needed. High school students with asthma also have reported higher incidents of bullying and cyberbullying than their counterparts without asthma [37]. Further worsening the problem, those students with both asthma and depression were at a higher risk for bullying [37], compounding the adverse effects of depression in this population.

In the same way that peer dynamics can potentially be a hindrance to care, when used appropriately, they may also improve care. Peer support networks and online support groups can provide ways for teenagers to engage with others in a similar situation, providing mutual support and minimizing isolation [16]. Providers should screen for bullying and potential social stigma of their asthma with their adolescent patients, especially when a pattern of nonadherence surrounding social, athletic, or school events is demonstrated. In addition, resources for peer support groups, including asthma camps, should be offered to patients and families.

Nuances and Adherence to Guidelines-Based Medical Management

Clinical Vignette

Justin is a 13-year-old male with severe persistent, poorly controlled asthma despite the use of budesonide-formoterol 160/4.5 mcg two puffs inhaled with a spacer twice daily, montelukast 5 mg by mouth daily, nasal fluticasone two sprays in each nostril daily, and cetirizine 10 mg by mouth daily. He has had

three ED visits and two hospitalizations in the last year for asthma exacerbations triggered by URIs and allergen exposures. When calling the pharmacy, his doctor discovers that Justin has not filled his prescriptions in 5 months. When Justin's physician discusses adherence with Justin, he tells her that he is "too busy" and "just forgets" to take his medications. He does not see why he needs to take them because none of his friends are on "so many" medications.

NHLBI EPR-3 [20] and GINA [38] guidelines provide a blueprint for the medical management of asthma in adolescents, including preferred controller therapies and escalation of care. However, adolescents may be in a precarious place in these guidelines in that they are grouped with patients aged 12 years and older. This affords adolescents some benefit in that they are often the first age bracket to be introduced to new medications approved either simultaneously or shortly after in adults, including most recently omalizumab, mepolizumab, and tiotropium. However, this age grouping presumes similar underlying physiology and response to therapy in adolescents as that seen in older patients. Obviously, adolescence is a time of substantial physical growth and developmental changes not seen in adults. As medicine progresses toward tailored, personalized therapy, interventions should be made to examine the unique effects of age and puberty on controller medications as well as biomarkers specific to the adolescent population to guide effective controller selection.

While intuitive, controller therapies are only effective if they are taken as instructed. Unfortunately, as previously discussed in Chap. 4, adolescents are poorly adherent to the use of controller therapies, with multiple factors contributing to their poor adherence (Table 8.4). A focus group of adolescents identified forgetfulness, including "being busy" or "in a hurry," as the main reason for lack of adherence, followed by lack of perceived need or beneficial effects [39]. A separate survey of adolescents taking inhaled corticosteroids demonstrated that necessity beliefs and sufficient medication knowledge were associated with better adherence, suggesting that improving knowledge about asthma treatments and stimulating positive perceptions toward medications and necessity of use may improve adherence rates [40]. Peer support was borderline significantly associated with higher chance of inhaled corticosteroid adherence [40].

When choosing controller therapies, it is important to choose a therapy that can be easily incorporated into an adolescent's lifestyle. While metered-dose inhalers are easy to transport and administer, they require a spacer for optimal medication delivery. Adolescents may forget or not want to carry a spacer with them, placing a limitation on this mode of delivery. A breath actuation device, a mist dispenser, or a medication with a built-in spacer may be more usable in this population. Furthermore, a medication that may only require once-a-day dosing could be ideal for improving adherence in an adolescent with a busy schedule.

In the aforementioned focus group study addressing adherence, adolescents expressed interest in smartphone apps with reminder functions and access to online

Table 8.4 Factors contributing to poor adherence in adolescents

Attitude toward health-care providers and parents
Comorbid psychiatric conditions
Denial of illness
Familial socioeconomic constraints
Forgetfulness
Mode of drug delivery
Parent and clinician support
Peer dynamics
Perceived or actual lack of medication efficacy
Perceived or actual medication side effects
Poor health literacy
Responsibility to take own medications
Risk-taking behaviors
Treatment complexity
Secondary gain from poor disease control
Understanding of illness and severity
Understanding of medications

information as potential strategies to enhance adherence [39], once again suggesting a role for technology in their management. Electronic monitoring devices are a new strategy to monitor medication use while also reminding patients to take their medications and providing real-time feedback on adherence [41]. Studies utilizing these devices in children and adults have demonstrated an increase in adherence but mixed results on clinical outcomes [41]. A proof-of-concept study combining an app with an electronic monitoring device that delivered visual reminders to take inhaled corticosteroids improved inhaled corticosteroid adherence and ACT scores and reduced short-acting beta-agonist use [42]. Electronic monitoring devices can be a potential tool to engage adolescents in their medication adherence and health care in the future, but broad implementation will require a reduction of device cost and associated clinical reimbursement.

Transitioning into Adulthood

Clinical Vignette

Luke is a 17-year-old high school senior with moderate persistent asthma currently well controlled on mometasone-formoterol 100/5 mcg two puffs inhaled with a spacer twice daily and montelukast 10 mg by mouth at bedtime. In addition to his asthma, Luke has allergic rhinitis for which he uses nasal fluticasone and fexofenadine. After graduating, he is planning to attend a college that is 4 hours away from home on a basketball scholarship. When asked about his triggers, Luke knows he has to take his albuterol prior to

exercising, but he does not know about any environmental triggers. When asked about which medications he takes, he says “a blue one and a red one” and defers to his mother on medication names, doses, and need for refills. Luke does not know the name of his health insurance plan nor where he will refill his medications while at college. His mother is worried that after many years of well-controlled asthma, Luke will have an exacerbation while at college and not know when or where to seek medical care.

Knowing the persistent prevalence of asthma in adolescence, the potential long-term sequelae of asthma on lung function, the difficulty with adherence, and the associated unique psychosocial comorbidities in this population, it is imperative that adolescents learn to assume care of their own asthma as they reach adulthood. This can be accomplished through a formal transitional care plan beginning early in adolescence. The goal of transitional care is to provide patient-centered, flexible, comprehensive, and coordinated high-quality care that continues uninterrupted from adolescence to adulthood [43, 44]. Unfortunately, transitional care is often inexplicit, incomplete, and late, leading to a gradual drifting away from pediatric care rather than a clearly planned handoff [44]. Times of transition can be especially dangerous for adolescents, with increased rates of congenital heart disease deaths, renal transplant failures, and decreased clinic attendance, as demonstrated in other chronic diseases [45]. In a study examining the effects of transition, patients with noncomplex chronic conditions, which included asthma, demonstrated an increase in health-care costs, hospital admissions, and ED visits following transition [46], underpinning the need to ensure appropriate transition readiness.

Limited studies exist examining transition patterns and readiness in adolescents with asthma, requiring extrapolation from other chronic diseases to examine barriers to transition. Risk factors for a delayed transition include chronic disease, public health insurance or no health insurance, and living in a lower-income neighborhood, all factors associated with asthma and the psychosocial impact of the disease [47, 48]. Barriers to transition are systemic, provider-related, and patient-related (Table 8.5). Only by addressing barriers in all three domains can transition be successful both now and in the future.

A study surveying international and interdisciplinary care providers identified ten outcomes constituting a successful transition of care for adolescents and young adults: quality of life, understanding characteristics of conditions and complications, knowledge of medication, self-management, adherence to medication, understanding health insurance, attending medical appointments, having a medical home, avoidance of unnecessary hospitalization, and having a social network [49]. All of these outcomes can, and should be, obtained when transitioning an adolescent with asthma.

When focusing on a specific disease state, such as asthma, primary care physicians should work in coordination with subspecialists to ensure that transition is comprehensively being addressed. Asthma care providers are encouraged to tailor

Table 8.5 Barriers to transition

Systemic barriers	Provider barriers	Patient and family barriers
• Lack of formalized systematic process • Insurance barriers at the time of transition • Poor reimbursement for providers • Lack of formalizing training in transition • Lack of research to identify best practices • Limited tools to assess readiness transition	• Poor communication between providers • Lack of vetted adult providers • Limited staff training • Lack of identified staff person responsible for transition • Lack of time to address transition • Lack of familiarity with conditions by adult providers • Providing only minimal patient records	• Lack of education about transition process • Anxiety • Lack of patient self-efficacy

Table 8.6 Proposed asthma-specific transition readiness milestones

Able to explain what asthma is to someone else
Demonstrates ability to utilize asthma action plan
Demonstrates proper technique with inhaled medications
Knows how to mitigate or avoid triggers
Knows how to obtain refills of controller and quick-relief medications
Recalls when to take controller medications
Recognizes symptom triggers
Recognizes when to seek urgent care for an exacerbation

the transition process, including the transition readiness assessment, for elements that would be necessary for successful asthma care (Table 8.6). Adolescents should be encouraged to identify personalized goals of their care, which may extend beyond symptom reduction and exacerbation prevention. In terms of basic asthma management skills, adolescents should be able to recognize the triggers for their allergic disease, to avoid or mitigate exposure to allergens and other environmental triggers, and to utilize their asthma action plans when experiencing symptoms [50]. During patients’ teens, providers should take part of each visit to address an aspect of transitional care in a formalized manner to assure that the care and control achieved now in adolescence are continued throughout their lifetimes.

Conclusions and Next Steps

Adolescence is a time of rapid physical and psychosocial changes in a patient’s life, leading to potential adverse health outcomes, even without the presence of a chronic condition such as asthma. Poor medication adherence, comorbid psychiatric conditions, peer social dynamics, and substance abuse may further complicate successful asthma management. Parents and health-care providers should work with teenagers to develop trusting partnerships that allow them to address an adolescent’s physical

and emotional health while encouraging self-efficacy. A personalized approach to guiding medication choice, ensuring adherence, and addressing comorbid conditions should be employed with each patient. As patients, families, and providers strive to reach these goals, several areas of adolescent asthma management require additional exploration, including the impact of controller medications specifically on adolescent asthma, the development of biomarkers to direct controller selection in this population, the effects of transitional care on young adult health outcomes, the standardization and tailoring of transitional care specifically for asthma, and the incorporation of technology in adolescents to improve adherence and clinical outcomes. By actively engaging adolescents in their care now, parents and providers can lay the foundation for successful asthma management for a lifetime.

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Chapter 9

Food Allergies: An Overview



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Background

Food allergy (FA), a pathologic immunologic response to food proteins, affects 8% of children and adolescents in the United States [1] and has been increasing in prevalence [2]. In general, the overall economic cost of FA for families and society is estimated to be \$24.8 billion annually [3]. The most common food allergens include peanut (25.2% of children with food allergy), milk (21.1%), shellfish (17.2%), tree nuts (13.1%), egg (9.8%), finfish (6.2%), wheat (5.0%), and soy (4.6%) [1]. Additionally, many children and adolescents with food allergy are allergic to more than one food [1]. FA is classified into immunoglobulin E (IgE)-mediated, non-IgE-mediated, and mixed reactions; this chapter will focus on IgE-mediated food allergy.

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The onset of a pathologic food allergy response is *sensitization*, during which a T helper 2 (Th2) cell response is initiated against a food antigen, resulting in antigen-specific IgE production by B cells. Once antigen-specific IgE antibodies (sIgE) are in production, an individual is considered to be sensitized to the antigen. Importantly, sensitization is not equivalent to clinical allergy; it is not uncommon for an individual to produce sIgE antibodies to foods that are clinically tolerated. Once in circulation, IgE binds to high-affinity receptors on the surface of mast cells (inside tissues) and basophils (inside blood vessels), thus priming these cells for activation. Mast cells, located in the skin, gut, and respiratory tract, are the primary agents of the allergic response. Upon reexposure to the antigen, mast cells degranulate, releasing histamine and a variety of cytokines, chemokines, enzymes (e.g., tryptase) and eicosanoids (e.g., leukotrienes, prostaglandins, and platelet-activating factor) into the extracellular space. Histamine, in particular, is responsible for several of the responses typically associated with acute allergic reactions, including urticaria, angioedema, nausea/vomiting, coughing/wheezing, hypotension, and increased nasal mucus production and heart rate. **Table 9.1** presents common symptoms associated with anaphylaxis [4]. These symptoms may occur alone or in combination and typically begin within minutes of ingestion of the food antigen. When symptoms involve two or more organ systems (e.g., skin and cardiovascular), the reaction is classified as *anaphylaxis*, a severe and potentially life-threatening allergic reaction which requires immediate treatment with epinephrine. Among children with food allergy, 38.7% have experienced a severe reaction [1].

In addition to the possibility of allergic reactions, including severe reactions and anaphylaxis, food allergies are associated with a range of comorbid conditions (e.g., asthma, atopic dermatitis, and allergic rhinitis), as well as negative outcomes such as limited social interactions and decreased quality of life for affected individuals and their families [5]. This chapter will review diagnosis, treatment, prognosis, and common misperceptions of IgE-mediated food allergies.

Table 9.1 Common signs and symptoms of anaphylaxis

Skin or mucosal tissue	Rash, generalized urticaria, flushing, pruritus, angioedema, oral pruritus or tingling, conjunctival erythema
Respiratory system	Dyspnea, cough, laryngeal edema, wheezing, stridor, chest tightness, rhinorrhea, nasal congestion, sneezing, nasal pruritus, hoarseness
Cardiovascular system	Chest pain, palpitations, tachycardia or bradycardia, cardiac arrest, syncope, feeling faint/dizzy, confusion, altered mental state
Gastrointestinal system	Nausea, vomiting, diarrhea, cramps, abdominal pain, difficulty swallowing
Central nervous system	Anxiety, feeling of impending doom, seizures, headache, irritability, confusion

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Diagnosis

Clinical History

A comprehensive clinical history is essential to distinguish food allergy from other food-related adverse reactions and to accurately diagnose and manage FA. Information to be collected includes the route and quantity of exposure of the suspected food allergen, symptoms, timing of onset, duration, and reproducibility of symptoms, as well as treatment administered and response to the treatment. Family history and medical history should also be obtained, as well as factors such as concurrent alcohol consumption, exercise, fever, and/or drug use, which have the potential to exacerbate allergic reactions [6]. Dietary history, including any food that the patient may be avoiding, can help narrow down suspected food allergens. For example, if a food has been tolerated and is included in the diet, further testing for that food is not needed. If it is not clear to which food an individual is showing adverse reaction, the possibility of cross-contact should be considered.

Physical Examination

The physical examination may help identify acute symptoms of an allergic reaction if conducted within minutes to hours after exposure to the suspected food allergen. More commonly, it leads to identification of atopic diseases which have a high rate of co-occurrence with food allergy, including atopic dermatitis, asthma, allergic rhinitis, and/or allergic urticaria [7]. The physical examination also provides an opportunity to assess growth parameters, nutritional status, and chronic oropharyngeal, gastrointestinal, pulmonary, and/or cutaneous symptoms. These factors may be suggestive of other food-related sensitivities which may warrant further investigation.

Diagnostic Testing

With supportive evidence from the clinical history and physical examination, various tests can be utilized to assess and confirm suspected IgE-mediated food allergy. Allergen-specific IgE (sIgE) testing is an *in vitro* assessment which measures blood serum levels of IgE to a specific allergen. It is important to note that sIgE only reflects immunologic sensitization to an allergen and is not indicative, in and of itself, of clinical food allergy. Thus, panel testing of large numbers of allergens is not recommended in diagnostic practice. sIgE should only be conducted in the case

of specific foods that are in question for causing a reaction and *not currently tolerated* in the diet. While general practitioners may perform sIgE testing, an elevated result (≥ 0.35 kU/L) warrants referral to an allergy specialist for further testing and management.

Skin prick testing (SPT) is an *in vivo* assessment performed by an allergy specialist in which a small amount of allergen is introduced into the epidermis to assess allergen-induced mast cell activation. In sensitized individuals, a wheal and flare reaction at the site of placement develops within minutes and is compared to positive and negative controls. A wheal ≥ 3 mm larger than the negative control is often considered an elevated result and indicates that sIgE is bound to cutaneous mast cells. While SPTs are indicative of sensitization and have a strong negative predictive value (NPV $\sim 95\%$), they have a poor positive predictive value (PPV $\sim 50\%$). Therefore, SPTs should not be used as a definitive diagnostic test for clinical food allergy [2]. For both sIgE and SPT results, the size of the test result can indicate the likelihood that a food allergy may be present, when the clinical history is highly suggestive. An elevated IgE by itself does not diagnose food allergy. In addition, the size of the IgE result does not indicate the severity of future reactions but can only be utilized to help determine the likelihood that a food allergy may be present.

The most accurate method for food allergy diagnosis is the graded oral food challenge (OFC), in which the patient ingests incremental amounts of a food allergen under close monitoring for the appearance of any symptoms of an allergic reaction. If the patient exhibits symptoms consistent with an IgE-mediated reaction during the challenge, a food allergy is considered present and the patient should avoid the food. If the patient successfully consumes a full serving of the food without symptoms, they may include the food in the diet. OFCs are often used in cases of an indeterminate patient history, inconclusive IgE tests, and/or to test if an allergy has been outgrown. **Table 9.2** lists testing thresholds for SPT and sIgE tests [8]. Due to the risk inherent in OFCs, the procedure should only be performed in a specialized medical facility under the supervision of a qualified allergy specialist.

Table 9.2 Predictive value of SPT and sIgE testing for OFC outcome

Food allergen	>95% PPV		~50% NPV	
	Serum-specific IgE (kU/L)	SPT wheal (mm)	Serum-specific IgE (kU/L)	SPT wheal (mm)
Egg white	≥ 7	≥ 7	≤ 2	≤ 3
Cow's milk	≥ 15	≥ 8	≤ 2	–
Peanut	≥ 14	≥ 8	≤ 2 if history of prior reaction; ≤ 5 if no history of prior reaction	≤ 3

Modified with permission of Elsevier from Sampson HA, Aceves S, Bock SA, James J, Jones S, Lang D, et al. Food allergy: a practice parameter update—2014. *Journal of Allergy and Clinical Immunology*. 2014;134(5):1016–25.e43

Clinical Vignette

Jon, a 15-year-old African American male, referred by his primary care physician, presents with a history of chest tightness, urticaria, and vomiting after eating clam. He has a medical history of asthma which is currently well-controlled with as needed use of albuterol and daily budesonide. Three weeks prior to his visit, he tried clam chowder for the first time and developed full-body urticaria and chest tightness within 5 min of consumption. After 10 min, he complained of nausea and started vomiting. He was driven to the emergency department, and upon epinephrine and albuterol administration, his symptoms subsided. He also reports an episode of urticaria 1 month ago following consumption of a bowl of lobster bisque containing lobster and a combination of fish and clam broth. Within 5 min after consumption, his mother noticed urticaria on his torso, arms, and legs. Symptoms resolved following administration of diphenhydramine. He has had previous exposure to lobster and did not have any history of previous adverse reactions. Currently, he eats wheat, egg, soy, milk, tree nuts, and peanuts without a problem. Prior to this month, he regularly consumed salmon and shrimp with no complaints. He does not recall eating other finfish, scallops, or oysters.

His father has a history of allergy to peanuts, cats, and horses. His mother and younger brother do not have a history of food allergy or any other atopic disease. The patient lives with his mother, father, younger brother, and their dog. He has no smoke exposure in the house.

Physical Examination

General appearance: Well-developed 15 year-old boy. Not in acute distress.

HEENT: No eye discharge/erythema/swelling. TMs clear bilaterally, no bulging/erythema. No nasal discharge, polyp, or airway blockage. No angioedema of lips. Moist mucous membranes. No erythema or swelling on nasopharynx.

Chest: Inspection normal. No urticaria/scar/lesion. Clear to auscultation bilaterally.

CV: Regular rate and rhythm. + S1/S2. No murmur/gallop/rubs.

Abdomen: No urticaria/scar/lesion on inspection. Bowel sounds positive in all four quadrants. No mass/tenderness on palpation.

Skin: No erythema/urticaria/scar.

Laboratory Data

In light of the clinical history, SPT and sIgE testing were performed for shellfish and finfish. SPT results were elevated for clam (5 mm), oyster (3 mm), and scallop (3 mm) and negative for finfish, lobster, crab, and shrimp. sIgE testing was elevated for clam (9 kU/L), oyster (0.9 kU/L), and scallop (0.78 kU/L).

Differential Diagnoses

Food poisoning, viral gastroenteritis, food intolerance, acute generalized urticaria, alcohol consumption, scombroid syndrome

Treatment Plan and Follow-Up

The patient and his family were counseled on the prognosis of food allergy, signs, and symptoms, treatment of allergic reactions and anaphylaxis, and lifestyle modifications including dietary avoidance. The patient was instructed to avoid clam. Since he has no history of eating oysters and scallops, recommendation for OFC was made and scheduled. He was told that he could continue consuming lobster, crab, and shrimp but was counseled on the risks of cross-contact. A food allergy action plan was developed and discussed along with the use of an epinephrine auto-injector. A follow-up visit was scheduled in 1 year.

Treatment: Medications***Epinephrine***

Epinephrine (adrenaline) is the only lifesaving medication that can terminate anaphylaxis. It should be prescribed for patients with a history of anaphylaxis, a prior systemic allergic reaction, comorbid asthma and food allergy, and/or a known food allergy, especially to peanut, tree nuts, fish, and shellfish, all of which are associated with increased risk for future anaphylaxis. However, since allergic reactions to food are inherently unpredictable (i.e., they may vary among patients and between exposures within a given patient), prescription of epinephrine should be considered for all patients diagnosed with an IgE-mediated food allergy.

Epinephrine plays a critical role in the reversal of *all* symptoms of anaphylaxis. Epinephrine administration results in blood vessel constriction, effectively reversing anaphylaxis-induced decreases in blood pressure by increasing peripheral vascular resistance. Epinephrine binding to α -adrenergic receptors elicits an increase in coronary artery perfusion. Additionally, vasoconstriction in other systemic vessels including the skin and mucosal surfaces prompts a decrease in angioedema, urticaria, and potentially systemic absorption of the allergen. Epinephrine also binds to β_1 -adrenergic receptors, causing an increase in heart rate and contractility, and to β_2 -adrenergic receptors which leads to inhibition of cytokine release and mediates bronchodilation [9]. See **Fig. 9.1**.

Epinephrine Effects

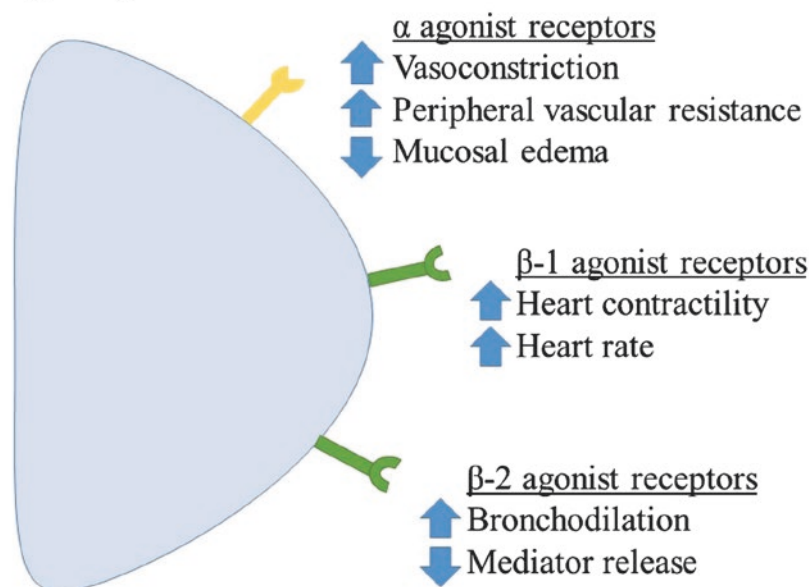


Fig. 9.1 Epinephrine treatment effects

Epinephrine auto-injectors (EAI) are used to deliver a single dose of epinephrine into the thigh muscle and are available in 0.15 mg (patients weighing 15–25 kg) or 0.3 mg (≥ 25 kg) doses according to patient weight, with recent approval for a 0.1 mg dose for infants who weigh less than 15 kg. Previous literature suggests that >35% of patients experiencing anaphylaxis required >1 dose of epinephrine, and, therefore, two EAIs should be carried at all times [10]. It is important to note that epinephrine should be administered immediately upon suspicion of anaphylaxis. The risks of administration are low and delayed administration is associated with poorer outcomes and higher mortality rates [11]. To administer an EAI: (1) remove the safety cap, (2) press the auto-injector into the lateral thigh, and (3) hold for 3–10 s (depending on the manufacturer). Following the initial injection, 9-1-1 should be called for transfer to a medical facility for further monitoring and treatment. If symptoms persist after 5–15 min, a second dose of epinephrine should be administered. Patients should also be aware of the possibility of biphasic reactions, in which signs and symptoms resolve but recur after a period of hours. The recommendation to seek emergency care after any use of epinephrine is based upon the potential for symptoms to be partially treated or return. Thus, additional monitoring is indicated for anyone who has anaphylaxis. Reviewing this indication and ratio-

nale can be helpful for adolescents and parents, who may misinterpret the need for emergency room care as being due to dangers or side effects stemming from the epinephrine auto-injector. Hence, they may be reluctant to use their epinephrine when indicated.

Antihistamines, Albuterol, and Steroids

Antihistamines such as diphenhydramine (Benadryl) and cetirizine (Zyrtec) are frequently administered for mild allergic reactions including urticaria and pruritus. However, while antihistamines may be palliative for mild symptoms, they do not halt the progression of an allergic reaction and should therefore be considered an adjunct to epinephrine in the case of suspected anaphylaxis. They are typically slow to act (30–60 min) and have no significant effect in the treatment of anaphylaxis [12].

Asthma medications, such as short-acting bronchodilators (e.g., albuterol), should be used adjunctively during an allergic reaction to address respiratory symptoms, especially for patients with a history of asthma or bronchospasm. In those with a history of asthma, lower respiratory symptoms (e.g., wheeze, cough) should always be treated with epinephrine during a food-induced allergic reaction. Corticosteroids have no role in the acute management of anaphylaxis due to their delayed onset of action. Corticosteroids have traditionally been given to patients with anaphylaxis in an effort to prevent a biphasic reaction from occurring, but a recent meta-analysis demonstrated no protective effect [13].

Treatment: Lifestyle Modification and Environmental Controls

Although epinephrine is safe and effective for the emergency treatment of anaphylaxis, lifestyle modifications are necessary for effective FA management and the prevention of allergic reactions to food.

Avoidance

Strict avoidance of food allergens is the only certain way to prevent allergic reactions. While exposure to food antigens may occur via the skin (cutaneous exposure), mouth (oral exposure), or lungs (inhalation exposure), severe reactions most

commonly develop following oral exposure [14]. For example, previous literature suggests that children with peanut allergy do not experience a systemic or respiratory reaction following peanut exposure via cutaneous or inhalation routes [15]. It should be noted that while food odors cannot elicit a clinical reaction, food proteins that are aerosolized during cooking may provoke respiratory symptoms in children with food allergy and asthma. Additionally, due to the possibility of cross-contact, patients should be counseled to avoid foods that are manufactured or prepared in environments in which their allergens are present, unless strict allergen containment precautions are known to be in place.

Food Labels

In order to effectively avoid food allergens, patients and families should be counseled to pay attention to food ingredients and labels. In 2004, the Food Allergen Labeling and Consumer Protection Act (FALCPA) was passed, requiring food manufacturers to clearly state if a packaged food sold in the United States contains any of the top eight food allergens (peanut, tree nuts, milk, egg, wheat, soy, finfish, and shellfish) as ingredients [16]. It is important to note that such labeling is not required for meat, poultry, certain egg products, or alcoholic beverages, if allergens are in the form of highly refined oils, if scientific evidence establishes that food ingredients do not contain allergenic protein(s), and/or if the FDA determines that a food does not prompt an allergic response in sensitized individuals. It should also be emphasized that labeling for possible cross-contact during the manufacturing or packaging process is not required. While some manufacturers choose to utilize precautionary allergen labeling (PAL), such labeling is voluntary and phrasing is not standardized. These phrases include “may contain,” “may contain traces of,” and “manufactured in a facility that also processes.”

Education on Anaphylaxis Management

Due to the possibility of accidental exposures to food allergens despite best efforts at avoidance, it is important for patients and families to learn how to manage an allergic reaction. Families should be counseled on how to recognize common symptoms of an allergic reaction, the identification of anaphylaxis, and appropriate administration of epinephrine. An emergency action plan should be completed by the clinician and reviewed with the patient periodically. This form includes patient-specific food allergen(s), guidelines for treatment, and emergency contact

information. Templates can be found on the American Academy of Allergy, Asthma, and Immunology (www.aaaai.org) and American Academy of Pediatrics (www.aap.org) websites in English and Spanish.

Past research indicates that despite the fact that adolescents are at greater risk for severe reactions and fatal anaphylaxis due to food, this age group is less likely to report their allergic reactions as “anaphylactic,” even when symptoms indicate anaphylaxis [17]. With increasing independence, risk-taking, and activities outside the home, this age group in particular should be counseled on the risks and symptoms of anaphylaxis and the safety and effectiveness of epinephrine administration.

Dining Out

A large proportion of food-induced fatal reactions are related to eating food not prepared at home [2]. Although five states (Illinois, Maryland, Massachusetts, Rhode Island, Virginia) and two cities (New York City, NY, and St. Paul, MN) have legislation related to restaurants and food allergies in place, dining out requires that patients with food allergy take additional precautions. Before planning to eat out, it may be useful for families to check menus online to see if there are any safe options and/or to call ahead to ask about ingredients and methods of preparation, including the possibility of cross-contact. Fried foods, baked goods, and desserts may be at particularly high risk for cross-contact. It is often advisable to communicate directly with the chef in order to obtain accurate information. Food allergies should be disclosed to wait staff prior to ordering. The patient should always carry epinephrine while dining out, and in the event of anaphylaxis, epinephrine should be administered immediately. Similar precautions should be taken while dining out at athletic events, camps, church events, workplaces, and when traveling.

School

Up to 25% of students experience their first allergic reaction at school [18]. Since food exposures may occur in a variety of ways during the school day (e.g., meals and snacks, classroom activities, celebrations, school events), successful management of food allergy at school requires collaboration between the student’s family, school staff, and medical professionals. Clinicians can provide guidance to families on federal and regional school policies and should encourage families to talk with school administration and health staff about establishing appropriate

precautions and preparedness plans. It should be noted that every state in the United States is currently required to allow students to self-carry and self-administer an EAI at school and that nearly every state allows or requires that schools stock undesignated (nonstudent-specific) epinephrine on the premises. Families may also be counseled on the types of health management plans that may be put in place for students, including emergency action plans, individualized healthcare plans (IHPs), and Section 504 Plans [19]. Additionally, counseling is necessary for common concerns that may arise for school age children including reluctance to carry or use an EAI or to disclose their food allergy to school peers [20]. The use of a medical alert bracelet may also be suggested, particularly for younger children. Finally, clinicians can work directly with school administrators in the development and implementation of school policies for the prevention and management of allergic reactions.

College presents unique challenges for students with food allergy. Students should be encouraged to discuss food allergy policies and protocols with school administration prior to enrollment and during orientation. Dining hall precautions and safe food options, housing options, and EAI training of college staff should be covered, and students may wish to schedule an appointment with the staff nutritionist. Patients approaching drinking age should also be counseled on the potential effects of alcohol consumption on food allergic reactions.

Advocacy and Food Allergy Awareness

In addition to counseling patients on food allergen avoidance, clinicians can support patients and their families in advocating for effective food allergy policies and increased food allergy awareness among the general public. Patients and families should be supported and empowered to advocate for themselves and for policy changes and may be directed toward resources to assist them in doing so. Food allergy advocacy organizations, support groups, and peer education materials may be useful sources of information.

Common Misperceptions

Differential Diagnosis

Food allergies may be misdiagnosed as other adverse reactions to food. For accurate diagnoses, it is important to distinguish the mechanism of a reaction: immune-mediated or nonimmune-mediated. Immune-mediated disorders are a result of an

abnormal immune response. Common immune-mediated disorders that are often mistaken for food allergy include:

- Celiac disease: An autoimmune disorder in which gluten consumption causes damage to the small intestine. Symptoms include abdominal pain, diarrhea, vomiting, weight loss, and malabsorption. It is typically hereditary and occurs in genetically predisposed individuals.
- Eosinophilic gastrointestinal disorders: Examples include eosinophilic esophagitis and allergic inflammation in the esophagus. Symptoms include failure to thrive, vomiting, dysphagia, or food impaction. The GI tissue can be affected.
- Food protein-induced enterocolitis syndrome (FPIES): A non-IgE-mediated immune reaction that impacts the GI system. Common triggers include dairy and soy, but rice, oat, and barley are also known triggers. Symptoms include delayed onset vomiting and diarrhea (typically 2–3 h after ingestion) which cease when the trigger food is removed.
- Oral Allergy Syndrome (OAS): May occur among individuals with seasonal allergies. Proteins found in some fruits, vegetables, and some tree nuts are similar to those found in pollen. The immune system recognizes both pollen and the similar proteins in food being consumed and prompts an allergic response. Symptoms do not usually progress beyond the mouth and quickly subside upon food ingestion or removal. Symptoms include itchy mouth, scratchy throat, swelling lips, mouth, tongue, and/or throat. Common associations include (1) birch pollen (apple, almond, carrot, celery, and cherry), (2) grass pollen (celery, melons, oranges, peaches, and tomatoes), and (3) ragweed pollen (banana, cucumber, melons, sunflower seeds, zucchini). Interestingly, the proteins that cause OAS are labile, and patients can often tolerate the same fruits/vegetables that cause symptoms if those foods are cooked, peeled, canned, or processed.

Nonimmune-mediated disorders include:

- Auriculotemporal (Frey) syndrome: A rare neurological disorder consisting of unilateral sweating and flushing after eating.
- Gustatory rhinitis: rhinorrhea caused by spicy food.
- Food intolerance: Consists of digestive problems when consuming food. Onset is gradual and includes symptoms such as nausea, stomach pain, diarrhea, vomiting, gas, cramps, bloating, and headaches. Reactions are not life-threatening.
- Pharmacologic reactions: Examples include adverse effects related to caffeine, tryptamine, or alcohol consumption.
- Toxic reactions: Examples include scombroid food poisoning or food poisoning in general. Scombroid food poisoning occurs upon consuming decayed fish. A toxin related to histamine is produced during the decay process. Food poisoning

is the result of consuming spoiled or contaminated food. Symptoms include nausea, vomiting, and/or diarrhea.

- Psychological reactions: Food aversions or food phobias.

Quality of Life

The management of food allergy often presents psychological and economic burdens on patients and their families; see Chap. 10 for an in-depth discussion. The avoidance of allergen exposure not only requires constant vigilance but can impose limitations on social interactions and induce strain in familial and peer relationships [5]. Children and adolescents with food allergy may experience a range of emotions around their diagnosis and the threat of an allergic reaction, including anxiety, fear, embarrassment, stress, and isolation. Adolescence, in particular, is a transitional period during which patients begin to take on increased personal responsibility for managing their food allergy. Expectedly, greater independence is often accompanied by greater anxiety. Food allergy-specific quality of life questionnaires, primarily for research purposes, have been established and may be a useful tool for clinicians to utilize in assessing the quality of life effects of food allergy on patients and their families. Referral to a clinical social worker or therapist may also be beneficial for some patients; these professionals may support patients and their families in developing strategies to combat food allergy-related anxiety and stress. Furthermore, ensuring that patients and families feel empowered to manage their food allergy and prepared to respond in the event of a reaction can help improve health-related quality of life for patients with food allergy and their families.

Prognosis: Outgrowing Food Allergy

It is not uncommon for children with food allergy to develop tolerance to a food allergen, also known as “outgrowing” a food allergy. Past studies indicate that many children outgrow egg, soy, wheat, and milk allergies. In one study, 82% of patients had developed tolerance to egg by age 16, 69% of patients had developed tolerance to soy by age 10, 65% had developed tolerance to wheat by age 12, and 80% had developed tolerance to milk by age 5 [21]. Allergies to peanut, tree nuts, shellfish, and finfish are less frequently outgrown. Periodic assessment by an allergy specialist will help determine whether a patient may be outgrowing a food allergy. If sIgE and SPT testing indicate that a patient may have outgrown an allergy, an OFC may be conducted. Following a successful OFC, the food may be introduced back into the diet in accordance with allergist recommendations.

Conclusion

Food allergy is a growing public health concern, impacting 8% of children and adolescents in the United States. Strict allergen avoidance and prompt treatment of anaphylaxis with epinephrine are currently the mainstays of food allergy management. Additionally, patients should be counseled on ways to effectively manage food allergies while out of the home. It is important to raise food allergy awareness among family, friends, school personnel, and the general public to better protect children with FA.

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Chapter 10

Food Allergies and the Teenager



Nancy S. Rotter and Michael Pistiner

Background

The typical adolescent behavioral, biological, and psychosocial development discussed earlier in this book (see Chaps. 2 and 3) complicates the management of food allergies in teenagers. Developmentally, teenagers are increasingly independent, spend more time with their peer group, and engage in more risk-oriented behaviors as they transition toward adulthood. The ultimate task of this developmental stage is for teenagers to acquire the skills to live and function on their own. However, during the emancipation process, teenagers and their parents often struggle with each other's readiness for the adolescent's independence. Difficulties can arise in which parents may be reluctant to give up control over dietary management due to their own concerns about their child's safety and decision-making with respect to food allergies. From a biological standpoint, this is compounded by research on the adolescent's not-yet fully developed prefrontal cortex of the brain, which plays a role in problem-solving, impulse control, and judgment, combined with the already developed nucleus accumbens which is associated with pleasure-seeking/reward. Thus, adolescents are more responsive to rewards and pleasure yet lack ability to think critically and carefully about choices and decisions. Teenagers spend increasingly more time outside of the family home participating in social and recreational

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activities, sports, or work. Peer pressure and the natural desire to avoid embarrassment further impact teenage decision-making, potentially increasing safety risks for the food allergic teen. Taken together, normal developmental issues specific to teenagers with food allergies – such as allergen avoidance and independent use of medications – make the transition to food allergy self-management uniquely difficult. Effective food allergy management is necessary at all times and in all situations.

The two pillars of successful food allergy management are prevention and emergency preparedness. Any person with a food allergy needs to implement strategies that will prevent an allergic reaction from occurring and be prepared to manage an allergic reaction. Very small amounts of food allergen can cause anaphylaxis, a potentially severe, life-threatening, allergic reaction. To prevent accidental exposure with food allergens, those responsible for children or adolescents must effectively read labels, prevent cross contact and communicate efficiently and clearly. It is also critical to be prepared for allergic reactions and anaphylaxis. Those responsible must be able to recognize any allergic reaction, including anaphylaxis, have epinephrine available, and know when and how to use epinephrine. Those responsible will also need to, and know how to, contact emergency services. These strategies are always necessary and there are some unique challenges and situations that arise as the adolescent transitions to a place of almost complete self-management.

The diagnosis of food allergy in the adolescent is essentially the same as in all age groups; see Chap. 9 for a detailed explanation. The focus of this chapter will be on food allergy management as it relates to psychosocial, emotional, and risk-taking behavior of adolescents.

The ultimate goal for the food allergic teen is to assume complete self-management. As with all tasks of adolescence, these skills develop gradually over time. For example, parents of a preschool-aged child can model reading ingredient labels to ensure food safety, while parents of an early elementary school-aged child may role-play strategies for attending birthday parties, where the child may not be able to eat the cake that is served. As they age, children should be encouraged to practice skills such as ordering food in restaurants and carrying their own epinephrine auto-injectors, with coaching from their parents. This scaffolding approach allows children to develop independent skills while still receiving parental support and guidance. Upon reaching adolescence, teenagers begin to assimilate these skills with decreased parental oversight in the context of encountering decisions about risk-taking behaviors, such as experimentation with alcohol and drugs. In addition, risk-taking specific to food allergies occurs, such as eating out without notifying restaurant staff about dietary restrictions or managing friendships and intimate relationships. Additionally, these decisions may be complicated by parental anxiety regarding a food allergic teen's self-management as well the teenager's self-esteem, self-confidence, and overall psychological functioning. A recurrent theme throughout this textbook is to allow for years of preparation and to have a plan in place to prepare teenagers for their transition to independence, which particularly applies to food allergy management.

There are many issues complicating the typical development for food allergic teenagers. Being attuned to *the current information regarding some of these specific issues can be very helpful in tailoring interventions to the specific family and adolescent. The use of education, empowerment, and partnerships can improve self-care, adherence, and quality of life.*

Although the authors have identified the topics within this chapter below as major issues influencing food allergy management in the adolescent, this list is not all-inclusive and many of the issues are overlapping and influence each other. While the focus is on teenage years, current published literature includes young adults in addition to adolescents. Most of the management strategies and challenges can be overlapping and shared between adolescents and young adulthood (Fig. 10.1).

Clinical Vignette

This is a composite of several adolescent case examples that have been combined to illustrate the complex issues discussed in this chapter that may arise for the individual teenager.

Lucy is a 15-year-old girl with a history of tree nut allergies to walnuts and pecans. She was diagnosed at 2 years of age after eating a chocolate chip cookie containing walnuts and experiencing lip swelling and vomiting. Although she experienced one mild reaction involving hives at age 6 from cross contact, she had not had any other allergic reactions since that time. Over the last few years, she and her parents questioned whether she may have outgrown her allergy, and at times she and her family were inconsistent about her food choices and ingredient label checking. Lucy also became inconsistent in carrying her epinephrine auto-injector as she felt she was low risk for having a reaction and it was bulky to carry. While away at camp, Lucy's cabin group went on an overnight away from campground in the woods. Lucy ate the evening meal of pasta with pesto, which she had eaten before in her home and at the local restaurant, as she was not allergic to pine nuts. She did not inquire about specific ingredients or read the label. She developed hives, lip swelling, and severe abdominal pain. She felt embarrassed in the presence of her cabinmates that she was having a reaction and that she had not checked the ingredient label. Lucy and one of her counselors went back to the camp, and the nurse administered epinephrine. Lucy was taken to the hospital where she was observed and released. As Lucy learned later, the pesto she had eaten contained walnuts. Following this incident, Lucy developed anxiety about eating when she was not with her family and limited peer and social activities. She became hypervigilant about allergen avoidance strategies and making sure that she carried her auto-injector. At the follow-up visit with her allergist, food allergy management strategies were reviewed with Lucy and her family, a plan was made to get necessary health communication and documentation to camp and school health, and a plan for periodic follow-up was established. Additionally, Lucy met with the pediatric psychologist who was part of the team of providers in her allergist's office for several sessions to help her manage anxiety about having another anaphylactic episode while maintaining appropriate self-management skills. Lucy was able to resume social activities and eating outside the home after several sessions of cognitive behavioral therapy. Lucy's family got involved with their regional nonprofit food allergy organization where she became involved in the teen activities and occasional support groups.

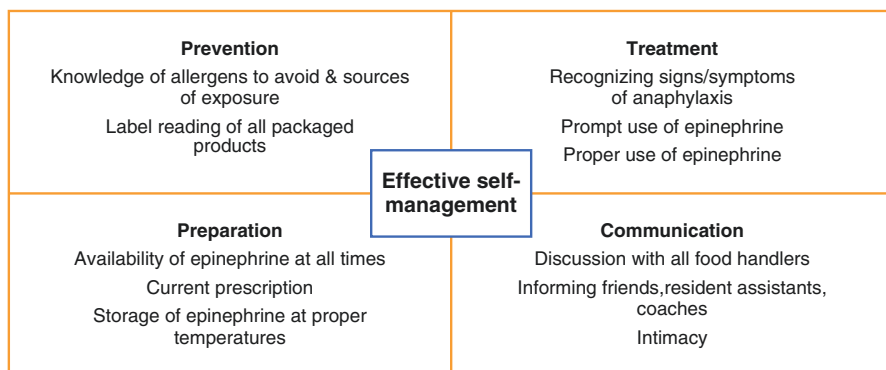


Fig. 10.1 Areas of focus for effective self-management of food allergies

Food Allergy-Related Mortality

Background

Food allergy-related mortality is an important issue to address, especially in the adolescent and young adult. Fortunately, death from food-induced anaphylaxis is rare. Umasunthar et al. published a study that estimated the incidence rate of death from a food allergy-related reaction in a child aged 19 years or younger to be 3.3 per million person-years [1]. Using food allergy statistics estimating an 8% prevalence and up to six million US children [2], we can estimate that approximately 20 food allergy-related deaths occur in the United States in children per year. This number can be put in perspective when compared to deaths caused by unintentional injuries (traffic related, drowning, poisoning, burns, falls, etc.), where annually more than 12,000 children and adolescents under age 19 die from unintentional injuries [3].

When looking at registries of fatal and near fatal food allergic reactions, the vast majority of cases were associated with delayed or lack of administration of epinephrine. Research supports that delays in treatment with epinephrine increase the chance of fatality. These registries reinforce the need for strategies that address recognition of anaphylaxis and emergency preparedness [4, 5]. Mortality data suggest that a disproportionately high number of cases of fatal anaphylaxis occur in teenagers and young adults. Approximately 70% of the mortalities reported in a registry were between ages 12 and 21, with risk-taking suspected to be a major factor. It is also important to recognize that a higher incidence of fatalities is associated with adolescents who also have asthma, in addition to the delay in the administration of epinephrine [4–8]. Risk-taking behavior may play a major role not only in food allergy-related mortality in adolescents and young adults but in this age group's overall mortality risk. Accidents, suicide, and assault are among the most common causes of death in this age group. The CDC published the major causes of mortality in the United States in 2014, by age [9]. In ages 10–14, 750 deaths were caused by accidents, 425 were caused by suicide, and 156 were caused by assault. In ages

15–19, 3724 deaths were caused by accidents, 1837 by suicide, and 1406 by assault [9]. Discussing the behaviors that may compromise effective food allergy management is important. Giving teens the knowledge, resources, confidence, and encouragement to care for themselves is key to supporting this at-risk group.

Challenge

Although mortality from food allergy is a rare event, risk-taking and compromised judgment can increase the likelihood of anaphylaxis. Directly discussing the importance of maintaining food allergy management without scaring or overwhelming teens can be challenging within the confines of a short office visit with the health-care provider.

Management Strategies

Adolescents with food allergies and their families should be educated and empowered in order to best understand and then manage risk. The importance of consistent and evidence-based allergen avoidance, as well as the availability and timely treatment of anaphylaxis with epinephrine, must be communicated and understood. Healthcare providers should be trained to deliver consistent teaching of effective food allergy management strategies. We must emphasize education, identification, and management, as well as the establishment of policies and procedures that will support children with food allergy wherever they are and whomever they are with.

Risk Taking

Background

It is well known and observed that adolescence is a time of exploration and experimentation in which risk-taking is inherent. Food allergic teenagers encounter an additional level of risk when they do not attend to necessary food precautions or emergency preparedness. Adolescent risk-taking is influenced by a multitude of factors, including peers, family stress, socioeconomic level, parental support, risk perception, sleep, emotion regulation, and self-esteem. A study examining risk-taking in a general population of adolescents revealed that those teenagers who received explicit information about the risk involved in a task reduced their risk-taking behaviors compared to those in the non-informed group [10]. Healthy self-esteem and future orientation have been identified as protective factors against engaging in risky behaviors in a general population of adolescents [11].

Adolescents with food allergies ($N = 174$; 13–21 years) participated in an Internet-based study designed to assess risk-taking behaviors and coping strategies to help identify intervention targets for this population [12]. Findings revealed that risk-taking was impacted by social situations and perceived risks. Sixty-one percent of those surveyed “always” carried an epinephrine auto-injector. Participants indicated that they were more likely to carry their epinephrine auto-injectors when they traveled (94%) or went to restaurants (81%) but less likely to do so if they were wearing tight clothing (53%) or engaging in sports (43%). More than half (54%) reported that they purposefully ingested an unsafe food. Study implications reinforced the importance of educating both food allergic teenagers and their peers as strategies for reducing risky behaviors.

Greenhawt et al. [8] surveyed a total of 513 college students with 57% reporting an allergic reaction to food. 36% of those that reported a food allergy identified symptoms consistent with anaphylaxis, 48% reported that they had an epinephrine auto-injector, and 6.6% reported that they always carried the device. Only 40% reported always avoiding the foods that they were allergic to [8].

Challenge

Managing a developmentally typical set of behaviors (risk-taking) in the context of a medical condition that has the potential for severe consequences in adolescents.

Management Strategies

Based upon research about adolescent brain development and risk-taking behaviors, both generally and as they relate specifically to those with food allergies, management and prevention are best addressed through early and ongoing education as well as open communication with parents, trusted adults, and peers.

Laying the groundwork for management from an early age and building on this as children get older are the keys for both children and their parents. Providing children with basic, age-appropriate education about their food allergies as young as age 2 or 3 helps to normalize their experience. Educating family members, teachers, coaches, and other adults in the child’s community with the child present models open and clear communication about allergen avoidance and emergency preparedness and sets the stage for children to learn how to implement this with peers. Parents who model skills such as always carrying an epinephrine auto-injector, checking ingredient labels, and making consistent food choices facilitate early development of these self-management skills in children. As children reach school age, parents can engage in live coaching of children ordering their own meals at restaurants, reading labels at grocery stores, and practicing the use of their epinephrine auto-injectors with a trainer device. These strategies are dual-fold: They allow

children to practice new skills, make mistakes and manage these challenges with guidance, while simultaneously building trust in their parents that they are becoming increasingly capable of handling their food allergies independently. Education about the importance of allergen avoidance as a first-line and very effective strategy for allergy management, with the use of epinephrine as the backup intervention, is an essential point.

Adolescents will make mistakes and engage in behaviors that parents wish they would not, regardless of whether or not they have food allergies. Keeping the lines of communication open by letting teens know that they will not be punished harshly or judged for making mistakes with respect to risk-taking will allow for ongoing discussions about safety, communication, and decision-making.

Excessive caution or anxiety on the part of parents of food allergic children can interfere with the adolescent's ability to develop necessary self-management skills. For instance, parents who limit their food allergic children's attendance at certain social functions, participation in sports, or dining at restaurants communicate messages that prevent their children from developing skills and confidence necessary to live independently. Some parents and children hold unrealistic beliefs in regard to which scenarios pose greatest risk for potential food allergen exposure and risk of anaphylactic reaction. Focusing on real-world food allergy management strategies including practical food allergy avoidance and plans that insure prompt treatment with epinephrine for anaphylaxis helps alleviate undue concern. These strategies can reduce unnecessary social isolation and allow the adolescent to participate in activities such as athletic events, outdoor activities, and visiting entertainment venues. Psychologists knowledgeable about food allergies can provide parental guidance interventions to assist parents who are prone to be anxious about having children engage in expected activities such as school, recreational, and social activities outside of the home. Cognitive behavioral therapy provided by a psychologist can be very useful for children and teenagers who experience significant anxiety from their food allergies, particularly if it interferes with their coping and functioning. In addition to cognitive behavioral therapy, the use of proximity challenges under allergist supervision can be a useful strategy to help address concerns for both parents and adolescents.

Peer Influence

Background

Healthy, typical adolescent development assumes that teenagers are spending more time with their peers and relying on them for support, direction, and guidance as part of their transition to adulthood. The impact of peer beliefs and opinion is generally considered to play a role in an adolescent's behavior, though this relationship is complex and affected by a variety of factors.

The literature suggests that peer support has the potential to positively impact health outcomes for adolescents with chronic medical conditions. Kohut et al. [13]

reviewed 11 studies which revealed significant improvement in both behavioral and emotional symptoms such as social engagement, school attendance, health-related quality of life, and attitudes toward illness and adherence; however, there were no significant differences in physical symptoms of chronic illness. Another literature review [14] found evidence that social support from peers facilitates child and adolescent adaptation to illness and may also help with aspects of adherence. Additionally, peer group affiliations for adolescents were associated with health-promoting behaviors. These authors concluded that helping children and adolescents to disclose their medical conditions to peers was important for illness management.

Studies specific to food allergic teenagers and young adults also highlight the importance of talking with friends and house/roommates about their food allergies [8, 12]. Sampson et al. [12] also found that only 60% of food allergic adolescents tell friends about their food allergies, but a higher percentage (68%) believe that living with food allergies would be easier if their friends knew more about their allergies.

Challenge

Empowering adolescents to make healthy and safe choices and decisions while depending on their peers for support and guidance.

Management Strategies

Communicating with peers is an important part of food allergy management and again begins in early childhood with parental modeling of these skills with family members and other adults, such as teachers. In elementary school, for some it can be helpful to have the food allergic child, parent, and school nurse jointly teach the child's class about food allergies while normalizing their medical condition and focusing on ways that the student is similar to their peers. Schools play an important role in creating communities of support. They can encourage awareness and understanding for students and staff.

As adolescence approaches, pre-teenagers can practice their communication and assertiveness skills with siblings or close friends, by educating them about their food allergies, the need to avoid allergens, and the use of epinephrine. Once a teenager is spending time away from parents, an actual rehearsal with friends about what to do in the event of severe allergic reaction can be helpful (e.g., call 911). Dining at restaurants and eating away from home are central to social interactions for teenagers. It can be very useful to develop and practice a plan for eating away from home, focusing on communication and preparation in case a reaction occurs (Table 10.1).

Table 10.1 A checklist for suggested strategies to approach dining out with food allergies

• Always have epinephrine auto-injector immediately available when dining out
• Always communicate with wait staff, manager, and/or chef regarding food allergens to avoid and inquire about safety of menu items from cross contact. If there is a lack of understanding or challenges in communicating, then politely leaving is the safest
• Consider reviewing restaurant website ahead of time to learn about existing food allergy policies/statements
• Consider reviewing menu items prior to visiting to identify availability of safe allergen-free choices
• Consider obtaining or creating an index card (chef card) that clearly outlines the foods that need to be avoided as well as need to avoid cross contact or shared preparation equipment

Bullying/Hazing

Background

Survey data have reported that 35% of children age 5 or above have been bullied, teased, or harassed because of their food allergy. In some cases, such events can be physical and include holding an allergen near or rubbing the allergen on individuals with a food allergy. Food allergy-specific bullying was also found to be associated with decreased quality of life (QOL). Through participation in fraternities, sororities, and other organized social groups, there are also stories of hazing regarding food allergen exposure, including cases that have resulted in severe allergic reactions and resulting litigation and charges being filed. Shemesh et al. [15] surveyed over 250 families and found that 31.5 and 24.7% of the surveyed children and their parents, respectively, indicated that they were bullied or harassed by classmates because of their food allergy. The authors also demonstrated an association between bullying and negative impact on QOL. The parents were aware of the behavior in 52% of the cases, and the authors concluded that parental awareness was associated with improved QOL [15].

Challenge

In the case of food allergy-related bullying, there is increased risk for both psychological and physical harm, as allergen exposure can lead to an allergic reaction.

Management Strategies

Encourage open communication and establish trust. In cases of bullying, act to curtail episodes and offer support for anyone being bullied. Families and health-care providers can assist schools to create a culture that is supportive and inclusive

to children with food allergies, including rules and policies that curtail bullying both in general and specific to food allergy. If bullying occurs in the school/college setting, families should involve the school/college. Involvement of the principal, school nurse, school psychologist, and teachers is important in taking charge of bullying in school. Encouraging children to share their feelings with supportive adults is key. Being bullied, teased, or harassed can make a child feel ashamed about having food allergies and further distressed about the ways in which they are different from their peers. Let them know in clear terms that there is nothing to be embarrassed about. Convey that communicating with adults can help stop the behavior. Consult a mental health professional if there is a significant change in school performance, participation in activities, sadness, anxiety, or any other concerning changes. Increasing overall awareness throughout the school community is an effective way to ward off further bullying. Students are influenced by the messages of their teachers, parents, and others in their schools. Bullying may arise when there are misperceptions and negative attitudes about food allergies. Replacing these with education can create an environment of support and understanding. Educating staff and parents can change the attitudes of children. Direct education to students may be very effective. Children also can play an important role in teaching each other, their parents, and play a critical role in establishing a supportive community. We all play our part in creating communities of support.

Long Interval Since Last Known Reaction

Background

For some teenagers and young adults, the last clinical reaction to a food allergen may have been several years ago and at an age where there is no recollection of the reaction. Some adolescents and their families may question the current presence or potential severity of their food allergy. They may not believe that it still is an issue. As adolescents are sensitive to peer pressure, they may be more apt to take dangerous risks. Mortality studies demonstrate that in fatal and near fatal allergic reactions, many of the cases were preceded by only mild reactions. One might postulate that perhaps in those cases, vigilance and emergency preparedness could have been compromised, leading to preventable catastrophic reactions [5].

Challenge

Families may be lost to medical/allergy follow-up or not realize that avoidance measures must still be followed and vigilance upheld.

Management Strategies

Regular follow-up visits with the adolescent's allergist are important for many reasons, including epinephrine refills, updating emergency care plans, and reevaluation with the potential for development of tolerance over time. Even if there is no change in the status of the teenager's food allergies, regular follow-ups with their allergists/healthcare provider provide reinforcement of necessary food allergy management strategies as well as an opportunity to review the challenges related to the transition to adulthood.

Drugs and Alcohol

Background

Experimentation and use of drugs and alcohol can compromise the health and well-being of adolescents and young adults. Food allergies can pose additional risk to this population when alcohol and drugs are being used.

Alcohol and drugs not only can affect decision-making and behavior but also can cause physiologic changes that can decrease the threshold for allergic reactions, and potentially increase severity of allergic reactions. When "under the influence," judgment, the ability to perform the necessary prevention strategies, and emergency preparedness may be compromised. Avoidance strategies like label reading and avoiding cross contact may be more difficult to implement. Emergency preparedness may also be compromised with a decreased ability to recognize a reaction, have epinephrine available, and know when to administer it, in addition to decreased motor coordination to be able to administer epinephrine.

Alcohol has been shown to act as a cofactor in anaphylaxis, decreasing the threshold for allergic reactions, and/or increasing severity [16, 17].

Challenge

Imparting knowledge and education about the potential increased danger of drugs and alcohol in adolescents and young adults.

Management Strategies

Begin discussions of respecting one's body and brain and the potential unhealthful and damaging effects of drugs and alcohol in general terms early in adolescence. Explaining the potential compromise in judgment and physiologic effects may help adolescents come to an understanding and realize the importance of not compromising food

allergy management strategies, especially in the setting of drugs and alcohol. Role-playing, practicing assertiveness skills, and talking openly with parents and role models can be helpful in avoiding lapses in food allergy management. The ingredients of the alcoholic beverage itself must be considered in addition to things mixed with it. It is also important to discuss that current labeling laws do not apply to alcoholic beverages and clear notification of potential food allergens may not occur.

Exchanging Saliva/Kissing

Background

In adolescence and young adulthood, kissing and other physical displays of affection are normal and expected. Adolescents and young adults also share beverages, as well as beauty and healthcare products such as lipstick or lip balm. In some situations, having a food allergy can make any activity or situation where saliva is exchanged from one person to another a potential source of cross contact with allergen. Maloney et al. [18] studied the salivary levels of 38 subjects that consumed two tablespoons of peanut butter. Samples were taken at different time points and after different interventions including brushing teeth, brushing and rinsing, rinsing only, waiting then brushing teeth, and waiting then chewing gum. Although all interventions decreased detectable peanut protein by varying amounts, the only intervention that resulted in undetectable levels was several hours after a peanut-free meal. The authors concluded that waiting several hours and ingesting a peanut-free meal are more effective at reducing salivary peanut protein than immediate interventions [18]. There are anecdotal reports of severe allergic reactions, and possible fatal reactions associated with open mouth kissing and accidental salivary transfer of allergen.

Challenge

Teenagers and young adults can find it awkward to talk to the person that they are considering kissing, about the potential transfer of food allergens in saliva. There are some social circumstances where communication between potential partners is limited, creating increased risk.

Management Strategies

Healthcare providers, school health personnel, and parents can have frank discussions about the potential for salivary transfer of allergens and the importance of communication with a potential partner. Although conversations and role-play can

feel awkward, it may help prepare for circumstances where without preparation the teen or young adult may compromise their safety.

Transition to College/Workplace: Independent Living

Background

Living in a dorm on a college campus or in a shared living situation away from the family home represents a significant shift for the young adult with respect to food allergy self-management. While independence skills could be practiced while still living with parents, moving out requires complete self-reliance and responsibility of the young adult to select safe foods, carry epinephrine, and manage situations involving potential risk. Challenges related to eating and preparing foods are common when there is no access to a kitchen, there are limited allergen-free menu item choices available in dining halls, and eating in buffet style college cafeterias can increase risk of cross contact. Additional points to consider include the management of food allergies in the workplace (job interviews, meetings, shared food storage, etc.)

Greenhawt et al. [8] conducted an internet-based survey of university students. Of the respondents, 293 identified as having food allergies. As noted earlier, they found that about one fifth of college students in their study made arrangements to have their epinephrine auto-injector, while less than 7% always carried their device. Greater than 60% of students who reported having an allergic reaction, indicated they continued to consciously ingest a self-identified allergen, though this was lower for those reporting prior anaphylaxis. Less than 50% of respondents told their roommate or housemate that they had a food allergy, while just over 65% shared this information with a close friend.

Challenge

Transition to complete self-management of allergies while adapting to a new, independent lifestyle can be difficult.

Management Strategies

Preparation for leaving home encompasses a wide range of self-management skills from doing laundry to managing finances. While allergy self-management skills have likely been developed, preparation for living in a new environment is essential. Several months prior to starting college, meeting with staff in the Disability Services

office and then in dining services to discuss their food allergy management practices in the dining halls is important for the college-bound student. Learning about the student health service and campus emergency response is also important in the event of an anaphylactic reaction.

Communicating with roommates about food allergies, in advance of moving in together, will improve the comfort and safety of shared space. Discussing strategies for maintaining clean surfaces, should allergens be brought into the room, and keeping foods separate if there is an in-room refrigerator, are examples of safe practices in roommate/housemate living situations. Additionally, the food allergic student should educate roommates, residence hall advisors, and friends about their allergies as well as recognize allergic reactions. As noted earlier, being aware of the increased risk of drug and alcohol use for those with food allergies, which will be prevalent at college, is important for students.

Additional Considerations

As addressed throughout this textbook, it is important to involve the healthcare team and have an open line of communication to help educate, empower, and reinforce necessary adherence with management strategies. This becomes critical in addressing fear and worry related to anaphylaxis and epinephrine administration, addressing teenagers who have had reactions and supporting adolescents with a new diagnosis of food allergies during their teenage years.

Conclusion

Understanding typical adolescent development provides an essential framework from which to apply the challenges faced by teenagers with food allergies. While having food allergies can cause additional hurdles in the transition to adulthood, there are many strategies that can be utilized for successful management. Strategies can be introduced in early childhood and practiced throughout adolescence to help both food allergic children/teenagers and their parents manage challenges effectively and facilitate a smooth transition to adulthood (Table 10.2). Given the unique factors impacting each teenager and their family, these approaches can be tailored to each individual and family. The healthcare team, which can include allergists, nurses/school nurses, nutritionists, pediatricians, psychologists, and social workers, can help families apply these general concepts to help each individual food allergic adolescent and their family.

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Table 10.2 Strategies for fostering allergy management and anxiety prevention per developmental stage

Infant/toddler (ages birth – 2 years)	• Educate family, friends, and caregivers about safe food preparation and feeding practices • Ensure that parents/caregivers have adequate support in managing child's food allergies
Early childhood (ages 3–5 years)	• Use concrete explanation of food allergies and dietary limitations • Focus on foods that can be eaten and are enjoyed by the child and have safe treats available • Begin to model label reading, as young children imitate adults • Use specific and clear language (e.g., “this is your special bread without wheat”) • Use metaphors (e.g., “animals have different diets to keep them safe and healthy, just like you do”) • Develop rituals and traditions that do not focus on food/eating
Latency age (ages 6–12 years)	• Focus on similarities between child and their peers (e.g., “You like to play soccer, videogames, and skate, just like your friends”) rather than differences • Role-play social situations including sharing with others about food allergies, turning down offers of food that may contain allergens, etc. • Empower children to make choices (how to handle food at birthday parties, sporting events, etc.) • Practice label reading, preparing food/packing lunch, and ordering in restaurants • Normalize prevention of accidental ingestion and role of epinephrine when mistakes occur
Adolescence (ages 13–18 years)	• Encourage teenagers to communicate with friends about their food allergies • Coach teens in strategizing about eating out with friends and getting help from friends in event of an allergic reaction • Keep lines of communication open with adolescents to assist in handling mistakes and accidents • Strategize with teenagers about carrying their epinephrine auto-injectors given clothing choices, etc. • Have open discussions about handling food allergies at parties that may involve alcohol or drugs

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Chapter 11

Atopic Dermatitis: Overview



Benjamin T. Prince and Rekha Raveendran

Clinical Vignette (Part 1)

A 10-month-old male presents to his pediatrician for evaluation of new rash. His parents report that it began approximately 1–2 months prior and has worsened since that time. The rash began on the extensor surface of his bilateral elbows and has since progressed to involve bilateral ankles and cheeks. The rash is described as red and very itchy. He has been unable to sleep throughout the night secondary to extreme itching. This affects him most nights of the week. The parents report trying topical diphenhydramine without much success and have avoided using any other topical or systemic medications. He is not currently taking any other medications.

The patient has otherwise been growing and developing normally and his parents deny any history of recurrent infections or fevers. His vaccinations are up to date and he has not had any adverse reaction to any foods or medications. He has been exclusively breastfed until 6 months of age when he was introduced to solids. His diet includes several fruits and vegetables, grains (including wheat), and egg. The parents are concerned that the introduction of these foods may have contributed to the development of the rash but deny any immediate worsening with ingestion of these foods. They report bathing him once a week without soap to prevent “loss of skin oils.”

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They currently live in a house that was recently built. They have a dog and cat that have been in the home for 10 years, and he does play with the animals often. There is no smoke exposure in the home. This is their first child.

Family history is not significant for atopic disease.

His physical examination is remarkable for an erythematous, scaling rash with overlying areas of excoriations on bilateral extensor surfaces of elbows and around both ankles. On his face, he has an erythematous, weeping rash with some mild crusting on bilateral cheeks. The patient appears uncomfortable and is actively scratching on examination.

Parents are hesitant to use any medications given the age of their son and are inquiring about possible alternative therapies to help improve his symptoms.

Introduction

Atopic dermatitis (AD) is a chronic, relapsing, and pruritic disease that classically develops between 3 and 6 months of age, with 90% of individuals developing it by 5 years of age. While the majority of affected individuals experience resolution, 10–30% persist into adulthood [1]. Descriptions of this condition appear to have been around as early as the eighteenth century. Initially, the more general term “eczema” was used, but in the 1930s, the correlation between eczema and other atopic conditions was first recognized. Since that time, the term atopic dermatitis has been used interchangeably with eczema to describe this chronic disease [2]. Emollients were the mainstay of treatment until the advent of hydrocortisone in the 1950s, which revolutionized the treatment of AD [3]. Atopic dermatitis affects 10–20% of children in developed countries. There have been high indirect and direct costs associated with AD, which is estimated to range anywhere from 364 million to 3.8 billion dollars per year [4].

There appear to be many contributing factors in the development of this disease, including both genetic and environmental interactions, which ultimately lead to impaired epidermal barrier function and immune dysregulation [5]. While there have been some specific gene mutations that have been associated with the development of AD, such as filaggrin, they do not account for the majority of cases [6]. Approximately 70% of individuals have a positive family history of atopy. Children with one atopic parent have a two- to threefold higher risk for developing AD, which increases to a three- to fivefold risk if both parents are atopic. Having a parent with a higher level of education and being of black race both appear to be associated with an increased risk of disease. When evaluating for other risk factors—including differences in gender, type of birth delivery, maternal/infant diet, early antibiotic exposure, and pet ownership—studies have been inconclusive [1].

The pathophysiology of AD is complex and starts with a disruption in the structural integrity of the skin. Filaggrin and other proteins are important in maintaining the integrity of the skin barrier, and mutations in these elements result in a more porous epithelium. This allows for the immunologic exposure of both environmental and food antigens, resulting in epicutaneous sensitization [5]. Studies have shown that 90% of individuals with AD have lesions colonized with *Staphylococcus aureus*. Toxins produced by this bacterium can exacerbate inflammation causing regulatory T-cell dysfunction and immune dysregulation, ultimately resulting in the intense pruritus associated with this disease [7].

In the remaining sections of this chapter, we will focus on the diagnosis and treatment of AD as well as review common pitfalls encountered in the management of this disease.

Diagnosis

The diagnosis of atopic dermatitis is based upon clinical history and presentation. Hanifin and Rajka initially proposed a set of criteria in 1980, which is comprehensive and continues to be the gold standard for use in clinical trials. Due to numerous criteria that are often poorly defined or too specific, widespread implementation in clinical practice has not occurred. The UK Working Party attempted to pare down the Hanifin and Rajka criteria to be more fit for use in clinical practice, but this was not applicable to very young children. In order to remedy this, there was an attempt to revise the original Hanifin and Rajka criteria in 2003 by the American Academy of Dermatology (AAD) to make it inclusive of all ages. The AAD criteria take into consideration essential characteristics of AD, important patient features, as well as less specific associated skin findings (Table 11.1). This is currently the most widely used clinical criterion in the United States [1, 2].

AD has a variable presentation depending upon age. Infants tend to develop lesions on face, neck, and extensor surfaces of their body. With increasing age, flexural involvement of the extremities becomes more prominent. In older children with severe disease, lesions can become hypopigmented and lichenified (Fig. 11.1a–c, Table 11.1).

When making the diagnosis of AD, it is important to exclude conditions that present with similar erythematous, scaling, and pruritic rashes. The differential diagnosis of atopic dermatitis differs according to age and encompasses common infections as well as rare immunologic disorders (Table 11.1). During infancy, common similarities include seborrheic dermatitis, viral exanthems, and contact dermatitis. Nutritional deficiencies such as zinc and biotin have also been associated with eczematous rashes. As infants progress into childhood, conditions such as keratosis pilaris, tinea corporis, impetigo, scabies, and drug reactions become

Table 11.1 American Academy of Dermatology clinical criteria for the diagnosis of atopic dermatitis

<i>Essential features (must be present)</i>
1. Pruritus
2. Eczema (acute, subacute, chronic)
A. Typical morphology and age-specific patterns
– Facial, neck, and extensor involvement in infants and children
– Current or prior flexural lesions in any age group
– Sparing of groin and axillary regions
B. Chronic or relapsing history
<i>Important features (seen in most cases)</i>
1. Early age of onset
2. Atopy
A. Personal and/or family history
B. Elevated IgE
3. Xerosis
<i>Associated features (suggest the diagnosis)</i>
1. Atypical vascular responses (facial pallor, white dermatographism)
2. Keratosis pilaris/hyperlinear palms/ichthyosis
3. Ocular/periorbital changes
4. Other regional findings (perioral changes, periauricular lesions)
5. Perifollicular accentuation/lichenification/prurigo lesions
<i>Exclusionary conditions</i>
Examples of similarly presenting conditions
1. In infancy
– Seborrheic dermatitis
– Viral exanthems
– Contact dermatitis (allergic or irritant)
– Nutritional deficiencies (zinc and biotin)
– Primary immune deficiency
2. In childhood
– Keratosis pilaris
– Tinea corporis
– Scabies
– Impetigo
– Drug reactions
– Ichthyoses
3. In adulthood
– Psoriasis
– Photosensitivity dermatoses
– Cutaneous T-cell lymphoma
– Other causes of erythroderma

Adapted with permission of Elsevier from Eichenfield LF, Tom WL, Chamlin SL, Feldman SR, Hanifin JM, Simpson EL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. J Am Acad Dermatol. 2014 Feb;70(2):338–51; and also adapted with permission of Elsevier from Eichenfield LF, Hanifin, JM, Luger TA, Stevens SR, Pride HB. Consensus conference on pediatric atopic dermatitis. Journal of the American Academy of Dermatology. 2003;49(6): 1088–1095



Fig. 11.1 The variable presentations of atopic dermatitis. **(a)** Rough, dry patches distributed over the neck, trunk, and extensors in an infant. **(b)** Papular dermatitis with focal scaling over the knees and antecubital fossa in a child. **(c)** Thick, lichenified plaques at the elbow and dorsum of the hand in an older child with severe atopic dermatitis

more common. Similar appearing rashes, including psoriasis and photosensitivity dermatoses, appear later in adolescence and adulthood. While most of these rashes are benign, there are some serious immune-hematologic conditions that present similar to or in conjunction with AD. Most of these serious conditions present in infancy as primary immune deficiencies. Eczematous rashes can be a symptom of Netherton's syndrome, DOCK8 deficiency, Wiskott-Aldrich syndrome, and severe combined immunodeficiency (SCID). In adolescents and adults, cutaneous T-cell lymphoma can be a concern, particularly in a patient without prior history of AD [8] (Table 11.1).

Once the diagnosis of AD has been made, various scoring systems have been developed to assess disease severity. These have been used extensively in clinical trials to more objectively define differences in severity and response to various therapies. One of the more commonly used scales is the SCORAD. It uniquely incorporates both objective physician assessments and subjective patient ratings. The physician estimates the extent of skin involvement and the severity of lesions, whereas the patient scores their itch and loss of sleep. Both of these measures are input into a formula that results in a severity score. Mild AD is defined as <25, moderate as 25–50, and severe as >50 with a maximum possible score of 103. Many of the other scoring systems only focus on either objective physician assessments or subjective patient ratings [1].

Treatment

The development of AD is dependent on multiple factors and therefore requires a multifaceted approach. The mainstay of treatment involves maintenance of the skin barrier through pharmacological and/or non-pharmacological means (Table 11.2).

Table 11.2 Therapeutic options for atopic dermatitis

Type	Examples	Pros	Cons
<i>Pharmacological therapies</i>			
Topical corticosteroids	Numerous options that range from low potency (Class 7) to superpotent (Class 1)	– Cost-effective – Few systemic side effects – Can be used as acute and maintenance therapy	– Hypopigmentation – Skin atrophy – Striae – Acne – Telangiectasias – Hypertrichosis
Topical calcineurin inhibitors	– Tacrolimus (0.03 and 0.1%) – Pimecrolimus 1%	– Steroid sparing – Can be used as acute and maintenance therapy	– Burning – Skin malignancy/ lymphoma^a
Antimicrobials	– Mupirocin 2% – Bleach baths (0.005% sodium hypochlorite) – Oral antibiotics	– Decrease <i>Staphylococcus aureus</i> colonization	– Antimicrobial resistance – Burning
First-generation oral antihistamines	– Diphenhydramine – Hydroxyzine	– Improve sleep – Decrease itch	– Sedation – Anticholinergic effects – Concern for incident dementia with cumulative use
Second-generation oral antihistamines	– Cetirizine – Fexofenadine	– Decrease itch – Less sedation/ anticholinergic effects than first-generation antihistamines	– Sedation
Systemic corticosteroids	– Prednisone – Methylprednisolone	– Rapidly effective for severe, diffuse eczema	– Hypothalamus-pituitary-adrenal (HPA) axis suppression – Rebound flares upon discontinuation – Agitation – Weight gain – Poor sleep

Table 11.2 (continued)

Type	Examples	Pros	Cons
Systemic immunosuppressants	– Cyclosporine – Azathioprine – Methotrexate – Mycophenolate mofetil (MMF)	– Steroid sparing – Effective for severe, diffuse eczema	– Infection risk – Gingival hyperplasia – Hypertension – Renal/hepatic dysfunction – Malignancy
Biologics	– Dupilumab (anti-IL-4/IL-13)	– Steroid sparing – Effective for severe, diffuse eczema – Decrease itch	– Hypersensitivity reactions – Conjunctivitis/keratitis – Herpes simplex virus reactivation – Expensive – Infection risk
Allergen immunotherapy	– Subcutaneous immunotherapy (SCIT) – Sublingual immunotherapy (SLIT)	– Can treat specific triggers – May improve other atopic conditions – Steroid sparing	– Hypersensitivity reactions – Limited evidence for efficacy in eczema
<i>Non-pharmacological therapies</i>			
Moisturizers	– Petroleum jelly – Ceramide containing emollients – Fragrance-free/dye-free barrier creams	– Foundation for both acute and maintenance therapy – Cost-effective – Minimal side effects	– Greasy – Burning
Phototherapy	– Narrow-band UVB – UVA1	– Steroid sparing – Effective for refractory, diffuse eczema	– Actinic damage – Altered pigmentation – Malignancy
Wet wraps	– Emollient wet wraps – Topical corticosteroid wet wraps	– Effective for severe eczema – Decrease itch – Cost-effective	– Cumbersome – Time-consuming – Increased systemic absorption of topical steroids
Irritant avoidance	– Dust mite/pet allergen avoidance measures – Avoidance of dyes/fragrances	– Cost-effective	– Best used adjunctive therapy

^aCausal relationship not established

Non-pharmacological Therapy

Moisturizers

Moisturizers and skin hydration are the foundation for prevention of transepidermal water loss. Daily soaking baths in lukewarm water for at least 10 min are recommended to help hydrate the skin (Table 11.3). The use of moisturizers shortly after bathing is essential in keeping the skin hydrated. There are many types of moisturizers including emollients (e.g., ceramides, glycols) to soften the skin, occlusives (e.g., petrolatum, mineral oil) to prevent transdermal water loss, and humectants (e.g., alpha hydroxy acids, hyaluronic acid) to provide moisture to the deeper skin layers. Clinical trials have shown that consistent use of moisturizers reduces pruritus, erythema, and lichenification. Three randomized, controlled studies have demonstrated that moisturizers can be the mainstay of treatment in mild AD and can reduce the amount of prescription medications in moderate to severe AD [9]. While there is a general consensus that frequent and generous application is optimal, there are no such studies to define the minimal amount of application.

There are a variety of vehicles for moisturizers including gels, creams, foams, lotions, and ointments. Lotion use is commonplace but has a high percentage of water that leads to quick evaporation, making it less effective than other moisturizers. While ointments are more hydrophobic and are a better protective barrier, they are greasy and not as well tolerated for some patients. Creams have a good balance of barrier protection and tolerability, making them a good compromise between lotions and ointments. More recently, prescription barrier creams have been developed which contain specific quantities of lipids in an effort to mimic the natural skin

Table 11.3 Maintenance skin care for atopic dermatitis

<i>I. Bathing</i>
– Bathe daily for 10 min in lukewarm water
– Use only fragrance-/dye-free moisturizing soaps
– Bleach baths 2–3 times weekly if indicated
<i>II. Moisturizers</i>
– Apply within 2–3 min after bathing to minimize transdermal water loss
– Apply frequently throughout the day
– Use only fragrance-/dye-free creams and ointments (avoid lotions)
<i>III. Medications</i>
– Low-potency topical corticosteroids (Class 5–7) applied 2–3 times weekly to problem areas
– Topical calcineurin inhibitors applied 2–3 times weekly to problem areas
– First-generation antihistamines before bedtime as needed for itch
– Second-generation antihistamines daily as needed for itch
<i>IV. Irritant/allergen avoidance</i>
– Dust mite encasements (if testing suggests dust mite allergy)
– Pet allergen avoidance measure if applicable (if testing suggests allergy)

environment. Although these have been found to be clinically effective, studies have failed to demonstrate their superiority when compared to more inexpensive, over-the-counter moisturizers [10]. While there are many options for moisturizers, it is most important to choose an agent that is free of both fragrances and dyes as these are known to be irritating to the skin (Table 11.2).

Wet Wrap Therapy

Wet wrap therapy is a more intensive moisture replacement that is used in severe atopic dermatitis. First developed in 1987, it involves the placement of an emollient on affected skin followed by a wet wrap and then covered with a dry dressing. A wet wrap consists of a breathable, nonirritating fabric such as gauze or cotton cloths that are soaked in water. The wraps can be worn up to 24 h and soften the skin by preventing water loss. They also act as a physical barrier to protect against scratching. Studies have shown that wet wrap therapy can significantly improve AD severity and can decrease the need for systemic immunosuppressive therapy [11]. The wraps can be used alone or in conjunction with topical steroids (Table 11.2).

Irritant Avoidance/Allergen Immunotherapy

Atopy is a hallmark of AD and includes aeroallergen sensitization. The most commonly implicated aeroallergen is dust mite. While there are many species of dust mite around the world, many of the allergens they produce are cross-reactive. Dust mite allergens are proteases that are proinflammatory, particularly in individuals with AD, through both IgE- and non-IgE-mediated mechanisms [12]. Dust mite avoidance measures aim to reduce exposure and remove mites from the environment. These measures include mattress and pillow encasements, humidity reduction in the home, washing bedding frequently, and pesticides. Allergen immunotherapy may also be effective in dust mite-sensitized individuals. There is not enough evidence, however, to make a strong recommendation for its use, and more quality studies need to be done [13] (Table 11.2).

Phototherapy

Lastly, there has been some evidence that phototherapy can be an effective treatment for AD. Phototherapy can be used alone or in conjunction with topical therapies. Narrow-band ultraviolet B (NB-UVB) and medium-dose ultraviolet A1 (UVA1) phototherapy are the preferred modality in pediatric populations and have shown reduction in severity and extent of skin involvement. There appears to be a sustained treatment response months after therapy has been completed. Studies have also shown improvement in quality of life scores in patients treated with phototherapy [13–15] (Table 11.2).

Pharmacological Therapy

Topical Corticosteroids

Of all the pharmacological therapies used in AD, topical corticosteroids (TCSs) are the most widely used and most versatile. They are divided into seven different classes with Class 7 categorized as low potency and Class 1 superpotent. Steroids affect a broad range of immunologic cells and change cell processing and signaling, ultimately decreasing inflammation [10]. While the mechanism of topical steroids is similar and does not vary based upon class type, Class 1 steroids are over 1500 times more potent than Class 7 steroids. Similar to moisturizers, the vehicle of delivery plays an important role in absorption of the steroid and therefore dictates the potency. Ointments contain fewer preservatives and are more effective than creams because of their occlusive effect. While foams and oils of the same steroid are less potent than ointments and creams, they can be more effectively applied to large surface areas as well as the scalp and other areas with hair [16, 17].

Topical corticosteroids are the first-line treatment when consistent dry skin care alone is ineffective in controlling symptoms. They can be used acutely for flares or on a weekly basis for maintenance therapy. When choosing the appropriate steroid to use for an acute flare, it is important to determine the severity and location of the disease. For lesions of the neck, face, and intertriginous areas, it is best to use steroids from Classes 6 and 7 as more potent topicals can be harmful to these areas of more delicate skin. Severe, lichenified lesions of the body may warrant a higher potency topical steroid. Because AD is a heterogeneous disease, the wide range of options allow for patient-specific regimens that may include more than one topical steroid. When examining TCS use among providers, there is variability in the approach for acute management. Some providers start with a more potent steroid for rapid disease control and quickly wean, while others start with a lower potency steroid and increase with treatment failure [10].

In regard to steroid application, there is no standard quantity; however, most suggest applying a fingertip amount to the approximate surface area of two palms [17]. Twice-daily application is the most common frequency for acute flares, although there is some evidence that once-daily application of some potencies may be sufficient. The most important factor in determining length of treatment is the improvement of the lesions, which can take up to several weeks of daily treatment to resolve. Continued use of moisturizers during times of acute flares is also vital for improvement. Traditionally, moisturizers were felt to be the sole agent for maintenance therapy. In patients with frequent, repeated flares in the same location, maintenance TCS therapy has also been shown to be effective. Scheduled application to these relapsing areas once to twice weekly with a low- to mid-potency steroid has been shown to decrease rate of relapse and increase time to next flare as compared to just moisturizers alone [10].

While TCSs are generally well tolerated, there are some local and systemic side effects with use. Local side effects are the most common and include striae, hypopigmentation, acne, telangiectasias, and focal hypertrichosis. The likelihood of devel-

oping these local side effects is dependent upon the steroid potency as well as the duration and location of use. As previously noted, it is important to avoid high-potency TCSs on thinner skin including the face, neck, and intertriginous areas. While most of these side effects will improve over time after discontinuing treatment, striae are permanent [10, 17]. Systemic side effects with TCSs are rare but can occur with prolonged high-potency use and when used in conjunction with wet wraps, with hypothalamus-pituitary-adrenal (HPA) axis suppression being the most common [3] (Table 11.2).

Topical Calcineurin Inhibitors

Topical calcineurin inhibitors (TCIs) are FDA approved for acute flare and maintenance therapy in both children and adults. They are naturally produced by *Streptomyces* bacteria and inhibit the activation and cytokine production of T cells, keratinocytes, and Langerhans cells [3]. Because they affect a more narrow range of cells compared to steroids, they are not associated with the same adverse effects and can be used as a steroid-sparing agent. They have even been shown to be effective in reversing TCS-induced side effects such as skin thinning.

Currently, there are two preparations of TCIs, with pimecrolimus available as a cream and tacrolimus available as an ointment. Tacrolimus ointment is available in a 0.03% and 0.1% strength, whereas pimecrolimus cream is only available as 1% strength. Studies have shown that twice-daily dosing is more effective than daily dosing. When compared with low to moderate TCS use on the face and neck, TCIs have been shown to be clinically superior in reducing severity of lesions. In one randomized controlled trial, patients preferred tacrolimus 0.1% to fluticasone propionate 0.005% ointment for moderate to severe facial atopic dermatitis [18]. Similar to TCSs, TCIs can be used two to three times a week in problem areas as maintenance therapy by reducing the number of exacerbations and increasing the number of flare-free days. For severe disease, the combination of TCSs with TCIs has been shown to have greater efficacy than either agent alone. While TCIs are currently FDA approved down to 2 years of age, there is evidence that they can be used safely in infants [10].

Local reactions like stinging and burning are more common in TCIs than in TCSs. These symptoms appear to lessen with continued treatment and can be minimized when TCI application is preceded with topical steroids. Lastly, there is a black box warning on TCIs due to concerns for increased risk of malignancy. Calcineurin inhibitors are immunosuppressive agents that are used systemically to prevent graft rejection in transplant patients. Post-transplant lymphoproliferative disorder (PTLD) that can sometimes progress to lymphoma is a well-known complication with systemic use in these situations. TCIs, in comparison, have been not shown to have significant systemic absorption or immunosuppression. In response to these concerns, surveillance studies that are ongoing have not shown any increased rates of malignancy relative to the general population. Given this information, there has been a recent movement to have this black box warning removed [10] (Table 11.2).

Antimicrobial Therapy

Due to a compromised physical barrier and immune dysregulation, individuals with AD are more susceptible to superinfection of skin lesions, particularly with *Staphylococcus aureus*. In an attempt to decrease colonization of *Staphylococcus aureus*, studies have looked at the use of both systemic and topical antimicrobials. Some studies have shown that addition of antimicrobials may reduce bacterial colonization, but this does not appear to improve disease severity. In fact, some studies have even shown that TCS therapy alone can significantly reduce *Staphylococcus aureus* colonization. A similar effect has been seen with the use of TCIs. This phenomenon is thought to be secondary to decreased inflammatory cytokines that ultimately inhibit antimicrobial peptide production [19]. Because of the mixed evidence of antimicrobial use in patients with atopic dermatitis, this therapy is reserved for patients with clear secondary bacterial infections (Table 11.1).

Other forms of antimicrobial therapy aimed at decreasing colonization include bleach baths. One double-blinded placebo-controlled study showed that twice-weekly bleach baths made with ½ cup of bleach in a full tub of water along with intranasal mupirocin significantly decreased severity of AD [3, 13] (Table 11.2).

Antihistamines

Pruritus is a universal symptom of AD and has significant adverse effects on sleep and quality of life [20, 21]. There are many etiologies of the pruritus associated with AD including histamine release as well as other neuropeptides. Scratching has also been shown to exacerbate pruritus and leads to further breakdown of the skin barrier. Due to the multifactorial nature of pruritus in AD, it is often very difficult to control. Maintenance of the skin barrier is crucial to improving pruritus. Antihistamines may also be used to alleviate itch [22]. There are two generations of antihistamines that differ in their central nervous system and anticholinergic effects. First-generation antihistamines, including hydroxyzine and diphenhydramine, are commonly used in atopic dermatitis at night for their sedative qualities. Improvement with these agents has been more attributed to improved sleep rather than direct pruritus control. Nonsedating second-generation antihistamines at standard dosing have not shown significant benefit in regard to itch reduction or AD control. A few studies have shown that increasing the dose of second-generation antihistamines up to four times the standard recommended dose may have some benefit in reducing pruritus, body surface area involvement, and lichenification. These results are thought to be secondary to the sedating effects seen with increased dosing of these medications (Table 11.2). While oral antihistamines may have some benefit, topical antihistamines should be avoided, as they have no proven benefit. They can also be sensitizing and lead to contact dermatitis in some patients [15].

Systemic Therapies

Systemic steroids are one of the oldest and most commonly prescribed therapies for AD. They provide rapid resolution of even the most extensive and severe disease. Commonly used formulations include prednisone, methylprednisolone, and triamcinolone acetonide that can be given orally or intramuscularly. In pediatric patients, dosing is weight based and ranges from 0.5 to 1 mg/kg. Unfortunately, they also have significant, undesirable side effects that limit their utility in AD. In addition to commonly encountered steroid side effects such as HPA axis suppression, weight gain, agitation, and poor sleep, AD patients also experience significant rebound flares upon discontinuation. Long steroid tapers can minimize these effects but may not eliminate them, which is why this is not a recommended therapy for AD [3, 15] (Table 11.2).

Systemic immunosuppressant therapy has been used in severe, refractory AD as steroid-sparing agents. Several medications have been used off-label with varying efficacy and include cyclosporine, azathioprine, methotrexate, and mycophenolate mofetil (MMF). Of these, cyclosporine is the most well studied and appears to be the most efficacious in the treatment of severe AD. It also has the potential for many severe adverse effects including hepatic/renal impairment and increased risk of malignancy. Upon discontinuation of cyclosporine, there is potential for withdrawal and worsening skin disease, though it is not as severe as observed with systemic steroids. Azathioprine has been shown to decrease disease severity and improve quality of life, when compared to placebo. Myelosuppression, transaminitis, and gastrointestinal symptoms are known side effects of azathioprine use. Metabolism of azathioprine is dependent upon the enzyme thiopurine methyltransferase (TPMT). Genetic polymorphisms within this enzyme lead to variable enzyme function among the general population. Because of this, it is important to assess TPMT activity levels prior to prescribing azathioprine. Methotrexate has been shown to be effective and safe in severe AD. The extent of efficacy is difficult to assess, however, because there is inconsistency in dosing and duration of therapy among studies. While there are few studies assessing the adverse effects of methotrexate use in AD, the side effect profile of methotrexate is well known given its extensive use in other diseases. These commonly include nausea and other gastrointestinal symptoms. More rarely, bone marrow suppression, pulmonary fibrosis, and malignancy can occur. MMF is another agent used in refractory AD and has been shown in one study to be comparable to cyclosporine once patients achieved maintenance therapy. Prior to reaching maintenance, however, individuals treated with MMF required systemic steroids to control symptoms. Unlike cyclosporine and systemic corticosteroids, MMF does not have withdrawal rebound symptoms and is also generally well tolerated. Side effects are usually transient and commonly include nausea, vomiting, and abdominal pain [13, 15] (Table 11.2).

Biologics

Biologics are an area of active research with several promising medications currently in development. Dupilumab, a monoclonal antibody that blocks both interleukin-4 and interleukin-13 receptors, has recently been approved for adult patients with AD. In a double-blind placebo-controlled study of patients with moderate to severe AD, the addition of dupilumab to other topical therapies improved both disease severity and pruritus as well as reduced rates of flares. It also improved other patient-reported symptoms such as depression, anxiety, and quality of life. Side effects to dupilumab are minimal and include injection site reactions and conjunctivitis. Because of their efficacy and mild side effect profiles, biologic therapies have a promising future in the treatment of patients with AD [23] (Table 11.2).

Pitfalls

Treatment Adherence

Atopic dermatitis is a complex disease and therapy is usually a multistep approach. As with most chronic diseases, adherence with therapy can be difficult. Physicians should assess for treatment adherence issues in patients that appear to be refractory to standard therapies. Nonadherence is responsible for more than half of treatment failures. There are several contributing factors for poor adherence to therapy in AD. Frequent treatment applications are often cumbersome and time-consuming. One study showed that increasing to twice-daily application of TCSs decreased compliance to 60% after just 3 days [24]. Poor understanding of disease pathogenesis and appropriate treatment strategies is a common pitfall in AD. It has been shown that almost half of caregivers are unable to identify the potency of prescribed TCSs or the indication for other topical medications. Educational programs have been shown to improve treatment adherence. While formal, structured educational programs have the highest efficacy in improving adherence and disease control, they are also time-consuming and costly. Other less efficacious but more practical options include educational videos, nurse-led educational sessions, written action plans, and pamphlets. One study noted that nurse-led educational sessions showed improved patient satisfaction that was equal to doctor-led care [25]. Lastly, steroid phobia is a phenomenon that significantly affects AD treatment adherence. Over 80% of caregivers reported steroid phobia relating to potential local and systemic side effects [24]. One study demonstrated that several factors were associated with steroid phobia including female gender, parental history of AD, and frequent changing of clinics. Interestingly, disease severity did not correlate with steroid phobia [26].

Pitfalls with treatment adherence can also be secondary to physician error.

Topical therapies are dispensed in a variety of sizes; inadequately prescribed amounts can lead to the inconvenience of refilling medications frequently, along

with added cost. It is important for physicians to assess the extent of involved skin in order to dispense the adequate amount of medication [17].

Sleep Deprivation

Sleep disturbance is a problem for patients with AD and can affect both mental and physical health. Pruritus is the driving factor, but studies have shown that there may be other factors such as altered melatonin secretion, dust mite sensitization, and elevated total IgE levels. One study showed that patients with AD had reduced sleep efficiency, longer sleep onset latency, and more fragmented sleep with decreased rapid eye movement stages. This study showed that the severity of disease was associated with greater sleep disturbance. Obesity and hypertension have also been linked with sleep disturbance in AD. As discussed above, traditional AD therapies are effective in improving overall sleep quality. Other nonconventional therapies that are directed specifically at improving sleep quality include melatonin supplementation, light therapy, and improvement in sleep hygiene. All three interventions have been shown to be effective in patients with AD [21].

Allergic Contact Dermatitis

Allergic contact dermatitis (ACD) is a condition that presents with eczematous lesions that can complicate AD. The prevalence of ACD in patients with AD can range anywhere from 6 to 60% depending on the study but is at least as prevalent as the general population. While it is not uncommon to develop ACD to many different allergens, there is a small subset of patients who develop reactions to TCSs. This can affect anywhere from 0.5 to 5.8% of the population. In patients with refractory or worsening disease, particularly in the area of TCS application, ACD should be considered. Patients may develop a reaction to both the topical steroid itself, as well as preservatives such as lanolin. Patch testing is the gold standard to diagnose ACD [13, 25].

Food Triggers

Foods have been implicated as a trigger in approximately 30% of AD patients [27]. Sensitization to foods is common in these patients secondary to their defective skin barrier. This sensitization does not always correlate with clinical reactivity. Foods should not be eliminated from the diet of a sensitized individual in the absence of other clinical symptoms. Because there are multiple triggers of AD including irritants, infection, and stress, it is important to establish a true cause-effect

relationship when there are concerns about food triggers. This can be done by having patients eliminate and reintroduce the foods over the period of no more than 2–3 weeks while documenting symptoms in a diary. Even if a symptom diary identifies a food trigger, complete removal is not without consequence. One study showed that food removal in AD was associated with the development of immediate IgE-mediated reactions in 19% of patients without a previous history of IgE-mediated food allergy. While the majority of these patients had cutaneous symptoms, 30% developed anaphylaxis upon reintroduction of the previously eliminated food [28]. Recent studies have demonstrated that infants with moderate to severe AD are at higher risk of developing peanut allergy. This has led to guideline changes advocating for early peanut introduction and maintenance in the diet. Because of adverse effects of eliminating foods in these patients, panel testing is not recommended [29]. Evaluation by an allergist is important in these patients.

Clinical Vignette (Part 2)

The vignette described at the start of the chapter illustrates a typical presentation of a child with AD. The patient has scaling and weeping lesions, which is consistent with moderate severity AD and represents the typical infant distribution. The crusted lesions on the face bring up the question of *Staphylococcus aureus* superinfection and may warrant bacterial culture to confirm. This vignette also addresses several common pitfalls seen in AD including sleep deprivation, steroid phobia, and concern about food triggers.

This patient would benefit from an improved skin care regimen, which is the crux of AD treatment. Daily soaking baths along with use of cream moisturizers may help improve and maintain his impaired skin barrier. Due to the severity of his symptoms, TCS therapy should also be initiated. If he has refractory facial lesions despite the use of low-potency TCSs, TCIs can also be considered. Topical antihistamines should be discontinued given their poor efficacy and risk of contact dermatitis. Instead, sedating first-generation oral antihistamines may be used to improve his quality of sleep. In regard to food concerns, screening food allergy panels would not be recommended. Eliminating foods from his diet may have little benefit and also place him at risk for developing immediate IgE-mediated reactions. Given his moderate AD and increased risk of peanut allergy, referral to an allergist is strongly recommended.

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Chapter 12

Atopic Dermatitis Pertaining to Adolescents



Rekha Raveendran and Benjamin T. Prince

Clinical Vignette (Part 1)

A 16-year-old female with a history of asthma and atopic dermatitis since childhood presents with worsening skin rashes over the last year. She has had difficulty controlling her atopic dermatitis, and this was her third follow-up for this issue.

On previous visits, she has been given a multitude of topical medications without significant relief including hydrocortisone 2.5% for her face, triamcinolone 0.1% ointment for her body, and tacrolimus 0.1%.

The patient states that while she was initially using her topical medications daily, she has been less compliant more recently. She often forgets and complains that the medications cause a burning sensation. Her mother, who recently changed jobs and has been working long hours, was unable to comment on the patient's skin care regimen but does state that the patient has been buying lots of fragranced skin products. The mother also reports that she has been having increasing difficulty waking her daughter up for school and that she appears constantly fatigued.

Physical examination is significant for erythematous scaling rash diffusely over her face and neck. There are hyperpigmented, lichenified lesions with associated excoriations on bilateral wrists and hands.

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During the examination she had a flat affect, avoided eye contact, and had slouched posture.

Mom is concerned that the patient has not been herself recently and feels that her atopic dermatitis and its effects on her appearance could be playing a role.

Introduction

Atopic dermatitis (AD) is chronic, relapsing disease that is secondary to an impaired skin barrier. This disease commonly affects infants and children and usually remits before adulthood. Later onset, more severe disease and longer persistence of AD in childhood, however, is associated with persistence into adulthood [1]. Adolescence is defined as the period of life from the onset of puberty during which a young person transitions into an adult. This transition is associated with increased maturity but can also come with increased vulnerability and anxiety, which can play a role in treatment of chronic diseases. In this chapter, we will address important concepts to consider in the transition of AD care from childhood to adolescence and associated pitfalls that may occur during this process.

Diagnosis

Atopic dermatitis persists from childhood through adolescence in 10–20% of individuals. There are several risk factors associated with persistent AD, including female gender, allergic sensitization to inhalants and foods, allergic asthma, and allergic rhinitis. Occasionally AD may begin during adolescence and is usually seen during puberty, which may suggest an underlying hormonal role. AD in adolescence presents differently than in childhood. As noted in Chap. 11, AD generally affects the head, neck, and extensor surfaces in childhood. In adolescence, the distribution typically changes to include flexural surfaces, palms, and soles, in addition to the head and neck. In contrast to lesions in childhood that are associated with *Staphylococcus aureus* infection, head and neck lesions in adolescents are often associated with *Malassezia* infection [2, 3].

While there are many diagnostic criteria, the most commonly used in the United States is the American Academy of Dermatology (AAD) criteria. The AAD criteria take into consideration essential characteristics of AD, important patient features, as well as less specific associated skin findings [4, 5] (see Table 11.1). There are also standardized measures to rate severity of AD. The most commonly used measures is the SCORAD which takes into account both objective physician assessments and subjective patient ratings [4].

Table 12.1 Differential diagnosis of atopic dermatitis in adolescents

Disease	Distinguishing features
Contact dermatitis	Irritant or allergic mediated rash localized to the area of direct exposure. Symptom resolution 2–3 weeks after removal of the offending agent
Psoriasis	Demarcated erythematous patches of skin covered with silvery scale generally located on extensor surfaces. Often associated with a family history and nail pitting
Ichthyosis vulgaris	Generalized dry and thick skin with scales resembling that of a fish
Tinea corporis	Annular erythematous scaly plaque with a raised border and central clearing. Unlikely to improve with topical steroids
Scabies	Pruritic, erythematous, clustered papules with linear tracks often present in finger webs. Other family members may be affected. Not likely to improve with topical steroids
Seborrheic dermatitis	Greasy, flaky lesions often localized to the scalp
Keratosis pilaris	Dry, rough papules localized to upper arm and thighs. Not likely to improve with topical steroids
Drug eruptions	Erythematous, widespread exanthem that can be pruritic and lead to skin desquamation. Associated with an eliciting drug
Dermatographism	Transient, pruritic wheel and flare that can be linear. Triggered by scratching
Cutaneous T-cell lymphoma	New onset of a pruritic, eczematous rash in a patient without a previous history of atopy. Associated with enlarged lymph nodes and will not improve with topical steroids

When making the diagnosis of AD, it is important to exclude other conditions that can present similarly with erythematous, scaling, and pruritic rashes. There are certain diseases that can mimic AD and are specific to adolescents. The most common diseases to consider in the differential diagnosis for adolescents includes contact dermatitis, psoriasis, ichthyosis vulgaris, tinea corporis, scabies, seborrheic dermatitis, keratosis pilaris, drug eruptions, and dermatographism (Table 12.1). Cutaneous T-cell lymphoma is also included in the differential diagnosis. Although this is more rare, it should be considered in patients with refractory atopic dermatitis, particularly when they do not have a history of other atopic diseases. Contact dermatitis, including irritant and allergic triggers, is common. While irritant triggers are more common in childhood, allergic triggers are more often seen in adolescents because of repeated exposure to allergens. With older age, repeated exposure to common allergens increases and can lead sensitization. Common triggers in adolescents include fragrances, cosmetics, and jewelry. If contact dermatitis is suspected, patch testing should be performed to determine the underlying allergen (Table 12.2). The development of psoriasis can affect any age but usually peaks in adolescence. While AD lesions in adolescents are often flexural, psoriasis involves the extensors, which can be helpful in differentiating the two. Seborrheic dermatitis peaks in infancy and then again during puberty secondary to hormone-driven sebum production. This is often associated with *Malassezia* infection because it has a predilection for sebum rich skin. Keratosis pilaris is a common skin condition that

Table 12.2 The process of patch testing

<i>Step 1: Identify potential eliciting allergen</i> – History of skin exposures preceding the rash is imperative – Symptoms typically develop 48–72 h after skin contact and can become chronic with continued exposure – While distribution commonly follows skin exposure, the eliciting allergen can be transferred to other body areas (e.g., hand to face)
<i>Step 2: Application of patches</i> – There are several vehicles available for use. Prepackaged groupings can be purchased that include a set of preselected allergens that are commonly associated in contact dermatitis (e.g., T.R.U.E. Test, allergEAZE). Customized testing can also be performed by manually placing suspected allergens in Finn chambers for skin application – Patches are placed on the back – Patients are advised to avoid strenuous activity that may lead to sweating and submerging in water (including baths) to prevent accidental removal of patches and to maintain skin contact with the patches
<i>Step 3: Removal of patches</i> – Patches are removed 48 h after placement – Reactions are documented using a graded scale of 1+ to 4+ based on severity at the time of removal – The amount and degree of erythema determines level of scoring
<i>Step 4: Final reading of patches</i> – Final reading of patches occurs at 72–96 h to differentiate between irritant and allergic contact dermatitis – Persistent reactions at the time of the final read are consistent with allergic contact dermatitis. Reactions that have improved from the time of patch removal are consistent with irritant contact dermatitis – Some allergens may have a more delayed reaction that may take up to a week (e.g., gold thiosulfate)

manifests as small papules with variable erythema. It is usually located on the extensor surfaces of the arm and legs but can also appear on the face. While this condition is benign, it is important to recognize because of the aesthetic implications in this patient population [3, 6]. It is important to consider cutaneous T-cell lymphoma in older patients presenting with eczematous rashes without prior history of atopy. While presentation prior to age 50 is rare, there has been an increasing incidence in adolescents over the past 10 years. It often presents with widespread, hypopigmented macules that resemble pityriasis alba. If cutaneous T-cell lymphoma is suspected, referral to dermatology should be made for skin biopsy [6].

Treatment in the Adolescent

Treatment for AD focuses on maintenance of skin barrier through pharmacologic and/or non-pharmacologic means (Table 12.3). AD has a relapsing and remitting nature that requires constant and consistent care. While treatment options are

Table 12.3 Therapeutic options for atopic dermatitis

Type	Examples	Pros	Cons
<i>Pharmacological therapies</i>			
Topical corticosteroids	Numerous options that range from low potency (Class 7) to super potent (Class 1)	– Cost effective – Few systemic side effects – Can be used as acute and maintenance therapy	– Hypopigmentation – Skin atrophy – Striae – Acne – Telangiectasias – Hypertrichosis
Topical calcineurin inhibitors	– Tacrolimus (0.03 and 0.1%) – Pimecrolimus 1%	– Steroid sparing – Can be used as acute and maintenance therapy	– Burning – Skin malignancy/lymphoma^a
Antimicrobials	– Mupirocin 2% – Bleach baths (0.005% sodium hypochlorite) – Oral antibiotics	– Decrease <i>Staphylococcus aureus</i> colonization	– Antimicrobial resistance – Burning
First-generation oral antihistamines	– Diphenhydramine – Hydroxyzine	– Improve sleep – Decrease itch	– Sedation – Anticholinergic effects – Concern for incident dementia with cumulative use
Second-generation oral antihistamines	– Cetirizine – Fexofenadine	– Decrease itch – Less sedation/anticholinergic effects than first-generation antihistamines	– Sedation
Systemic corticosteroids	– Prednisone – Methylprednisolone	– Rapidly effective for severe, diffuse eczema	– Hypothalamus-pituitary-adrenal (HPA) axis suppression – Rebound flares upon discontinuation – Agitation – Weight gain – Poor sleep
Systemic immunosuppressants	– Cyclosporine – Azathioprine – Methotrexate – Mycophenolate mofetil (MMF)	– Steroid sparing – Effective for severe, diffuse eczema	– Infection risk – Gingival hyperplasia – Hypertension – Renal/hepatic dysfunction – Malignancy

(continued)

Table 12.3 (continued)

Type	Examples	Pros	Cons
Biologics	– Dupilumab (anti-IL-4/IL-13)	– Steroid sparing – Effective for severe, diffuse eczema – Decrease itch	– Hypersensitivity reactions – Conjunctivitis/keratitis – Herpes simplex virus reactivation – Expensive – Infection risk
Allergen immunotherapy	– Subcutaneous immunotherapy (SCIT) – Sublingual immunotherapy (SLIT)	– Can treat specific triggers – May improve other atopic conditions – Steroid sparing	– Hypersensitivity reactions – Limited evidence for efficacy in eczema
<i>Non-pharmacological therapies</i>			
Moisturizers	– Petroleum jelly – Ceramide containing emollients – Fragrance-free/dye-free barrier creams	– Foundation for both acute and maintenance therapy – Cost effective – Minimal side effects	– Greasy – Burning
Phototherapy	– Narrow band UVB – UVA1	– Steroid sparing – Effective for refractory, diffuse eczema	– Actinic damage – Altered pigmentation – Malignancy
Wet wraps	– Emollient wet wraps – Topical corticosteroid wet wraps	– Effective for severe eczema – Decrease itch – Cost effective	– Cumbersome – Time consuming – Increased systemic absorption of topical steroids
Irritant avoidance	– Dust mite/pet allergen avoidance measures – Avoidance of dyes/fragrances	– Cost effective	– Best used adjunctive therapy

*Causal relationship not established

similar from childhood through adulthood, there are some adolescent-specific issues that need to be considered when customizing an appropriate regimen.

Non-pharmacological Therapies

Moisturizers and Dry Skin Care

Preventing transepidermal water loss is the mainstay in AD treatment. Moisturizers and daily soaking baths, therefore, are important to maintaining the skin barrier. Patients with AD should be doing soaking baths for at least 10 min every day with

application of moisturizers shortly thereafter (see Table 11.3). It is crucial to seal in the moisture obtained from bathing. As discussed in Chap. 11, there are several different kinds of moisturizers including occlusives, emollients, and humectants. Emollients soften skin and are the most commonly used moisturizer. There are several different types of emollients including lotions and creams. Lotions have a high percentage of water and can easily evaporate which can lead to paradoxical dryness and can exacerbate AD. Creams are the preferred emollient as they have higher percentage of oils than lotions. Ointments are occlusive moisturizers that create a thick barrier on the skin surface to prevent transdermal water loss and protect the skin from irritants. Lastly, humectants can help to pull moisture into the deeper layers of the skin [7, 8].

In adolescents, dry skin care can be difficult to maintain secondary to the time commitment, cost, discomfort, and associated aesthetics. Dry skin care is time intensive and most effective when performed daily and consistently, which is challenging for most adolescents. In addition, this is the hallmark of skin healing and protection and thus should be performed at all times, even when active AD flares are not present. For adolescents, this can be a challenging part of their care as they often lack the ability to appreciate long-term consequences and do not understand that daily preventative strategies can reduce the frequency and severity of discomfort in the future. Reminder systems specific to their lifestyle and preferences may be useful. As with most medications, storing moisturizers in plain sight, as opposed to inside cabinets or drawers, can serve as a daily visual reminder and assist adherence.

Ointments and creams are thicker and can be greasy, which may be less aesthetically pleasing and can damage clothing and linens. Ceramide containing moisturizers can burn on application, which may deter adolescents from continued use. Prescription emollient devices, creams, and ointments may also be more expensive than lotions, which can be a financial barrier. Lastly, lotions often contain fragrances and dyes, which may be more appealing to the adolescent but can irritate their skin and contribute to AD flares.

Wet Wrap Therapy

For severe AD, wet wrap therapy is a proven and affordable treatment that can provide more intensive moisture replacement. In this therapy emollients are placed on the skin, which is then wrapped with breathable, non-irritating fabric that has been soaked in water. Dry dressings are placed over the wet wraps and left in place for up to 24 h. In severe AD, emollients can be replaced by topical corticosteroids for improved absorption and therefore more rapid resolution of lesions [9] (Table 12.3).

Wet wrap therapy, however, can be cumbersome and uncomfortable. In an adolescent, this therapy can be difficult to maintain. Wet wraps are often done in the evening and overnight, which may interfere with social events and busy school/work schedules. Wet wraps are time intensive and require commitment in order to offer benefit. Adolescents who have not previously utilized this treatment may not appreciate the potential benefit. Adopting use prior to leaving home can demonstrate

success of this therapy and may improve adherence for ongoing use when living independently.

Irritant Avoidance and Immunotherapy

Irritant avoidance is important to maintain AD control. Fragrances and dyes are ubiquitous in many skin care products including moisturizers, cosmetics, and sunscreen [8]. As atopy is a hallmark of AD, aeroallergens can also play an important role in flares. As discussed in Chap. 11, dust mite is one of the most commonly implicated aeroallergens in AD, but pet dander may also worsen symptoms in adolescents who are allergic [10]. These two exposures should be considered when evaluating housing, particularly if living with roommates.

During adolescence, much time and effort is spent on maintaining appearance. Fragrances and other beauty products are often used, which can lead to skin irritation and AD flares. While dust mite avoidance measures do not affect appearance, adolescents who are transitioning to living on their own may not put in the effort to do them. Allergy immunotherapy is time consuming and requires compliance in order to be effective. Frequent visits for immunotherapy without immediate results may discourage adolescent patients from continuing with treatment.

Phototherapy

Phototherapy can be used alone or in conjunction with topical therapies. The most commonly used modalities in AD are narrow band ultraviolet B (NBUVB) and medium-dose ultraviolet A1 (UVA1). Phototherapy can reduce AD severity and skin involvement, and its effects can last months after discontinuation [10–12] (Table 12.3).

Phototherapy does require a significant time commitment, which can be a deterrent for some patients. Since it uses UV light, it does lead to tanning of the skin. This side effect of treatment, in some cultures, may be seen as aesthetically advantageous and may make adolescents more likely to be compliant with therapy. However, this treatment will require effort to arrange, particularly for adolescents moving away from home to a new location. The challenges of identifying a new provider, establishing care, and ensuring regular visits after living independently must all be considered.

Pharmacological Therapy

The most commonly used and effective therapies for AD are topical medications. There are several issues that may decrease adolescents' access to these medications, including forgetting to renew/transfer prescriptions or take current prescription to

their new location, misplacing the tubes after moving, high cost, and insufficient quantities often prescribed. In addition, AD is often relapsing and remitting; thus adolescents may feel fine for extended periods and lapse on their routine skin care. When AD flares occur, they can be extremely uncomfortable and disruptive to the daily routine. The importance of anticipatory guidance and having prescription topical medications available at all times should be actively discussed with adolescents prior to their transition to independence and planned for accordingly.

Topical Corticosteroids

As discussed extensively in Chap. 11, topical corticosteroids (TCS) are versatile and widely used in the treatment of AD. They are available in seven different classes that vary in potency from low potency (Class 7) to superpotent (Class 1). TCSs can be used for acute and maintenance treatment of AD. In patients who have more severe or relapsing disease, application of low to medium TCSs once to twice weekly has been shown to decrease rate of relapse and increase time to next flare [8] (Table 12.3).

While TCSs are considered the first-line pharmacological therapy and are generally well tolerated, the potential side effects can be off putting for an adolescent. These therapies are associated with hypopigmentation, striae, acne, and skin atrophy. Striae, in particular, can be troublesome as it is permanent. These side effects can be minimized or avoided by choosing an appropriate TCS potency for the affected areas. Higher potency TCSs on more delicate, thinner-skinned areas can worsen these side effects and should be avoided. This therapy generally requires twice-daily application. Studies have shown that there is a decrease in compliance to 60% just 3 days after initiating twice-daily therapies [13].

Topical Calcineurin Inhibitors

Topical calcineurin inhibitors (TCIs) inhibit the activation and cytokine production of T cells, keratinocytes, and Langerhans cells [14]. There are currently two preparations available with pimecrolimus available as a 1% cream and tacrolimus available as a 0.03 and 0.1% ointment. These medications should be dosed twice daily (Table 12.3).

Similarly to TCSs, TCIs can be used for both acute flares and for maintenance. Unlike TCSs, however, TCIs do not cause hypopigmentation, acne, striae, or skin atrophy, which may make them a more palatable choice for adolescents. They can be very effective on thinner-skinned areas like the eyelids and the face. TCIs can sting and burn, especially on more inflamed areas, but this should dissipate with continued and consistent use and can be minimized if preceded by a TCS [8]. It is important to make the patient aware of these adverse effects in an effort to avoid noncompliance.

Antimicrobials

It is well known that lesions in AD are often colonized with *Staphylococcus aureus*. Toxins produced by this bacterium can exacerbate inflammation causing regulatory T-cell dysfunction and immune dysregulation ultimately resulting in the intense pruritus associated with this disease [15]. Some studies have shown that the addition of antimicrobials may reduce bacterial colonization [16]. Twice-weekly baths made with 1/2 cup of bleach in a full tub of water have also been shown to reduce AD severity [10, 14] (Table 12.3).

As with ointments and creams, topical antimicrobials can also be greasy and may not be preferred. Antimicrobials are also used in addition to other topicals and may complicate the skin regimen and increase noncompliance, particularly in adolescents. With the evidence that both TCSs and TCIs decrease colonization of *Staphylococcus aureus*, it may be beneficial to optimize these regimens before adding topical antimicrobials [16]. Bleach baths may be beneficial and can be added to the daily soaking regimen. As adolescents transition to independent living, they may not have a tub available, which is necessary for this therapy.

Antihistamines

Antihistamines may be used to alleviate itch associated with AD. There are two generations of antihistamines that differ in their central nervous system and anticholinergic properties. Hydroxyzine and diphenhydramine are first-generation antihistamines and can be useful for their sedative properties. Because pruritus associated with AD is multifactorial and includes many etiologies other than histamine, second-generation antihistamines must be increased up to sedative doses to show improvement [17] (Table 12.3).

With adolescents, it is particularly important to consider the sedative impact that antihistamines can have on their daily routines. Due to their feeling of invincibility, they may not recognize the level of impairment that antihistamines can cause, particularly when performing tasks such as operating a motor vehicle. It may also impact their concentration leading to poor performance in school. Any adolescent taking or prescribed sedating antihistamines must be made aware of the potential for significant interactions with alcohol, which can combine to cause increased drowsiness, slow reaction time, and sedation. In contrast, sleep deprivation can also have significant effects including decreased quality of life and poor concentration so a balance of treating pruritus and limiting side effects must be achieved [18].

Systemic Therapies

One of the oldest and most commonly prescribed therapies in AD patients are systemic steroids because they provide rapid resolution of even the most extensive and severe disease [12, 14]. Systemic steroids have fallen out of favor, however, since

the advent of topical therapies because of their extensive side effect profile. Other systemic immunosuppressant therapies to consider include cyclosporine, azathioprine, methotrexate, and mycophenolate mofetil (MMF). While these agents have shown varying efficacy in patients with severe, refractory AD, which can limit use in adolescents in particular, increased infections, hepatitis, renal dysfunction, and malignancy are just a few side effects that are common to many of these medications [10, 12] (Table 12.3).

The rapid relief provided by systemic steroids can appear to be very attractive, especially in adolescents with severe, disfiguring disease, but should be avoided. It is important to explain the rebound effect seen with oral steroids that can ultimately worsen their disease. The dermatologic side effects seen with TCSs can also be seen with oral steroids. In addition, oral steroids can also lead to weight gain and central obesity, diabetes, agitation, and hypothalamus-pituitary-adrenal axis suppression. These side effects can lead to poor self-esteem and behavioral problems in an adolescent population. Immunomodulators may be necessary in refractory disease but do come with risks and side effects. Some of the side effects, particularly those seen with cyclosporine such as gingival hyperplasia and hirsutism, can affect appearance. This may be concerning, particularly for some adolescents, and therefore the risks and benefits should be discussed prior to initiating these medications.

Biologics

An emerging treatment option in AD is biologic therapy. Due to their specific mechanism of action, biologics tend to have fewer side effects than other systemic therapies used in AD. Dupilumab, a monoclonal antibody that blocks both interleukin-4 and interleukin-13 receptors, has recently been approved for adult patients with AD [19]. There are ongoing trials and this medication will hopefully be approved adolescents with AD in the future (Table 12.3).

Biologics are often injectable medications and may require office visits to administer. This may be a limiting factor in the adolescent population; however, these medications may have many benefits. In a recent study dupilumab was shown to decrease disease severity, pruritus, and rates of AD flares. It was also noted to improve other patient reported symptoms including depression, anxiety, and quality of life [19]. Because adolescents often struggle with psychosocial issues, this medication could be very impactful in this population. Other biologics are also being studied and will likely revolutionize the future treatment of AD patients.

Quality of Life in Adolescents with Atopic Dermatitis

While quality of life is affected in patients of all ages in AD, adolescence is a time of heightened vulnerability, insecurity, and anxiety. In a study of adolescents, AD had a highly negative impact on quality of life that was associated with disease

severity. Severe AD can be disfiguring, and Brenninkmeijer and colleagues also found that this can lead to decreased social interactions [2]. The majority of high school patients with AD reported being ashamed of their skin, and many avoided intimate situations and abstained from sports. They also reported problems that are common to other age groups including intense itching, sleep deprivation, and associated fatigue [3]. Adolescents with chronic medical conditions, such as AD, are at increased risk for bullying. A study evaluating chronic conditions and bullying showed that bullied adolescents were more likely to be depressed, have poor relationships with parents, more physical symptoms, and be victims of violence. One in five adolescents report being bullied and are three times more likely to experience exclusion, which leads to fewer friends and less support [3, 20]. It is important to be aware and address the social stigmatization and psychological consequences in adolescents with AD.

Pitfalls

Nonadherence

Please see Chap. 11 for a discussion of specific factors associated with nonadherence in the treatment of atopic dermatitis. Here, we would like to consider some reasons for noncompliance that apply specifically to adolescent population [21, 22] (Table 12.4). Adolescence is a time of both physical and cognitive maturation. Cognitively, they progress from concrete to more abstract thinking. They have a difficult time appreciating long-term consequences of their current behavior. They have a tendency for egocentric thinking and often feel invulnerable to consequences, which leads to more risk-taking behavior. This is also a time for increased independence. Chronic diseases such as AD may cause feelings of helplessness and loss of control over their life. In order to gain control, adolescents may purposefully stop taking their medication and miss appointments [23]. Time management is a skill that is developed during the transition to adulthood. Adolescents may choose other

Table 12.4 Common reasons for nonadherence in atopic dermatitis

<i>General reasons for nonadherence</i>
– Running out of medication with lack of follow-up
– Concern for side effects of treatment (e.g., steroid phobia)
– Poor understanding of treatment plan
– Cost of therapies
<i>Adolescent-specific reasons for nonadherence</i>
– Poor understanding of long-term consequences of nonadherence
– Feeling of invincibility leading to high-risk behavior
– Poor time management
– Concern for adverse cosmetic effects of therapies
– Disfiguring disease can lead to depression and lack of motivation

activities over the time-intensive, therapeutic treatment strategies required for AD. As previously mentioned, appearance plays a big role during adolescence, and therapies with adverse cosmetic effects may also affect compliance. Severe AD can be disfiguring, and this can lead to lower self-esteem. A recent study demonstrated that the prevalence of suicidal ideation was increased in adolescents with both AD and itch compared to those without AD [24]. Factors that have a positive impact on adherence include a good family support system, close friends, personal sense of control, physician empathy, and rapidly effective treatments [23]. When treating adolescents with AD, it is important to consider these specific reasons for nonadherence.

Sleep Deprivation

Sleep disturbance is a problem for patients of all ages with AD and can affect both mental and physical health. In adolescents, poor sleep can lead to behavioral problems, poor daytime performance, and neurocognitive defects. When compared to teens without AD, adolescents with AD scored 16 points lower on a composite IQ exam. Obesity and hypertension have also been linked with sleep disturbance in AD, which can lead to long-term health consequences and psychosocial issues related to image. In the adolescent population it is important to assess sleep quality and optimize therapy as this has been shown to correlate with less sleep disturbance [18].

Clinical Vignette (Part 2)

The vignette described at the start of this chapter illustrates some of the challenges in treating an adolescent with AD. Adolescence is a time of increased independence and instilling a good skin regimen at the start of symptoms can help patients remain compliant as they transition to living on their own. It is also a transitional time that can be fraught with psychosocial issues including poor self-esteem, social acceptance, and bullying. The patient has had significant difficulty in controlling her disease, and this has led to some behavioral changes that are suggestive of depression including flat affect, avoidance of eye contact, and slouched posture. It is important to identify this behavior in adolescent patients, as this can be a barrier in providing effective treatment. She identified side effects as an issue with her treatment, namely, burning. This may be preventing her from using the medications on a regular basis leading to her continued flares. In this patient, it would be beneficial to discuss adverse effects of treatment such as burning with TCIs and explain that those adverse effects can improve over time with consistent use. It may also be helpful to consider the addition of TCSs prior to TCI application. Identifying side effects before they occur can prepare patients and prevent

discontinuation of treatment, especially in cases where those symptoms may dissipate with continued use. The use of irritant products is another common issue in adolescent patients. These products are common in fragrances, lotions, cosmetics, and other skin care products. Counseling patients on the importance of avoiding these products is essential for minimizing AD flares. Adolescents are a unique patient population, and there are specific strategies to consider in order to effectively treat these patients.

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Chapter 13

Other Allergic Conditions: Venom Hypersensitivity, Drug Allergy, Chronic Urticaria/Angioedema, and Primary Immune Deficiency



Brian Schroer

Introduction to Other Allergic Conditions

While the most common allergic conditions affecting teenagers were discussed throughout this textbook, there are a few other topics which may impact adolescents and warrant discussion. This chapter will cover issues often seen in teenagers who present to both primary care physicians and allergy offices. These issues can range from very specific topics such as venom allergy and chronic urticaria to a broad range of potential issues such as drug allergy and immunodeficiency.

Venom Hypersensitivity

Stinging insects can be found all over the world and are the second most deadly insects that people will encounter on a daily basis. Mosquitoes are the leading cause of deaths across the world due to their role in transmission of parasites and viruses such as malaria, dengue fever, chikungunya, and other deadly diseases. When it comes to insects that use stingers to inject venom (they sting, and they do not bite), the main immediate danger is anaphylaxis. Anaphylaxis from venomous stings can be more severe and rapid in onset compared with food allergies due to the allergens being presented to the immune system by injection, rather than ingestion. The Centers for Disease Control and Prevention (CDC) suggests that, in America, stinging insects are the deadliest nonhuman animal in North America as approximately 90–100 people in the United States die from stinging insect hypersensitivity per

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year [1]. Despite those numbers, people are best served to remain calm when around stinging insects because most do not sting unless provoked.

In North America and Europe, the most common types of stinging insects that can cause allergic reactions are honeybees, fire ants, and wasps. Wasps include both hornets (a type of European wasp) and yellow jackets (a wasp with some unique identifying characteristics). The most common causes of stings in general are yellow jackets and African “killer” bees due to their aggressive behaviors. Most of these insects live in characteristic locations or have typical markings that can make them easier to identify. Yellow jackets are black with yellow marks and are found in both warm and cold climates. Their nests tend to be underground, and they are active around trash cans and any outdoor food or drinks. They are one of the few stinging insects which forage for both sugary and protein-based foods. Native honeybees are slower moving and fuzzy and have yellow and dark brown markings. They rarely sting unless provoked or accidentally stepped on, as they are not naturally aggressive. Honeybees have barbed stingers that connect to their venom sac, which is an internal organ and is typically pulled out of them after a sting, leading to their death. There are many types of wasps with a wide variety of size and colors. They tend to nest in higher areas of houses or trees. Paper wasps create characteristic nests in trees and under eaves on houses. Hornets can be variably colored and are typically larger than yellow jackets and wasps. They live in larger characteristic gray-brown paper nests in trees. Imported fire ants (IFA) are found in warmer climates, are reddish brown in color, live in large colonies, and mostly sting when the nest is inadvertently disturbed.

Types of Reactions

When most of these insects sting, the vast majority of people will not have an allergic reaction. However, symptoms often occur at the site of the sting, which are due to proteins in the venom. Redness, swelling, itching, and warmth are common symptoms from venom. This type of reaction is self-limited and does not cause prolonged symptoms. Supportive treatment with cold compresses, analgesics for pain relief, topical steroids to help reduce inflammation, and oral antihistamines is all that is typically necessary for alleviating symptoms associated with a normal response to stings.

If an allergic reaction to the venom does occur, there are two major types of reactions which have clinical implications for management: large local reactions and anaphylaxis.

Large Local Reactions

This type of reaction encompasses exaggerated redness and swelling which can cover a contiguous area from the site of sting and typically peaks in severity at 48–72 h but may last up to 1 week [2]. The size of the reaction can be dependent on

the number of stings and the location of the sting. Some large local reactions can cause swelling of an entire extremity. The area becomes red, warm, and itchy, and it can last for several days. Though it may feel hot to the touch, stings rarely lead to infections, and antibiotics are not indicated [3]. The heat is due to the local type IV delayed cell-mediated hypersensitivity response [3]. These types of reactions occur in 10–15% of adults [3]. Interestingly, the IFA sting will typically cause a pseudopustule (pimple-like reaction) which also looks infected but which is caused by necrotic tissue damage from the venom [3].

Many patients with large local reactions are referred for allergy evaluation due to concerns that the next sting will cause a more severe reaction. However, patients who have a history of a large local reaction have a 5–10% chance of having anaphylaxis when they are stung again, which is not elevated compared with the general population [2, 4]. Because of this, guidelines suggest that patients with large local reactions do not need allergy testing and allergen immunotherapy is not typically recommended [4]. If patients receive frequent or uncomfortably large local reactions, however, allergy testing with the intention of starting allergen immunotherapy can be performed with the goal of reducing the severity of reactions to future stings [5, 6].

Anaphylaxis

Anaphylaxis is a systemic reaction to the venom which causes symptoms that occur away from the site of the sting. These symptoms can include systemic itching; hives; swelling of the lips, face, throat, or other extremities; coughing from the throat or coughing from bronchoconstriction in the lungs (asthma-like symptoms of chest tightness, wheezing, trouble breathing); nausea; vomiting; feeling faint or light-headed or actually fainting due to the hypotension; and vasodilation of anaphylactic shock. And, as mentioned previously, death can occur in rare instances. When a patient has had one or more of these symptoms, then further evaluation by an experienced allergist is recommended, along with strong consideration for venom immunotherapy, which (when completed for at least 3–5 years) can lower risk of anaphylaxis with future stings from as high as 70% to less than 10% [2]. In addition, anyone with a history of anaphylaxis to a venomous sting must be prescribed an epinephrine autoinjector and counseled on appropriate recognition and treatment of anaphylaxis, should it occur in the future.

Helpful History

When available, the body of the insect can be helpful for identification purposes. This helps with both avoidance techniques and prescription of venom allergy immunotherapy. The clinical history is the most important part of the evaluation. The situation surrounding the sting can help narrow down the list of suspected insects. Other important questions to ask include:

- How many stings occurred?
- How long after the sting did symptoms begin?
- What symptoms started first?
- What came next?
- Pertinent negatives are important.
- What treatment was used? The only effective treatment for anaphylaxis is epinephrine. That being said, it is important to ask if the patient was given antihistamines or steroids either by themselves or at the advice of healthcare professionals.
- Review how long it took symptoms to resolve before they felt better and were completely gone.
- Finally, ask about any previous or subsequent stings and whether there were or were no any symptoms that occurred.

Prevention

There are a number of easy-to-follow recommendations about how to prevent a sting. Some are listed on the CDC website (www.cdc.gov/niosh/topics/insects/default.html) and summarized here [7]. It can help to wear light-colored clothes as flying stinging insects are attracted to dark colors. Wearing smooth clothes can help prevent the insect from getting stuck in the fibers. Perfumes or scents can attract insects and should be avoided when outdoors. Many stinging insects can be found inside flowering plants, surrounding garbage cans, or around open containers of food or drink; caution is recommended near these objects. It is advised to avoid swatting or attacking insect as this may provoke a sting. If a sting occurs, then people should run from the site and go indoors if possible. Africanized honeybees are known to hover over water and follow people for long distances. Finally, anyone known to have previous anaphylaxis or allergy to venom should always have self-injectable epinephrine immediately available.

Treatment

For patients with anaphylaxis to a stinging insect, the risk for a reaction on subsequent stings is generally considered to be around 50% [8, 9]. Further evaluation by an allergist can help determine if the reaction history warrants testing and treatment with venom immunotherapy. Generally, the only reason to do any testing for the venom is if the patient is a candidate for allergy immunotherapy. Teenage patients who experience *only* systemic itching or hives with no other systemic, respiratory, cardiovascular, or gastrointestinal effects are not recommended for immunotherapy as their risk of anaphylaxis with future stings is not elevated [2]. However, if those patients have frequent exposure or wish to pursue immunotherapy due to ongoing concern, then allergy testing with subsequent immunotherapy can be done.

Venom allergy immunotherapy (VIT) or venom allergy shots are a version of subcutaneous immunotherapy which has extensive evidence to support its efficacy. This therapy can prevent potentially fatal reactions and is an important preventative therapy [2]. There is evidence for efficacy for honeybees, all wasps, and fire ant immunotherapy [2]. Immunotherapy has been found to decrease the risk of anaphylaxis from a subsequent sting from between 30 and 70% to less than 5% [8, 9]. As with allergy shots for environmental allergens, venom immunotherapy is always given in the office because of the risk of potential systemic allergic reaction. Injections begin with more dilute doses and build up to a maintenance dose, which is most often a dose of venom equivalent to two stings. To get from the low dose to a higher dose quickly, most allergists use a cluster protocol. During this protocol the patient receives multiple progressively larger doses in 1 day. They return once per week until they reach a point where they will receive one shot per week while still building up the dose. Once the top dose (about the equivalent of two stings) is reached, the maintenance dose is usually given monthly. The recommended duration of shots is 3–5 years. Some patients may need lifelong therapy if they have had a severe reaction as their initial presentation, if they have a reaction to the allergy shots, or if they have had a reaction to a field sting while receiving maintenance dose therapy.

All patients with prior anaphylaxis, including those receiving immunotherapy, need to be trained on how to recognize the symptoms of anaphylaxis and know how to use self-injectable epinephrine. This should involve the use of an anaphylaxis emergency care plan which is available from a few different resources such as FARE (Food Allergy Research and Education) [10], AAAAI (American Academy of Allergy, Asthma, and Immunology) [11], AAP (American Academy of Pediatrics) [12], and AAFA (Allergy and Asthma Foundation of America) [13]. While many of these are templated for food allergies, the concepts are the same for venom anaphylaxis treatment.

Chronic Urticaria/Angioedema

I tell my patients that I want to put a sign on my door that says, “Hives happen.” Acute and chronic hives happen and are relatively common. They also often occur with associated swelling (angioedema). Despite looking like an allergic reaction, hives that occur on a consistent and frequent basis are not caused by any type of allergen or exposure. Hives can be both highly annoying and often worrisome to patients. Because hives occur during acute allergic reactions to foods, venoms, and drugs, many people assume that all hives occur due to an allergic response to something in the environment. However, this is not true. Many episodes of hives which have a typical presentation and timeline can be easily distinguished from true allergic reactions. This section will provide information to assist both clinicians and teenagers in understanding the etiology and natural course of hives and ideally avoid extensive testing to “find the cause.”

The History Is the Test

The words hives, urticaria, welts, or wheals mean many things to many people. It is important to distinguish hives from other chronic itchy rashes such as allergic contact dermatitis or atopic dermatitis. This differentiation can be difficult because many patients come to the visit with no hives to examine. Though teenagers will often bring pictures on their phones which can be incredibly helpful, it can still be difficult to differentiate true urticaria from other rashes, especially if the pictures are blurry. Therefore, a detailed history is necessary to differentiate the wide variety of rashes that can occur.

Hives, or urticaria, are a type of rash that is almost always itchy and are characterized by a raised patch or plaque that is pale in color (wheal) with surrounding redness (flare) (Fig. 13.1). They can be circular, or irregularly shaped, can occur as single or multiple lesions, and can coalesce into one larger hive. Patients often experience hives that wax and wane throughout the day for a few days before initially presenting for evaluation. Sometimes patients are seen right away and are treated with antihistamines, but then the hives return when the antihistamines wear off. Hives that are present for 24 or more hours or last less than 6 weeks are termed acute urticaria. According to clinical criteria, chronic hives are present more often than not or daily for >6 weeks. Approximately 50% of patients with chronic hives also experience angioedema, which typically occurs in characteristic locations including the eyelids, lips, face, hands, feet, and genitals (Fig. 13.2) but rarely causes swelling of the tongue or throat or difficulty breathing or swallowing. However, in adolescents who have persistent symptoms despite treatment with antihistamines, the rate of angioedema is reported lower than adults, at 28% [14]. Based upon clinical experience, many adolescent patients may describe a symptom of “throat closing” or “trouble swallowing.” This is often not associated with objective signs of shortness of breath and is typically secondary to anxiety about their hives. Eliciting a history to differentiate true oropharyngeal angioedema from subjective symptoms due to



Fig. 13.1 Typical urticaria

Fig. 13.2 Upper and lower lip angioedema



Table 13.1 Differentiating urticaria from dermatitis from urticarial vasculitis

Urticaria	Dermatitis	Vasculitis
Raised, flat	Raised	Flat or raised
Burning itching	Itching	Painful
Migratory	Stationary	Stationary
Associated with angioedema	No related issues	None or arthritis

anxiety can be difficult but should be attempted. Evidence or history suggesting true angioedema of the oropharynx should lead to evaluation of other causes of anaphylaxis before establishing a diagnosis of idiopathic urticaria.

When hives (with or without swelling) occur, specific questions can help differentiate from other rashes and reactions that may require testing or evaluation by a specialist. Angioedema without hives or itching raises concern about hereditary angioedema syndromes and drug allergies to nonsteroidal anti-inflammatory drugs (NSAIDs) (which can also cause hives) or ACE inhibitors (which can cause isolated angioedema without hives).

The following historical details can be useful to differentiate typical urticaria from other rashes (Table 13.1). Hives are often transient and migratory, typically lasting less than 24 h in any one location. Itchy rashes that last for more than 24 h in one spot tend to be a dermatitis or a different type of rash, such as vasculitis. Hives should be itchy and not painful. Pain instead of itching is associated with vasculitis [15]. Hives leave no residual marks, resolving as though they were never there. Hives due to urticarial vasculitis often leave a bruise as though the patient was hit by a ball (Fig. 13.3). Hives tend not to be symmetrical and can occur on any portion of the skin, regardless of area. The rash associated with hives does not present with fluid-filled papules. Fluid-filled papules are often found in patients with dermatitis, eczema, or bullous skin diseases. Many patients can feel their hives coming on before they are visible, often describing a tingling/burning sensation before the rash is present. There are usually no other symptoms such as fever, joint pains, blisters, stomach pain/swelling, mouth itching, nausea, vomiting, coughing, trouble breathing, or light-headedness. If these symptoms are present, then other etiologies such as autoimmune conditions, malignancy, or infection should be considered.

Fig. 13.3 Urticarial vasculitis with hives and bruising



Table 13.2 Acute/chronic hives vs food allergy

Acute/chronic hives	Food anaphylaxis
No particular cause	Only occur with food ingestion
Occurs with or without food exposure	Occurs within 2–4 h of meals
Skin only	Skin + mouth, throat, lung, gut symptoms
Returns after treatment	Does not return after treatment
Treat with antihistamines	Treat with epinephrine

As mentioned, many patients with hives worry that they are caused by exposure to a specific allergen. Details which can be used to differentiate hives from food allergies include (Table 13.2) hives not due to food allergies wax and wane for no apparent reason. They can appear when a person wakes up in the morning or several hours after ingestion of food. Most acute hives from food allergy reactions resolve within 6–8 h after food ingestion, even without treatment. Hives from food allergy reactions do not return after treatment and are not usually seen as a part of a biphasic reaction. As such, a reaction caused by a food eaten at dinner may cause hives that persist through the day/evening but should be resolved by the next morning. Another distinguishing factor suggestive of food allergy includes oral symptoms soon after eating the causative food or any other symptoms of anaphylaxis described in previous chapters. Food allergy reactions only occur when the food is eaten and occur every time the food is eaten. Food allergy reactions do not come and go with time; therefore if a patient is eating a food and it is not causing symptoms every time, then they are not likely allergic to that food. Patients with food allergies almost always identify their food, or meal, that causes symptoms, and allergy testing is useful to confirm their suggestive history. Most patients with acute or chronic urticaria that have concerns about food allergy cannot identify any specific foods, or have a long

list of suspected foods, that may be contributing. Many patients will experiment with dietary avoidance to see if their hives will resolve, but with no success. Patients should be asked if they have tried this approach, which can be very useful in both establishing the proper diagnosis and counseling. Reviewing these ideas and concerns with the patient can be therapeutic on its own.

There are a distinct group of urticarial syndromes where hives are caused by physical forces; thus, any patient with hives should be asked whether they have physical triggers. The classic example is dermographism, or dermographism, which occurs when scratching the skin or application of pressure causes the development of hives in the shape of the scratch, typically rapidly, within minutes (Fig. 13.4). Other common physical urticaria syndromes include cold urticaria, which is caused by exposure to cold air or cold water (Fig. 13.5). Heat-induced urticaria, or cholinergic urticaria, is caused by sweating, increased body temperature, or

Fig. 13.4 Dermographism



Fig. 13.5 Cold urticaria after ice cube test with some dermographism



physical activity. Delayed pressure urticaria occurs on areas of the skin subject to continuous pressure, such as the strap of a book bag, shirts, socks, pants, or undergarments. Other rare physical urticaria syndromes include solar urticaria which occurs when patients are exposed to certain ultraviolet wavelengths associated with sun exposure. Aquagenic urticaria is extremely rare and occurs with exposure to water, regardless of temperature. Some patients with acute or chronic urticaria have physical triggers associated with, but not the sole cause of their symptoms. When this occurs, the physically stimulated symptoms resolve when the underlying hives resolve.

When evaluating for other possible triggers of urticaria, it is recommended to always ask about use of NSAIDs. NSAIDs are a common cause of a pseudoallergic reaction leading to acute urticaria, with or without angioedema, in the setting of no previous history of urticaria. This is considered a pseudoallergic dose-dependent NSAID reaction called NSAID-induced urticaria and angioedema [16]. It is usually a class effect which can occur with all COX-1 inhibitors [16]. However, about 35% of patients with preexisting urticaria or angioedema may experience NSAID-exacerbated urticaria and angioedema in which the NSAIDs make the underlying urticarial disease worse [16]. Those patients should be counseled to avoid all NSAIDs and may safely use acetaminophen or available COX-2 inhibitors [17]. If NSAIDs are thought to be exacerbating factors, then evaluation with an NSAID challenge in a controlled setting under the supervision of a physician trained in NSAID challenges may be necessary to prove that it is safe to take NSAIDs again.

Further Evaluation/Testing

In general, patients with a typical history of acute or chronic urticaria do not require laboratory testing or skin prick allergy testing for environmental or food allergens. In a large case review of patients with chronic urticaria/angioedema, Lang and colleagues found that laboratory testing for evaluation of infection, autoimmune conditions, or allergies made little difference in further management or treatment [18]. It is now recommended to avoid routine laboratory testing unless there are concerning aspects of the history suggesting that the hives are due to a secondary condition (vasculitis, autoimmune diseases, infections, renal disease, gastrointestinal/hepatic disease) [17].

Treatment (Table 13.3)

The first treatment of acute or chronic urticaria is reassurance regarding the diagnosis, lack of associated allergies, and that the patient is not at increased risk for anaphylaxis. Many patients are relieved by the fact that this is not a food or contact allergy. Most patients want to know how long the hives will be present. While most

Table 13.3 Stepwise treatment algorithm for chronic urticaria

Step 1: Second-generation antihistamines
Step 2: Increase dose of second-generation antihistamines up to four doses per day
Step 3: Add H2 blockers or antileukotrienes
Step 4: Add first-generation antihistamine at night
Step 5: Omalizumab or immunosuppression

patients will experience spontaneous resolution at some point in the future, there is no way to predict how long that will be for an individual patient.

The treatment of acute or chronic urticaria should be aimed at providing symptomatic relief with the use of medications that have less side effects than the disease itself. While urticaria and angioedema can be miserable when they are associated with severe itching, there are no known short- or long-term sequelae. Patients should be advised that the goal of the therapy is to reduce the frequency and severity of the symptoms so that they can reduce interference with school, work, and social encounters but that 100% elimination of all hives may not be achieved. For those with physical triggers, avoidance of the provoking stimulus is the first treatment. Then, for most patients, the best medication to start with would be long-acting non-sedating antihistamines alone [17]. If a patient has incomplete relief, then dosing can be increased from once per day to twice per day. If that does not provide sufficient relief, then double doses twice daily or four times the typical daily doses of long-acting non-sedating antihistamines have been used effectively with little additional side effects, though the evidence for efficacy is weak [19].

Other medications can be added to the long-acting non-sedating antihistamines if they are not effective at high dose. Providers should always weigh the benefit of treatment with the potential for side effects from other medications. Because most additional medications used for hives have the potential for side effects, initiating therapy typically involves using a step-up approach as opposed to starting high and then tapering down. The first additional medication after high-dose second-generation antihistamines is usually a H2 blocker [18]. If that does not provide relief, an antileukotriene such as montelukast once daily can be added [18]. If those are not successful, then first-generation antihistamines such as hydroxyzine or doxepin can be used at bedtime, with warnings about the sedating effects and extreme caution in operating motor vehicles and drinking alcohol [17]. Doxepin is a potent antihistamine and has both H1 and H2 properties [20]. If hives remain poorly controlled, then increasing doses of first-generation antihistamines can be used until the side effects are not able to be tolerated. If none of these options are effective or tolerated, the anti-IgE antibody omalizumab has been FDA approved for severe refractory chronic urticaria [17]. Though it comes with a high cost (~\$1000 per injection which is administered once monthly), it is highly effective with minimal side effects [21]. Other systemic immunosuppressant drugs such as cyclosporine can also be considered, weighing the benefits of decreased symptoms with the potential side effects that can occur with immunosuppressant therapy [17].

Both acute and chronic hives are able to be temporarily relieved by systemic corticosteroid therapy. However, there is little evidence that oral steroids are necessary. Their short- and long-term risks are such that systemic steroids should be the last choice of therapy for patients with acute or chronic hives. One recent study in patients with acute hives showed that oral steroids in addition to long-acting antihistamines were no better at relieving symptoms than long-acting antihistamines alone [22]. In addition, the natural course of hives often lasts longer than the treatment course of oral steroids, which can cause a rebound effect once the medication is discontinued and, ultimately, additional treatment with steroids when symptoms return.

Adverse Drug Reactions

Adverse reactions to drugs encompass many different types. As with other topics in this chapter, dealing with drug allergies specific to adolescents is fairly similar to children or adults. One thing to consider in adolescents is clarification of proper management of any drug allergies before they leave home. Often the reaction occurred when they were infants or children. This makes it difficult for the teenage patient to recall anything about their reaction or appreciate the need for ongoing avoidance, if necessary. Once again, details surrounding the clinical history are the most important “test.” As such, clear documentation of the specific story of each reaction as soon as they occur in a location such as the electronic medical record, or in a place the patient can readily access, will make it easier for young adults to have an accurate record of drug reactions.

If there is a history of suspected penicillin allergy, patients should be evaluated by an allergist who can perform penicillin allergy skin testing and oral challenge. This can provide accurate clarification regarding need for potential avoidance or will likely remove the allergy from their reported list and allow them to use the most effective treatment option, should antibiotics be necessary in the future. Most people are told that once you are allergic to a drug, they need to avoid the drug forever, but that is not the case. As with all of medicine, the need to take a drug that has caused an adverse reaction needs to be weighed between the potential benefit of the drug, which is based on the specific clinical scenario, and the risk for any adverse event from occurring. The potential adverse effects could be similar to the past, or the drug can cause new types of reactions. This section will focus on the risk involved among patients with prior adverse reactions. The benefits will always be based on the clinical scenario at the time of need for the drug.

Categorizing Adverse Drug Reactions

Most drug reactions can be categorized into a few broad categories. Being able to correctly categorize the adverse reaction is the most important step to help determine whether it is safe to try the drug again or not. The categories are:

- *Predictable reactions*: These are most often dose dependent and due to the mechanism of action of the drugs [23].
- *Unpredictable reactions*: These are not typically dose dependent and include drug allergy (IgE penicillin anaphylaxis), pseudoallergic reactions (NSAID reactions such as aspirin-exacerbated respiratory disease (AERD)), drug intolerance, and idiosyncratic reactions [23].
- *Drug allergy* refers to immune-mediated responses to the drug which includes anaphylaxis and other types of hypersensitivity reactions. *Drug allergies* have been categorized by the updated Gell and Coombs classification system. However, this system does not fully embody the complicated nature of drug allergy and will not be covered here [23].
- *Drug intolerance* is an adverse effect which occurs at low or normal doses, are not due to lack of metabolism or excretion, and are not immunologically mediated [23].
- *Idiosyncratic reactions* are reactions that fall outside of the previous categories and have no defined mechanism [23].

The History Is the Test

This chapter will focus on important details of an effective history and available diagnostic testing based upon the history and the drug. When evaluating a patient with an adverse drug reaction, these details are helpful to categorize the reactions. If a physical exam is able to be done, the skin manifestations are the most important information to help determine the next step [23]. If they are able, all patients should be asked to take pictures at least once per day while the rash is present. These pictures are particularly helpful for the allergist, who is not likely to see the patient during the reaction.

The History and Physical

When discussing the reaction, specific details are important. Though many patients may not know the details due to their age at the time of the reaction, or time since the reaction, a focused and thorough set of questions can help elucidate important details. If a parent/caregiver is unavailable, then providing adolescents with a list of these questions will guide their conversation:

- *Why Did You Take the Medicine?* This helps narrow the drugs that may have been used and can also give information about whether the “reaction” was due to the infection itself. For example, if a patient had symptoms of severe sore throat and exudative pharyngitis for a week and then was treated with amoxicillin, the resulting maculopapular rash may be indicative of a rash due to treating Epstein-Barr virus as this is a known association in 30% of cases of mononucleosis treated with amoxicillin [24].

- *What Drug?* Some drugs are known to cause IgE-mediated reactions, most prominently penicillin antibiotics. Other drugs such as sulfa antibiotics or NSAIDs are less likely causes of IgE-mediated reactions. Sulfa antibiotics are known to cause characteristic immune responses such as fever with a fine maculopapular rash due to cell-mediated reactions. As discussed previously, NSAIDs cause pseudoallergic reactions such as AERD or hives and swelling.
- *What Dose?* This is especially important when symptoms may have been due to side effects or pseudoallergic reactions from NSAIDs, which can be dose dependent.
- *How Long Did You Take the Drug Before a Reaction Occurred?* An anaphylactic reaction which occurs minutes after the second dose will be categorized differently than a reaction such as serum sickness-like reaction (SSLR) from cefaclor which typically starts 1–3 weeks after the course was completed.
- *How Long After the Dose Did the Reaction Begin?* Hives and swelling starting 20 min after an intramuscular injection of penicillin G will most likely be IgE mediated, and a reaction that starts the morning after a dose is less likely to be IgE mediated.
- *What Symptoms Occurred?* Ask the patient “Tell me what happened?” Then fill in the gaps with specific questions similar to what was discussed about urticaria. If a rash occurred, was it raised, irregularly shaped, or flat with red flares? Was the rash blistering? Blisters would be concerning for Stevens-Johnson syndrome or toxic epidermal necrolysis. Was it itchy? Or painful? Did it leave any marks or bruises? Was it associated with fevers, joint pains, or change in urine color such as can be found in rare SSLRs? The pertinent negatives are just as important as the pertinent positives. Gastrointestinal (GI) symptoms such as cramping and diarrhea are a known side effect of many antibiotics. Isolated GI symptoms make any form of allergic/immunologic reaction less likely and indicate more predictable side effects.
- *What Did You Do to Treat the Reaction?* Did you stop or continue the medication? If you continued the drug, did the reaction get worse or stay the same while you remained on it? Did it resolve with no specific treatment? Did antihistamines help or not? Did it require a course of oral steroids?
- *How Long Did It Take for the Symptoms to Resolve?* This is important to differentiate IgE-mediated reactions from delayed reactions. An urticarial rash that started after a course of amoxicillin for a URI and lasted for 8 weeks may simply be chronic idiopathic urticaria that started during the infection.
- *Had You Ever Taken the Drug Before? If So, Did You Have a Reaction?* Tolerance of a drug before a reaction does not rule out an allergic reaction. However, it can provide valuable information to differentiate side effects from immune responses. It also suggests that they have had the potential to be sensitized to the drug.
- *Have You Taken the Drug Since? If So, Did You Have a Reaction?* This question gets to the heart of every drug allergy evaluation. If repeat exposure occurred and nothing happened, then they are at no more risk for a future reaction than anyone in the general population.

Now that you have determined a reaction occurred and the history and physical suggests an immune response or drug allergy, the next question remains, can this patient safely take this drug again? That answer is dependent upon the specific history. For some reactions, the drug should never be used again unless it is the only drug available and the need for the drug is life-threatening. This is typically the case with Stevens-Johnson syndrome or TEN, which can cause life-threatening reactions in up to 35% of cases [25]. Whereas serum sickness to snake antivenom can be a severe reaction, it is not always life-threatening and may be able to be treated [26]. In that case the risk of a reaction is necessary to take if a snake bite occurs again. If the reaction was consistent with a known side effect, repeat exposure may not provoke the same symptoms, or lower doses of the drug can be used. In the rare case where a teenage patient who has had a reaction to NSAIDs, and who needs an aspirin prophylaxis for stroke or cardiovascular events, a challenge can be performed up to the dose used for prophylaxis. They may tolerate that dose but not a higher dose of aspirin at 325–650 mg [27].

If the reaction was to penicillin antibiotics and the history suggests an IgE mechanism, then allergy skin testing is available to evaluate if a reaction will occur again. Negative skin prick and intradermal testing to the major determinant (benzylpenicilloyl polylysine/Pre-Pen) or the minor determinants (penicillin G) have been shown to have a high negative predictive value [28–30]. If the penicillin testing is negative, many patients will undergo a single-dose oral challenge in the office setting before being cleared for further therapeutic doses of penicillin. Therefore, if the skin testing and single-dose challenge are both negative, the risk for reactions to any formulation of penicillin is low and should be considered to be no greater than the general population [30].

Most of the time, the decision on what to do next will be based on the clinical scenario and the past reactions. The best time to do an evaluation is before the drug is necessary. Trained allergists able to do inpatient evaluation are not available in many hospitals. Severe infections often require early administration of antibiotics, and the inability to evaluate for the allergy leads physicians to use alternatives that may be more costly, have more side effects, and be less efficacious [31]. Other than skin testing to penicillin antibiotics and some chemotherapy agents, there are no validated skin or blood tests available to evaluate the risk for a future reaction to any other drugs. In that case, the best available test is an oral drug ingestion challenge, typically performed in a supervised setting where treatment can be given if a reaction occurs. In that case drug challenges are often deferred until the drug is necessary, because alternative agents are often available.

If a patient has been evaluated and deemed to be allergic to a drug, the general recommendation is to continue to avoid the drug and use equally efficacious alternatives as clinically indicated. Understanding what drugs do and do not need to be avoided based on the potential for cross-reactivity is important. For example, patients with sulfa antibiotic allergies can tolerate other sulfa-containing drugs as their chemical structure is very different [32]. Most patients with penicillin allergy can tolerate cephalosporins [33]. Seek expert advice when unsure if a drug has to be avoided based upon cross-reactivity.

If there are no equally efficacious alternatives or those alternatives cannot be taken, there are ways to give many drugs, if necessary. Induction of drug tolerance is a new term for drug desensitization [23]. This term describes all procedures used to allow patients who are truly sensitive to a drug to safely receive the drug whether IgE mediated or not. Induction of tolerance procedures varies widely in regard to safety and who performs them. Penicillin tolerance induction is usually supervised by allergists in a closely monitored inpatient unit. Hematologists/oncologists perform tolerance induction to chemotherapy in their infusion centers. Infectious disease specialists will often perform the tolerance induction procedure for sulfonamide antibiotics in their outpatient clinic. Even if a patient is allergic to a drug, if they need it, there may be ways they can get the drug safely. It is important to understand that induction of tolerance does not “cure” a patient of having that drug allergy. They will need to maintain consistent exposure on a daily basis in order to prevent a reaction from recurring; lapses in therapy can lead to another reaction.

Immunodeficiency

For teenagers, immunodeficiency encompasses a different differential diagnosis than in a younger child or an adult. It combines rare presentations of unusual congenital immunodeficiency syndromes as well as the complicating factors of illnesses which can lead to secondary causes of immunodeficiency (Table 13.4). However, primary immunodeficiency should be considered only after testing for HIV, a common cause of acquired immunodeficiency in teenagers. In regard to severe congenital immunodeficiencies, most infants/toddlers will die from infection if not diagnosed in a timely fashion or will already have a diagnosis and are being managed well enough to become teenagers.

Signs and symptoms of undiagnosed immunodeficiency cover many areas such as unexplained weight loss, recurrent fevers, frequent infections with common pathogens, less frequent atypical infections, difficult to treat infections, and invasive infections. The Jeffrey Modell Foundation suggests warning signs of immunodeficiency in a teenager or adult that can be used as a screening tool: two or more ear infections

Table 13.4 Age of typical diagnosis for possible immunodeficiency relative to adolescence

<i>Congenital immunodeficiencies which usually present before adolescence</i>
SCID, CGD, X-linked agammaglobulinemia, Omenn syndrome, DNA ligase deficiency, Nijmegen breakage syndrome, Wiskott-Aldrich syndrome, ataxia-telangiectasia
<i>Congenital immunodeficiencies which can be present in teenagers</i>
DiGeorge, hyper IgE, hyper IgM, PI3 kinase disease, primary ciliary dyskinesia, IgA deficiency, chronic mucocutaneous candidiasis, complement deficiency
<i>Secondary causes of immunodeficiencies in teenagers</i>
Malnutrition, anorexia, bulimia, cancer, infection, medications/immunosuppressants, protein-losing enteropathy, protein-losing nephropathy, intestinal lymphangiectasia
<i>Acquired forms of immunodeficiency presenting in teenagers</i>
CVID, AIDS

or sinus infections per year; one pneumonia per year; chronic diarrhea with weight loss; recurrent viral infections such as warts, herpes, molluscum contagiosum, and mucosal, skin, or invasive fungal infections; need for IV antibiotics to clear infections; atypical mycobacterial infections; or a family history of immunodeficiency [34]. These signs are merely screening tests, however, and should not be used to make a diagnosis of an immunodeficiency but can alert patients and providers alike to some potential warning signs.

The diagnosis of an immunodeficiency should be made based upon a very specific and clear history of undue susceptibility to infection, recurrent infections, or family history of known primary immunodeficiency. Relying on laboratory testing alone has pitfalls. In many cases, the laboratory studies used to screen for immunodeficiencies can be affected if the testing is done while a patient is acutely ill or receiving certain medications. Common tests used to establish a diagnosis of immunodeficiency include a CBC with differential, T and B cell enumeration studies, total antibody levels and specific antibody responses to vaccines such as diphtheria and tetanus, and encapsulated bacteria such as *Strep. pneumonia*, *Haemophilus influenzae*, or *Neisseria meningitidis* [35]. Some diagnostic tests, such as complement assays, are technically difficult or require specific specimen handling which can affect their results if performed incorrectly. If a patient presents with typical symptoms and/or the laboratory studies are abnormal, further evaluation by an experienced immunologist can be useful to confirm suspected diagnosis of the growing number of recognized immunodeficiency syndromes (Tables 13.5, 13.6, and 13.7). Correct diagnosis of a rare immunodeficiency is important as it has

Table 13.5 List of humoral immunodeficiencies

Common variable immunodeficiency
X-linked agammaglobulinemia
Autosomal recessive agammaglobulinemia
Specific antibody deficiency
IgA, IgG subclass, IgM (rare)
Transient hypogammaglobulinemia of infancy

Table 13.6 List of common combined immunodeficiencies

SCID
ZAP-70
Omenn syndrome RAG1/RAG2
DNA ligase IV deficiency
Complete DiGeorge
Nijmegen breakage syndrome
AD-HIES: STAT 3
AR-hyper IgE syndrome (HIES): DOCK8
Ataxia-telangiectasia
Hyper-IgM syndrome AID deficiency
Chronic mucocutaneous candidiasis
Wiskott-Aldrich syndrome
PI3 Kinase disease

Table 13.7 List of complement pathway immunodeficiencies

<i>Classical complement pathway deficiencies: C1, C4, C2</i>
Immune complex diseases such as SLE
C2 deficiency also leads to bacterial infections and cardiovascular disease
<i>Alternative pathway: factor B, factor D, properdin</i>
Pneumococcal and <i>Neisseria</i> infections
<i>Mannose-binding lectin pathway</i>
Pyogenic infections to pneumococcal, <i>Neisseria</i> , and <i>Saccharomyces</i> infections
<i>C3 deficiency: common branch for alternative, classical, MBL pathway</i>
Presents at young age with overwhelming infection
<i>Terminal complement pathway: C5–9</i>
Lead to <i>Neisseria</i> infections

significant clinical implications on specific treatment, follow-up, screening, genetic counseling, morbidity, and mortality. Therefore it is recommended to refer the patient to a specialist experienced with patients with all forms of immunodeficiency who can confirm or rule out the diagnosis and ensure appropriate management has begun.

Adolescents with known immunodeficiency who are transitioning to independent living will need to learn a vast array of self-management skills and become responsible for their own care. This transition process should begin far in advance of independent living and will need to entail a complete transfer of care to another specialist (if moving to a new location), identification of the nearest medical center experienced in caring for patients with immunodeficiency, and transfer of any home health needs, including weekly or monthly immunoglobulin infusions. Teens will need to recognize early signs of infection, know when and how to seek proper care, and then be able to follow through with all treatment recommendations, including proper use of antibiotics. In addition, teens with immunodeficiency must be made aware of how their overall health can dramatically impact their susceptibility to infection. This includes maintaining a stringent diet, sleep schedule, and exercise regimen. All of the developmental issues that make self-management of food allergies and asthma challenging can be magnified with teens who have immunodeficiency; their social interactions and dating may suffer if they are frequently ill, and their appearance may change if health is not optimized. While a full discussion of the specific issues pertaining to self-management of immunodeficiency falls outside the scope of this chapter, the themes presented throughout this textbook can be applied in this situation as well, thus preparing adolescents to manage their health as best as possible.

Conclusion

As with more common allergic conditions such as asthma and food allergies, adolescents with urticaria, drug/venom allergies, and immunodeficiency also need to learn important self-management skills prior to living independently. Early and repeated discussion with healthcare providers is paramount to successful navigation of this process.

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Chapter 14

What Now? Practical Steps for Adolescents with Allergies and Asthma to Manage Their Healthcare Independently



Marc L. Rubin and Mervat Nassef

Guide to Preparing for Independence

A number of years ago, a well-known credit card company had as its motto: “Don’t leave home without it.” If ever was there a saying so applicable, it is here! We previously published checklists to help teens who are transitioning to independence prepare for the issues related to their allergic conditions that they will face in their new setting [1]. Here we present a detailed guide for teens with allergies and asthma with general recommendations for managing their healthcare independently (Table 14.1) as well as specific recommendations regarding issues related to allergies, food allergies, and asthma (Tables 14.2 and 14.3).

Insurance Plans and Pharmacies

Health insurance cards are updated annually and not necessarily at the start of a new year. Most often, parents keep possession of their child’s cards so they are not misplaced, and teenagers may not even be aware of their existence. Also, many companies have different plans for each service, requiring multiple cards. It is important that the name on the card is that of the adolescent in order to reduce potential billing

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Table 14.1 The basic needs

• Medical cards: medical/dental/prescription
• Copies of most recent physician visit, laboratory tests, and allergy test results
• Up-to-date immunizations
• List of drug allergies
• Current list of medications, including seasonal prescriptions
• Dates for medication refills and expirations
<i>Before or upon relocation to the new home</i>
• Transfer all active prescriptions to the new pharmacy location
• Obtain new prescriptions for those medications which are part of normal therapy, but expired/out of refills
• Consider distance to hospital or ambulatory facility for emergency needs

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Table 14.2 College housing plan of action for environmental allergies and asthma

• Contact school regarding special accommodation policies, necessary paperwork, and the procedure for prescreening roommates
• Assess level of exposure to: allergens, pollutants (motor vehicle traffic, manufacturing plants)
• Inspect for mold, cockroaches, rodents, pets, tobacco smoke
• Heating and ventilation system: avoid forced-air central system, and <i>provide notification to allow for air conditioning if possible</i>
• Review environmental control measures, including dust control: use of HEPA and/or air conditioning during pollen season
• Hold discussion with potential roommate(s) regarding allergen/irritants to be avoided, and cleaning arrangements
• Uncarpeted environments are easier to maintain for someone with allergies and asthma
• Does the owner have a policy regarding pets? Do any of the neighbors have pets? Did the potential unit previously have pets? (dander can remain for months after pet removal)
• Is smoking allowed in the building? Did the prior renters smoke?
• Will the owner allow a mold checkup?
• Is the building near a commercial thoroughfare?

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errors and rejections. Since leaving home often incorporates new physicians and a new pharmacy, it is imperative that the new “adult” becomes familiar with accessing the insurance provider’s website to find medical providers within their plan to provide services in their new setting. The back of the insurance card also generally provides contact phone numbers and links to guide the user.

To ease the transition into a new physician practice, having a copy of current medical records (including last exam visit, lab work, allergy testing results, medica-

Table 14.3 Issues to consider pertaining to food allergies

• Provide new school, resident assistant, and roommates list of current allergens to avoid, including list of alternate names used on labeling
• Review how cross-contamination can occur during food preparation
• Role-play to help practice conversations with roommates, new relationships
• Consider touring food preparation facility, and meeting with the chef to discuss safe food preparation
• Review when and how to use self-injectable epinephrine
• Discuss high-risk locations and activities that may lead to accidental allergen exposure
• Consider obtaining medical identification jewelry
• Review and update anaphylaxis action plan

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tion list and drug allergies, updated vaccines) to give to the doctor provides the essential information needed to begin providing care. Without that background, there may be a delay in addressing an urgent issue or providing the best treatment approach. Knowing what has succeeded or failed with past treatment is important for achieving a more rapid and successful outcome. As well as looking for a new primary doctor, a person with allergic rhinitis, asthma, or food allergies may benefit from locating a board-certified allergist/immunologist in their new location. After relocating to a new home, new “triggers” may be experienced (pollens, mold, animal dander, etc.), and the allergy specialist can help identify and address this problem. Unless the new residence is near a large metropolitan area, or at a college campus, there can be difficulty locating a specialist. By contacting the insurer through the phone number on the medical card, telemedicine communication with specialists may be available if there are none located nearby.

In addition to finding a local healthcare provider, it is essential to identify easy access to a nearby pharmacy in order to keep medications readily available. With many national chains, it may simply be a matter of walking into the nearest branch, updating the contact information, and then all patient records are automatically transferred. If the move is to an area more rural, and there is not a local branch of the previously used pharmacy chain, it is important to check which local pharmacy is contracted with the specific insurance carrier, and the prescription card can be used for the contact information. In addition to finding which pharmacies are contracted, there may be mail-order requirements for maintenance medications, including intranasal and inhaled corticosteroids. This feature may have a dramatic cost difference in the price of the medications.

As noted in Table 14.1, the pharmacy will need to see the prescription card, a list of active prescriptions (originating pharmacy and phone number, prescription number, name of medication, physicians name), over-the-counter (OTC) medications (nasal sprays, antihistamines, cough suppressants, vitamins, and homeopathic remedies), medication and food allergies, and conditions being treated, e.g., allergic

rhinitis, asthma, and diabetes. For those prescriptions that are out of refills or expired, the pharmacist should be informed and can then contact the prescribing clinician to obtain new prescriptions.

Considerations for New Housing

The transition to independent living has many facets to address. With the basics now attended to, the next critical factor to prepare for is locating a new residence to live in that provides an allergen-safe, easy-to-maintain, clean environment. This encompasses two probable paths, with some issues in common and other issues unique to each setting: (1) housing on a college/university campus and (2) residence in an apartment or home. In both cases, it is important to set the rules upfront with prospective roommates regarding the environmental control measures that need to be in place to reduce exposure to allergens and irritants. Also, a contingency plan is helpful in case unexpected changes take place in the housing environment outside of one's control.

College/University Campus

The most common initial transition for most students is to live in an on campus dormitory, or student housing. While this may appear to be a straightforward event, many of the buildings are older and, as such, need close examination to minimize the risk of worsening allergy and/or asthma symptoms. Table 14.2 provides a plan of action to help maintain good health and quality of life. The transition to college life is stressful in and of itself, lest it be complicated by allergy issues. Flare-ups of allergy and asthma symptoms can impair sleep, concentration, and ability to focus on all of the challenges that lie ahead. For those moving into apartment living, most of these checkpoints still apply, and need to be fully addressed, since renting in a privately owned building would not be overseen by the school and may have a greater risk of allergen presence. Lastly, review the plan of action for environmental control. Verify air filtration, air conditioning, and housekeeping schedules (if available) to ensure from the very start that those factors most likely to affect allergic rhinitis and asthma will be kept to a minimum for achieving maximum control.

In addition to the housing accommodations, horticultural changes, differences in air quality/pollution, social activities, intramural sports, and campus events may increase exposure to unexpected triggers, requiring a newfound awareness of surroundings and being prepared to address them. Colleges and universities generally have medical services readily available to their students, when they are needed. For those participating in collegiate athletics, it is very important to inform coaches and team physicians of asthma and food allergies (and any other medical condition) at

the outset of the season. This will enable them to help maintain full participation and prepare for emergencies, should they arise.

Apartment/Rental Home

With the exception of contacting school personnel to assist in obtaining housing accommodations, all of Table 14.2 applies here, but with additional points to cover presented in Table 14.3.

As important as the housing review is when leaving for college, should allergy issues arise due to the accommodations, there is generally recourse with the housing administration to rectify the problems, including changing units. When committing to a rental/lease agreement, it can be difficult to achieve resolution, with potential financial loss and emotional stress. It is therefore important to investigate the future residence prior to moving in, as well as the steps involved with changing location (should the need arise) to ensure the greatest chance of success and good health.

Preparing for Food Allergies on a College Campus

The transition to college can be daunting for any adolescent who has food allergies (see Table 14.3). Thankfully, this transition is becoming easier as many colleges and universities are starting to increase their awareness and understanding of food allergen avoidance in their dining halls. It is strongly encouraged to start this conversation with prospective colleges well in advance of starting the academic year. Prospective students should reach out to the disability services office to inquire about their formal/informal food allergy management strategies on campus. Students may be required to file information about their food allergies and discuss specific accommodations that might be necessary. This will likely require documentation from their medical provider and teens should allow plenty of advance time for this process to occur. If the prospective school is not familiar with food allergy management and/or does not have formal practices in place, then teens and their parents may be their source of information. Most schools are more than willing to work with families to find safe accommodations. Clear communication, allowance for questions, and collaboration can go a long way in paving the path toward a smooth transition.

Any adolescent with food allergies who is enrolling in a college or university should speak directly with the dining services department to discuss their needs. A line of clear communication should be established early and it is much easier for dining services personnel to accommodate individual needs once they have a personal relationship and improved understanding. Each school may vary, but introduction and discussion with the registered dietician, head chef, or facility manager can serve as an excellent starting point. Students should clearly identify their food

allergens and inquire about food preparation practices and current understanding and knowledge of dining personnel in regard to safe food preparation and identify a list of “safe” foods that they can enjoy, as well as foods that should be avoided due to potential cross contact with their allergen.

Once on campus, and in the midst of busy class and/or work schedules, it can be challenging to maintain safe dining practices. Avoiding peak dining times may help prevent accidental ingestion of food allergens and it may be easier to identify safe dining options when lines are less busy. Teenagers should always have their epinephrine autoinjector immediately available and should never knowingly ingest a food that contains their allergen. It can be challenging, but teens should be encouraged to always inform the food handlers of their allergies and ask questions when ingredients are not clearly indicated. If it is not known to be safe, then it should be avoided.

There are also online resources available through each school’s website or from the Food Allergy Research & Education (FARE) website: www.college.foodallergy.org.

Additional Areas of Concern

Before leaving for the new home and prior to or during the final visit to the local doctor, in addition to obtaining a copy of medical records, labs, and new prescriptions to leave with, an updated medication action plan should be filled out and provided to all adolescents with asthma and/or food allergies. As stated earlier, new locations can easily bring new challenges, and having easily accessible and clear guidance can be useful. Also, review of proper device technique for nasal sprays, inhalers, and epinephrine autoinjectors should be conducted with feedback from the healthcare provider.

Once the new location is chosen, a final issue to address is air quality. Being aware of the changing air quality of where one lives allows planning for outdoor activity levels, as well as possible modifications to treatment. The three air quality points that one must pay attention to are:

1. Ozone levels
2. Particulate matter (from engine exhaust as well as industrial processes)
3. Pollen levels (including the particular plant type)

The two air quality references in Table 14.4 address these factors. They are easy to use and can offer results for any specific area according to zip code. The Airnow.gov link provides overall guidance of air quality, as well as specific to the zip code, and covers ozone and particulate matter. The Pollen.com site indicates both the pollen levels as well as the specific pollens in that area, which can aid in determining triggers not previously encountered. It can also send daily emails at the start of the day to guide avoidance strategies.

Table 14.4 Resources for self-directed information

• Find an allergist
– http://aaaai.org/find/
– http://acaai.org/locate-an-allergist
• Allergic rhinitis
– http://www.aaaai.org/conditions-and-treatments
– http://acaai.org/allergies/types/hay-fever-rhinitis
– http://www.allergyasthmanetwork.org/education/allergies/
• Air quality
– https://airnow.gov/index.cfm?action=aqibasics.aqi
– http://www.pollen.com
• Asthma
– http://www.aaaai.org/conditions-and-treatments/asthma
– http://acaai.org/asthma
• Food allergy
– http://www.aaaai.org/conditions-and-treatments/allergies/food-allergies
– http://acaai.org/allergies/types/food-allergy
– https://www.foodallergy.org/life-food-allergies/managing-lifes-milestones/going-college
– https://community.kidswithfoodallergies.org/forum/school_and_food_allergies
– http://www.allergyasthmanetwork.org/asthma-mom-video-blog-empowering-teens-self-manage/

Lastly, a successful life is often a reflection of continuous personal growth. Knowledge is constantly growing in the understanding of illnesses, and therapies continuously evolve to improve our quality of life. Table 14.4 provides vetted resources for self-management of allergic rhinitis, asthma, and food allergies from the American College of Allergy, Asthma, & Immunology (ACAAI; www.acaai.org). There are also several patient advocacy organizations that provide helpful information, including the Allergy and Asthma Network (www.allergyasthmanetwork.org), the Asthma and Allergy Foundation of America (AAFA; www.aafa.org), and Food Allergy Research & Education (FARE; www.foodallergy.org). These sites are consistently updated to aid in adjusting to seasonal changes and to prepare for what lies ahead.

Conclusions

There are several basic yet fundamental areas that must be addressed in order for adolescents with allergic conditions to safely navigate their transition to independence. This includes understanding health insurance, identifying a new physician and pharmacy, making necessary accommodations in housing and dining halls, and taking new responsibility for one's health. As repeated throughout this textbook,

preparation should begin early, starting years in advance. With planning and practice, adolescents will develop the skills they need to successfully manage their health in the midst of a busy (and fun) transition time in their lives.

Reference

1. Stukus D, Nassef M, Rubin M. Leaving home: helping teens with allergic conditions become independent. *Ann Allergy Asthma Immunol.* 2016;116:388–91.

Chapter 15

A Practical Approach for Clinicians to Prepare Adolescents for Independent Living



Brian Schroer

Relationship-Centered Communication Skills

This chapter will highlight relationship-centered communication to give the clinician some specific communication skills that can be utilized to help teens manage various allergic issues. These skills have been taught at the Cleveland Clinic using the R.E.D.E.SM Model and can make it easier to help a teenage patients navigate often complex medical interviews [1]. The R.E.D.E. model emphasizes the relationship as secret to helping patients. It is neither doctor-centered nor patient-centered. This model breaks a typical medical interview down into three parts:

- Establishing the relationship, which allows the patient to connect with and trust the provider before the history begins
- Developing the relationship, which allows the provider to understand the history and the patient's perspective about what is going on and how the disease is affecting her/him
- Exploring the patient perspective, which allows for insight into the patient's goals for therapy and collaborative decisionmaking

The individual skills that the remainder of this chapter will discuss include establishing the relationship with the patient by conveying value and respect with the welcome and setting the agenda, developing the relationship by eliciting the patient narrative and exploring the patient perspective using V.I.E.W., and engaging the patient to collaboratively develop a treatment plan using A.R.I.A. Throughout the interview, demonstrating empathy helps to build the therapeutic relationship.

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Establishing the Relationship

From the moment you meet a patient, it is important to develop a relationship that will allow the patient to feel comfortable working with you to provide help. To do this quickly, you can convey value and respect with the welcome by being prepared, formally introducing yourself to the patient and any others in the room, and making a brief social comment. Before exploring the history, it is important to collaboratively set the agenda. Having an agenda is an important way to start any meeting. The agenda should be discussed and agreed upon before moving into the medical history. This can help organize the visit by allowing the patient to provide a list of concerns he/she wants to cover and by reviewing what the clinician needs to cover. This step focuses the interview on what will be discussed for the rest of the visit. Doing this can provide the patient a road map for the visit and can prevent “door-knob” questions. It can also allow the patient to reveal concerns that may not be easy to talk about or that he/she forgot to mention first.

With teenagers, the most important issue may not be the first one mentioned, especially if it is a sensitive topic. Set the agenda by asking the patient to list all of their concerns or topics he/she wishes to cover during the visit. Encourage the patient to continue and get a complete list by asking: “What else?” Once you have a complete list of their concerns, you can provide the agenda. If the patient’s list is long, then ask which concerns are most important to cover during the visit. Once the patient and provider agenda is agreed upon, summarize it before tackling each agenda item: for example, “I hear that you want to discuss a recent reaction to a food allergen, your mother wants you to ask about your penicillin allergy before you go away to college and I want to make sure your asthma and allergic nose symptoms are well controlled. How does that sound?”

Develop the Relationship: Elicit the Narrative and Explore the Patient Perspective Using V.I.E.W.

This is the section where you elicit the patient narrative by allowing the patient to tell her/his story [1]. This is where you obtain details of the history which is vital to making the diagnosis and can help you gather information about goals or barriers to treatment. Start with open-ended questions allowing the patient to tell you their story, and then fill in the gaps using close-ended questions needed to make the diagnosis. While doing this, you should explore the patient’s perspective using the tool V.I.E.W. [1].

V.I.E.W. stands for:

- *Vital* activities: How is your problem affecting you day to day?
- *Ideas*: What do you think is wrong? What do you think caused this? How do you think this will get better? In allergy clinic, asking patients what *they* think is wrong and what *they* can do about it often leads patients to give their diagnosis and treatment plan on their own!

- *Expectations*: The patient will give you an idea of what he/she thinks is possible if the provider asks, “What are you hoping we can do today?”
- *Worries*: The provider can address those worries by asking patient, “What worries you about this?”

This information from V.I.E.W. helps the provider understand what kind of knowledge, attitudes, behaviors, questions, and barriers a teenager has, which can be used to engage the patient in shared decisionmaking at the end of the interview.

Engage the Patient in Collaborative Treatment Planning

Using the information from the interview and then engaging in shared decision-making is the end result of establishing and developing the relationship. Establishing a relationship early and being curious about the teen’s perspective over the course of the visit in this way can make the adolescent patient feel comfortable discussing and participating in developing a mutually agreed upon plan. This makes him/her more successful at achieving the goals of treatment. Start by providing the diagnosis, discussing the goals of treatment, and then providing the benefits, risks, and alternatives available to achieve those goals. Tailor this discussion using the patient narrative to highlight how this treatment may address daily activities, ideas of what is going on, expectations for treatment, and/or worries about what could happen. Ask the patient his/her preferences for the treatment, and use those to develop a mutually agreed upon plan to which the patient is more likely to be adherent.

Create a dialogue instead of a monologue by using A.R.I.A. A.R.I.A stands for:

- *Assess*: What do you know about this disease? What do you want to know? Have you heard about these treatments?
- *Reflect*: State back the patient’s meaning or emotion, or provide an empathetic statement; for example: “It sounds like you do not know much about hives. That is common, most patients do not know about chronic hives.” Or reflect back what they said; for example: “I hear you do not know much about hives. That is common. Let me tell you...”
- *Inform*: Provide information in understandable language in the context of the patient’s perspective and preferences.
- *Assess*: This is the teach-back portion to ensure the patient understood the information you gave him/her. You can ask the patient: “Just so I make sure I did an effective job of explaining the problem, can you review what you heard?” Or ask: “When you go home to your parents today, what are you going to tell them?” Then confirm commitment to the plan before closing the interview and arranging follow-up.

Throughout the interview, demonstrating empathy can help to help build the relationship by showing patients that we care. These statements of empathy can be used at times where the patient demonstrates emotion or discusses difficult topics. Nonverbal demonstration of empathy is useful but not sufficient. Examples include

embracing the pause, using a leaning forward, open posture, showing facial expressions of care, concern or curiosity, head tilt or nodding, moving closer to the patient, appropriate touch, gentle or slow pace of speech. The S.A.V.E. mnemonic gives ways to express empathy and to show the patient not only that you see or hear him/her but understand and appreciate his/her experience. S.A.V.E. stands for:

- *Support*: A statement of partnership, such as “I’m here for you” or “Let’s work together to...”
- *Acknowledge*: A statement recognizing how the patient feels, such as “This has been hard for you”; “I’m sorry for the wait, I value your time”; or “I wish there were better alternatives.”
- *Validate*: A statement that normalizes the patient’s feelings, such as “Most people would feel the way you do” or “Any one in your position would feel upset.”
- *Emotion naming*: A statement that clarifies the patient’s emotion, such as “You seem sad.”

Do what feels comfortable and genuine to you based on what is happening in the moment.

To conclude this chapter, examples of using these skills will be discussed in the context of two individual topics discussed in Chap. 13: venom hypersensitivity and chronic urticaria/angioedema.

Venom Hypersensitivity

Establishing the Relationship

Most patients come in to the doctor for evaluation of a reaction to stings because they are worried that they will have a worse reaction the next time they are stung and they want to know what to do in case they do get stung. When setting the agenda for this visit, you should ask the patient what she/he wants to discuss. Then review this list. If not already stated by the patient, you can complete the agenda by making sure to tell the patient you will need to cover what happened before and after the sting, discuss what kind of reaction she/he had and what needs to be done to prevent future stings, and, finally, discuss if further evaluation by an allergist is necessary.

Develop the Relationship: Elicit the Narrative and Explore the Patient Perspective Using V.I.E.W.

Allow the patient to tell her/his story without interruption. Use an open-ended question such as: “Tell me what happened.” Demonstrate empathy if needed by stating: “That reaction sounds scary (emotion name). Most patients would have reacted the way you did (validate).” Fill in the details of the history using the previously

reviewed questions. Once you have that information, ask the V.I.E.W questions. What vital activities may lead to another sting? Ask what ideas the patient has about her/his risk for future stings and how to prevent future stings. Review expectations for this and subsequent visits. Finally, ask what worries the patient has about future reactions. This should be driven by the patient to get information that can help to engage her/him when developing the treatment plan.

Engage the Patient in Collaborative Treatment Planning

First provide a diagnosis specifically stating if this was a reaction that is a large local reaction or anaphylaxis. You can then use A.R.I.A. Assess what the patient knows about this type of reaction and management. For example, if you are telling a patient that she/he had a large local reaction you can ask: “What do you know about large local reactions to stinging insects.” The patient may say: “I’ve heard that these reactions can be fatal.” Reflect by using an empathetic statement validating this common fear by saying: “Many patients are worried about that kind of reaction.” Inform the patient: “Evidence shows that risk among patients with large local reactions to progress to a more severe reaction is no higher than everyone else.” Assess again by asking: “What else did you want to know about this type of sting?” Let the patient guide most of the discussion. If she/he does not ask about specific info, you can suggest things to discuss such as avoidance and whether further evaluation is necessary. Assess the level of understanding of what was discussed using teach back: “To make sure I did a good job of explaining how to avoid a future sting, can you tell me things you will do to prevent being stung?” Reinforce what the patient understood correctly, and reflect and inform further about information which needs to be modified. At the end of the visit, you can ask: “What questions do you still have about what we discussed?” or “What do you still want to know about stinging insect allergies?” By the end of the visit, there should be a clearly understood plan about the risk of future reactions, how to prevent and treat any reactions, and what needs to be done to set up further evaluation and testing.

Chronic Urticaria/Angioedema

Establishing the Relationship

Using empathy to show the patient that you understand her/his concern for the hives allows the patient to realize you will provide support through this problem. Setting a collaborative agenda for a visit with a patient with hives is helpful as it often tells you that the patient is here for hives and swelling with no other atopic complaints. When you ask “What else do you want to cover,” most patients will have no other specific issues to discuss, though they may mention the angioedema she/he has been

experiencing or want to know what is causing this reaction. Setting the agenda can be as simple as stating: “We will discuss the hives and swelling, decide what type of rash it is, and then discuss what we can do about it. How does that sound?”

Develop the Relationship: Elicit the Narrative and Explore the Patient Perspective Using V.I.E.W.

After you get a feel for the story and have obtained specific information about hives such as type of rash, duration of symptoms, and exacerbating and alleviating factors, it is important to ask the V.I.E.W. questions. Vital activities: How have the hives affected you at school, sports, home? Ideas: What do you suspect is the cause, or what do you think is causing the rash? Most patients will be very specific with their ideas including individual food ingredients or detergents. Others will overtly say they have given up their search for a cause because there is no specific correlation with anything. Expectations: Many patients come into the visit asking for allergy testing to figure out what is causing the symptoms. That being said, every patient has different ideas, and it is interesting to hear her/his thoughts. Once the typical history is taken though, most often you will be able to discuss the fact that allergy testing for indoor and outdoor allergens or foods is not useful at identifying the cause of the hives since there is no specific cause. But, without being curious and understanding a patient’s expectations, you will not be able to meet her/his expectations. Nor can you address if these expectations are possible to achieve. Worries: What are your concerns about the hives? What are you worried may happen? It is almost universal in my clinical experience that patients are worried that if the hives and swelling are going on in their skin, then the reaction will involve their throat or be associated with more typical anaphylaxis symptoms. Empathize by validating those concerns by stating: “Many patients worry that the reaction will get worse.” Without asking, you will not be able to alleviate those fears.

Engage the Patient in Collaborative Treatment Planning

Once a diagnosis of acute or chronic urticaria is made, it is important to tell the patient what it is and what it is not. Tell her/him that hives and swelling are its own disease and that it is not caused by foods being eaten or things being applied to the skin. Assess what the patient knows about hives and swelling. If the patient says that she/he is worried it is an allergic reaction, then reflect by normalizing these thoughts by stating that most patients come in worried that the rash is due to allergies. Inform: Then tell the patient that in most cases food or topical allergies are not contributing to the hives and swelling. While it would be nice if avoiding a food or a topical allergen would make the hives resolve, these avoidance measures are not likely to

result in any improvement. **Assess:** Ask what else the patient wants to know before getting into specific therapy. It is important to teach the patient how to step up and step down therapy based on the frequency of the hives. Give the patient options of how to increase the medications at home if the initial therapy is not effective. Empower the teenage patient to take ownership of this ability and to advocate for how he/she wants to increase the medications. It is equally important to discuss stepping down the therapy if the hives have been gone for a significant period of time; in this way, the patient does not have to stay on unnecessary medications once the hives and swelling have resolved. Make sure to reassess the adolescent patient's understanding of the plan before ending the visit. One option would be to ask the patient: "Can you tell me what you would tell your parents who are not here today what you are going to start doing tonight to treat the hives? What you will do if the hives are not improved after one week? What you will do if the hives have not been present for one week?" Assessing the patient's understanding before closing the visit will make it more likely she/he can achieve control of their symptoms while feeling in control of the therapy. Finally, offer continued support by stating that you can be contacted at any time with questions, updates, or concerns before closing the interview.

Conclusions

Clinicians should adopt a relationship-centered approach to engagement with their adolescent patients transitioning to independent living. Using a standardized method such as the one outlined in this chapter will help encourage active participation from teens, address the most relevant issues related to their care, and ultimately lead to a greater investment from adolescents in their own well-being.

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Index

A

- ACD, *see* Allergic contact dermatitis
- Acute generalized urticaria, 142
- AD, *see* Atopic dermatitis
- ADHD, *see* Attention deficit hyperactivity disorder
- Adherence, 183
- Adolescent brain development and implications
- adolescent autonomy and illness management, 25–27
 - allergies
 - and psychopathology, 20, 21
 - and sleep, 22
 - QOL, 24, 25
 - cognition and executive functioning, changes in, 16, 17
 - emotions and psychopathology, 19
 - individuals age into early adulthood, 18
 - puberty induces hormonal and affective changes, 18, 19
 - social functioning
 - parents, relationship with, 22, 23
 - peer influence/risk-taking, 23, 24
 - structural changes, 17
 - variability in maturation, 18
- Adverse drug reactions, 214
- history and physical, 215–217
 - life-threatening reactions, 217
 - penicillin antibiotics, 217
 - physical exam, 215
- Aeroallergens, 11, 56, 58, 59, 69, 122, 177, 194
- Airnow.gov, 228
- Albuterol, 99
- Allergen immunotherapy, 177, 205
- Allergen-specific IgE (sIgE) testing, 139–141, 149
- Allergic conjunctivitis, 57, 58
- Allergic contact dermatitis (ACD), 183
- Allergic rhinitis (AR), 4, 225, 226, 229
- allergen avoidance, 59, 60
 - allergist/immunologist, 92, 93
 - antihistamines, 90
 - cat allergens, 61
 - classification, 56
 - cockroach allergens, 61
 - cognitive issues, 84, 85
 - decongestants, 91
 - definition, 55
 - determination of, 2
 - disadvantages, 72, 73
 - dog allergens, 60, 61
 - dust mite allergens, 61
 - exam performance, 55
 - fungi, 60
 - immunotherapy, 69
 - intranasal antihistamines, 67
 - intranasal corticosteroids, 63–67
 - intranasal medication technique, 67, 73
 - ISAAC Phase One, 3, 4
 - ISAAC Phase Two, 4
 - ISAAC Phase Three, 4
 - medication adherence, 91
 - nasal saline irrigation, 62, 63
 - ophthalmologic medication, 68
 - oral antihistamines, 63, 64
 - physical examination, 58
 - pollen season, 58
 - prevalence, 3, 55
 - psychosocial issues, 85
 - quality of life, 56, 83, 91

- Allergic rhinitis (AR) (*Cont.*)
 seasonal allergy, 82
 self-care, 82
 sensitization, 56
 severity, 57, 83
 skin prick testing, 58, 59
 sleep disturbance, 86, 87
 symptoms, 58
 traffic safety, 87, 88
 types, 55, 56
- Allergic rhinitis and its impact on
 asthma (ARIA), 61, 86, 87
- Allergic rhinoconjunctivitis, 2, 10
- Allergic sensitization, 2, 6, 9–11
- Allergy epidemic
 AD, 5
 allergic rhinitis, 3, 4
 asthma, 4, 5
 atopic disease history and prevalence
 studies, 2, 3
 barrier regulation hypothesis, 10
 environment vs. genetics, 8, 9
 food allergies, 5–8
 hygiene hypothesis, 9
 microbiome dysbiosis, 9
 microbiome hypothesis, 10, 11
 skin barrier disruption, 9
 viral hypothesis, 9, 11
- Allergy skin testing, 217
- American Academy of Dermatology
 (AAD), 171, 188
- American Academy of Family Physicians
 (AAFP), 39
- American Academy of Pediatrics
 (AAP), 39, 40
- American College of Physicians (ACP), 39
- Anaphylaxis, 138, 205
- Angioedema, 209
- Antihistamines, 90, 180, 196, 213
- Anti-inflammatory controller medications, 111
- Antimicrobials, 9, 174, 180, 191, 196
- Anxiety, 20, 21, 127, 128
- Aquagenic urticaria, 212
- A.R.I.A. (Assess, Reflect, Inform, Assess),
 231, 233, 235
- Asthma, 1, 2, 224, 232
 airflow obstruction, 121
 albuterol, 122
 anticipatory guidance and
 management strategies, 121
 anxiety and depressive disorders, 127, 128
 asthma-specific transition readiness, 132
 behavioral change approaches, 124
 comorbid conditions, 103–104, 126
 controller therapies, 129
 corticosteroids, 129
 daily controller medications, 120
 definition, 96
 diagnosis, 98–100, 103–105, 122
 diagnostic testing, 122
 differential diagnosis, 123
 electronic monitoring devices, 130
 endotypes, 97
 EVH, 103
 flow-volume loop, 124
 guidelines-based medical management,
 129, 130
 health-care expenditures, 120
 ImmunoCAP testing, 122
 inflammatory mediators, 96, 97
 ISAAC Phase One, 5
 lung growth, 121
 management, 120, 124
 medical care, 119
 medical management, 126, 129
 medication adherence, 122, 124, 129, 130,
 132
 morbidity, 119
 mortality, 95, 119
 new home, 228
 NHANES I, 4
 NHANES II, 4
 NHIS, 4
 NHLBI guidelines, 96, 105
 optimal medication delivery, 129
 pathophysiology, 96
 peer acceptance and social interactions,
 128
 personalized therapy, 129
 phase three, 5
 phenotypes, 97
 physical and financial impact, 120
 physical well-being, 120
 prevalence rates, 4, 95, 199
 psychiatric conditions, 126
 psychosocial aspects, 120, 126
 pulmonary function testing, 122
 quality of life assessment, 120
 resource utilization, 120
 risk factors, 96
 school-based programs, 124
 screening, 125
 self-management, 229
 severity and control, 105–108
 skin prick testing, 122
 smartphone apps, 125

- specific recommendations, 223
 - spirometry, 122
 - steroid resistance, 122
 - symptoms and medication tracking, 99–101, 125, 226
 - systemic steroids, 122
 - tobacco smoking, 126, 127
 - transition barriers, 132
 - transitional care, 131, 132
 - treatment, 125
 - goals, 115, 116
 - inhaled corticosteroids, 112, 113
 - LABAs, 114
 - medications, 111, 112
 - montelukast/leukotriene antagonist, 113, 114
 - self management skills, 109–110
 - stepwise approach, 111, 112
 - targeted biologic therapies, 114
 - written treatment plans, 110, 111
 - triggers, 101, 102
 - Asthma Control Test (ACT) scores, 125
 - Asthma inhaler technique, 48
 - Atopic dermatitis (AD)
 - clinical conditions, 170, 171
 - diagnosis, 171–173, 188–190
 - irritant avoidance, 194
 - ISAAC Phase One, 5
 - nonadherence, 199
 - pathophysiology, 171
 - quality of life, 197–198
 - risk factors, 188
 - sleep deprivation, 199
 - treatment, 174
 - ACD, 183
 - adherence, 182–183
 - antihistamines, 180–181, 196
 - antimicrobial therapy, 180
 - antimicrobials, 196
 - biologic therapy, 182, 197
 - food triggers, 183
 - irritant avoidance, 177
 - moisturizers, 176–177, 192–193
 - pharmacological therapy, 195
 - phototherapy, 177, 194
 - sleep disturbance, 183
 - systemic therapy, 181–182, 197
 - TCIs, 179, 195
 - TCSs, 195
 - wet wrap therapy, 177, 193–194
 - young person transitions, 188
 - Atopic march, 10
 - Atopy, 177
 - Attention deficit hyperactivity disorder (ADHD), 19, 21
 - Auriculotemporal (Frey) syndrome, 148
- B**
- Barrier regulation hypothesis, 10
 - Biologic therapy, 182, 197
- C**
- Cat allergens, 60, 61, 68, 69
 - Celiac disease, 148
 - Centers for Disease Control and Prevention (CDC), 4, 87, 203, 206
 - Childhood Asthma Management Program (CAMP), 121
 - Cholinergic urticaria, 211
 - Chronic nasal congestion, 57, 72, 81
 - Chronic urticaria, *see* Urticaria
 - Cockroach allergen, 61
 - Cognitive behavioral therapy, 20, 159
 - College housing plan of action, 224
 - Combined immunodeficiencies, 219
 - Communication with adolescent
 - adolescent patients and their families
 - adolescent mindset, 32
 - common communication
 - missteps, 35, 36
 - confidential communication, 33, 34
 - direct communication, 32, 33
 - mature minors, 34
 - respect, 34, 35
 - transition of care
 - AAP, 39, 40
 - adherence, 36, 37
 - collaborative decision-making, 40
 - definition, 38
 - EAP, 39
 - general plan of, 39, 40
 - in-control agent model of decision-making, 37
 - relational autonomy models, 37, 38, 40
 - SAHM, 40
 - self-management, 37
 - systemic barriers, 39
 - Complement pathway
 - immunodeficiencies, 220
 - Counseling teenagers, 84
 - Cow's milk allergy, 7
 - Creams, 193

D

Decongestants, 91
 Delayed pressure urticaria, 212
 Denial and depression, 45, 46
 Depression, 19–21, 45–46, 125–128
 Dermatitis, 209
 Dermographic urticaria, 211
 Dietary management, 153
 Dog allergens, 60, 71
 Doxepin, 213
 Driving test, 87, 88
 Drug allergies, 215
 Drug desensitization, 218
 Drug intolerance, 215
 Dry skin care, 193
 Dupilumab, 182
 Dust mite allergens, 61, 177
 Dust mite allergy, 85
 Dysbiosis, 10

E

Eczema, 170, 183
 Eczematous rashes, 173
 Emergency action plans, 147
 Emollients, 193
 Environmental allergies, 224
 Eosinophilic gastrointestinal disorders, 148
 Epinephrine, 2, 24–27, 71, 138,
 142–147, 154–161, 163,
 165–167, 205–207, 210
 Eucapnic voluntary hyperpnea (EVH) test, 103
 European Academy of Paediatrics (EAP), 39
 Executive functions, 16–18
 Exercise-induced bronchoconstriction,
 102, 103

F

First-generation antihistamines, 213
 Food Allergen Labeling and Consumer
 Protection Act (FALCPA), 145
 Food allergic teen's self-management, 154
 Food allergies (FA), 1, 2, 5, 138,
 142–144, 225, 227
 acute allergic reactions, 138
 adherence with management
 strategies, 166
 adolescent transitions, 154
 advocacy organizations, 147
 alcohol consumption, 147
 allergen avoidance, 154
 allergic reaction, 154, 161–166

anaphylaxis, 138, 145, 146, 150, 154
 antigen-specific IgE antibodies, 138
 anxiety prevention per developmental
 stage, 167
 awareness, 147
 basophils, 138
 behavioral, biological and psychosocial
 development, 153
 bullying/hazing, 161, 162
 classification, 137
 in college, 147
 comorbid conditions, 138
 counseling, 147
 developmental issues, 154
 diagnosis, 154
 dietary restrictions, 154
 dining hall precautions, 147
 dining out checklist, 161
 drugs and alcohol, 163, 164
 EAI, 147
 economic cost, 137
 egg, 137
 emergency preparedness, 154
 epinephrine, 138, 143, 154
 exploration and experimentation, 157
 finfish, 137
 food allergens, 137
 food antigen, 138
 histamine, 138
 housing options, 147
 IgE-mediated (*see* IgE-mediated food
 allergies)
 immunoglobulin E-mediated, 137
 kissing and other physical displays of
 affection, 164
 LEAP study, 8
 management strategies, 153, 154, 159
 mast cells, 138
 medical/allergy follow-up, 162
 medications, 154
 milk, 137
 misperceptions, 147–149
 mixed reactions, 137
 mortality, 156, 157
 NAMCS/ NHAMCS, 6
 non-IgE-mediated, 137
 OFC, 149
 outgrowing food allergy, 149
 pathologic immunologic response, 137
 patient counseling, 147
 peanut allergy, 6–8, 137, 149
 in pediatric population, 6
 peer beliefs and opinion, 159, 160

- peer education materials, 147
 - periodic assessment, 149
 - policies, 147
 - preschool-aged child, 154
 - prevalence, 7
 - prevention, 154
 - public health concern, 150
 - quality of life, 138
 - risk-taking behaviors, 153, 154, 157–159
 - at school, 146
 - self-management, 154, 156
 - sensitization, 138
 - serum IgE testing, 6
 - shellfish, 137
 - social interactions, 138
 - soy, 137
 - strategies, 154
 - strict allergen avoidance, 150
 - support groups, 147
 - T helper 2 (Th2) cell response, 138
 - transition to adulthood, 163
 - transition to college/workplace, 165, 166
 - treatment
 - antihistamines, 144
 - corticosteroids, 144
 - epinephrine (adrenaline), 142–144
 - lifestyle modifications, 144
 - short-acting bronchodilators, 144
 - strict avoidance of food allergens, 144
 - tree nuts, 6, 137
 - vigilance and emergency preparedness, 162
 - wheat, 137
 - Food allergy reactions, 210
 - Food-induced fatal reactions, 146
 - Food intolerance, 142, 148
 - Food labels, 145
 - Food poisoning, 142
 - Food protein-induced enterocolitis syndrome (FPIES), 148
 - Food safety, 154
 - Food triggers, 183–184
 - Fractional exhaled nitric oxide (FeNO), 105
 - Fungi (mold spores), 60
- G**
- Gastrointestinal (GI) symptoms, 216
 - Genome-wide association studies, 8
 - Global Initiative for Asthma (GINA), 61, 119
 - GotTransition.org, 39
 - Group-based asthma, 124
 - Guidelines-based therapy, asthma, 124
 - Gustatory rhinitis, 148
- H**
- Hay fever, *see* Allergic rhinitis (AR)
 - Health Examination Survey (HES), 4
 - Health insurance cards, 223
 - Health management plans, 147
 - Health-related quality of life (HRQOL), 24, 25
 - Heat-induced urticaria, 211
 - HEPA filter, 57, 61
 - Hives, *see* Urticaria
 - Hornets, 204
 - Humoral immunodeficiencies, 219
 - Hygiene hypothesis, 9
 - Hypoallergenic dog, 60, 71, 72
- I**
- Idiosyncratic reactions, 215
 - IgE-mediated food allergies
 - alcohol consumption, 142
 - allergen-induced mast cell activation, 140
 - clinical history, 139
 - diagnostic practice, 139
 - dietary history, 139
 - family history, 139 (*see* Food allergies (FA))
 - graded oral food challenge, 140
 - laboratory data, 141
 - medical history, 139
 - physical examination, 139, 141
 - prognosis, 142
 - skin prick testing, 140, 149
 - Immune-mediated disorders, 147, 148
 - Immunodeficiency
 - clinical presentations, 218
 - combined, 219
 - complement pathway, 220
 - diagnosis, 218, 219
 - humoral, 219
 - signs and symptoms, 218
 - treatment, 220
 - Immunoglobulin E (IgE) antibodies, 55, 56, 58
 - Immunomodulators, 197
 - Immunosuppressant therapy, 197, 213
 - Immunotherapy, 69–71
 - Imported fire ants (IFA), 204
 - In-control agent model, 37

- Independent healthcare
 - air quality, 228
 - food allergies, 227–228
 - health insurance cards, 223–226
 - new housing environment
 - apartment/rental home, 227
 - college/university campus, 226–227
 - paths, 226
 - triggers, 225, 226, 228
 - new physician and pharmacy,
 - identifying of, 228
 - patient advocacy organizations, 229
 - pharmacy prescriptions, 223, 224
 - Individualized healthcare plans (IHPs), 147
 - Indoor allergens, 11
 - Infectious disease specialists, 218
 - Infraorbital vasoedema, 57–59
 - International Study of Asthma and Allergies in Childhood (ISAAC), 3–5, 55
 - Intranasal antihistamines, 67
 - Intranasal corticosteroids, 63–67, 72, 83, 87, 89, 91
 - Irritant avoidance, 177, 194
 - Itchy rashes, 208, 209
- J**
- Jeffrey Modell Foundation, 218
- K**
- Keratosis pilaris, 189
- L**
- Learning Early About Peanut (LEAP) study, 7, 8
 - Long-acting beta-agonists (LABAs), 114
 - Long-acting non-sedating antihistamines, 213
- M**
- Medication allergy, 213
 - Metabolome, 11
 - Metered-dose inhaler (MDI), 110
 - Methacholine bronchial provocation test, 105
 - Microbiome hypothesis, 10, 11
 - Modified Allergic Rhinitis and its Impact on Asthma (m-ARIA) classification, 83
 - Moisturizers, 193
 - Montelukast, 68
 - Moodiness, 19
 - Motor vehicle accidents, 87, 88
- N**
- Nasal congestion, 85–87, 89, 91
 - Nasal saline irrigation, 62, 63
 - National Ambulatory Medical Care Survey (NAMCS), 6
 - National Health and Nutrition Examination Surveys (NHANES) I and II, 4
 - National Health Interview Survey (NHIS), 4
 - National Heart, Lung, and Blood Institute (NHLBI) asthma guidelines, 96, 105
 - National Heart, Lung, and Blood Institute Expert Panel Report-3 (NHLBI EPR-3), 124
 - National Hospital Discharge Survey (NHDS), 6
 - Native honeybees, 204
 - Nonadherence
 - allergic rhinitis, 44
 - asthma, 44
 - denial and depression, 45, 46
 - disease threat, 46, 47
 - factors, 44, 45
 - family, 48, 49
 - food allergy, 44
 - knowledge and skills, 47, 48
 - peers, 49
 - schedules and routines, 50, 51
 - school policy, 51
 - treatment
 - cost, 50
 - side effects, 50
 - value, 47
 - Nonallergic rhinitis, 2, 55–58, 72
 - Nonimmune-mediated disorders, 147–149
 - Non-sedating second-generation antihistamines, 180
 - Non-steroidal anti-inflammatory drugs (NSAIDs), 212
 - Nurse-led educational sessions, 182
- O**
- Ointments, 193
 - Omalizumab, 213
 - Oral allergy syndrome (OAS), 148
 - Oral antihistamines, 63, 64
 - Oral steroids, 214
- P**
- Paper wasps, 204
 - Paradoxical vocal cord motion, 122

Peak flow meters, 105
 Peanut allergy, 6–8, 184
 Penicillin allergy, 214, 217
 Penicillin tolerance induction, 218
 Personalized care, 132, 133
 Pharmacological therapy, 178, 195
 Phototherapy, 177–179, 194
 Pollen allergy, 83, 87
 Pollen.com, 228
 Pollinosis, *see* Allergic rhinitis (AR)
 Precautionary allergen labeling (PAL), 145
 Predictable reactions, 215
 Primary immunodeficiency, 218
 Pruritus, 180, 196
 Psoriasis, 189

Q

Quality-of-life (QOL), 24, 25, 83, 91

R

R.E.D.E.SM Model, 231
 Relational autonomy model, 37, 38, 40
 Relationship-centered communication skills
 A.R.I.A., 231
 collaborative treatment planning,
 233, 234
 R.E.D.E.SM Model, 231
 V.I.E.W., 231–233
 Respiratory syncytial viral (RSV)
 infections, 11
 Rhinitis, *see* Allergic rhinitis (AR)
 Rhinorrhea, 55, 57, 62, 63, 72
 Risk-taking behavior, 46

S

S.A.V.E. (Support, Acknowledge, Validate,
 Emotion naming), 234
 SAHM, *see* Society for Adolescent Health and
 Medicine
 School-based asthma education, 124
 Scombroid syndrome, 142
 SCORAD scale, 173, 188
 Self-directed information, resources for, 229
 Self-management skills training, asthma, 124
 Severe congenital immunodeficiencies, 218
 Skin prick testing, 57–59, 62, 69, 71, 72
 Skin testing, 83
 Sleep deprivation, 196
 Sleep disturbance, 183, 199
 Sleep pattern, 86–87

Society for Adolescent Health and Medicine
 (SAHM), 39, 40
 Solar urticaria, 212
 Spirometry, 103, 104
 Standard deviation of lateral position (SDLP),
 87, 88, 90
 Steroid phobia, 182
 Stevens-Johnson syndrome, 217
 Stinging insect allergy, *see* Venom
 hypersensitivity
 Subcutaneous allergen immunotherapy
 (SCIT), 69–71
 Sublingual immunotherapy (SLIT)
 tablet, 69–71
 Systemic corticosteroid therapy, 214
 Systemic steroids, 181, 196–197
 Systemic therapy, 181

T

T-cell lymphoma, 189, 190
 TCS, *see* Topical corticosteroids
 Thiopurine methyltransferase
 (TPMT), 181
 Topical calcineurin inhibitors (TCIs),
 179–180, 195
 Topical corticosteroids (TCS), 178–179, 195
 Traffic safety, 87, 88
 Tree nut allergy, 6

U

UK Working Party, 171
 Unpredictable reactions, 215
 Urticaria
 allergic response, 207
 collaborative treatment planning, 236, 237
 clinical criteria, 208
 evaluation/testing, 212
 food allergy reactions, 210
 vs. itchy rashes, 208, 209
 laboratory testing, 212
 NSAIDs, 212
 stepwise treatment algorithm, 213
 syndromes, 211
 treatment, 212–214
 V.I.E.W., 236
 Urticarial vasculitis, 209

V

Venom allergy immunotherapy
 (VIT), 205, 207

Venom hypersensitivity
 collaborative treatment planning, 235
 history, 205–206
 large local reactions, 204
 prevention, 206
 stinging insects, 203–204
 symptoms, 204
 treatment, 206–207
 V.I.E.W., 234, 235
V.I.E.W (Vital, Ideas, Expectations, Worries),
 231–234, 236

Viral gastroenteritis, 142
Viral hypothesis, 9, 11
Vocal cord dysfunction (VCD), 122, 123

W

Wet wrap therapy, 177, 193

Y

Yellow jackets, 204