

SECTION 4, MANAGING ASTHMA LONG TERM—SPECIAL SITUATIONS

Introduction

Patients who have asthma may encounter situations that will require adjustments to their asthma management to keep their asthma under control. Special situations described in this section include: EIB, pregnancy, and surgery.

Exercise-Induced Bronchospasm

The Expert Panel concludes that exercise may be the only precipitant of asthma symptoms for some patients. These patients should be monitored regularly to ensure that they have no symptoms of asthma or reductions in PEF in the absence of exercise, because EIB is often a marker of inadequate asthma management and responds well to regular anti-inflammatory therapy (EPR—2 1997).

EIB—which can limit and disrupt otherwise normal lives if not treated—should be anticipated in all asthma patients. EIB is a bronchospastic event that is caused by a loss of heat, water, or both from the lung during exercise because of hyperventilation of air that is cooler and dryer than that of the respiratory tree. Some, but not all, studies suggest that release of inflammatory mediators is involved in the etiology of EIB (Anderson 2004; Anderson and Brannan 2004; Carlsen and Carlsen 2002; Jarjour and Calhoun 1992; McFadden and Gilbert 1994; Tan and Spector 2002). EIB usually occurs during or minutes after vigorous activity, reaches its peak 5–10 minutes after stopping the activity, and resolves in another 20–30 minutes. Some reports indicate that there is a refractory period of less than 1 hour after EIB that allows for an asthma-symptom-free interval after warmup exercises (Edmunds et al. 1978). There is uncertainty, however, concerning the existence of a late-phase reaction hours after exercise (Chhabra and Ojha 1998).

DIAGNOSIS

The Expert Panel recommends that a history of cough, shortness of breath, chest pain or tightness, wheezing, or endurance problems during exercise suggests EIB. An exercise challenge can be used to establish the diagnosis (EPR—2 1997). Use of history alone has been shown both to underdiagnose and overdiagnose the problem (McKenzie et al. 2002; Tan and Spector 2002). VCD, in particular, can be confused with EIB (Huggins et al. 2004; Sullivan et al. 2001). An exercise challenge, useful for establishing the diagnosis, can be performed in a formal laboratory setting or as a free-run challenge sufficiently strenuous to increase the baseline heart rate to 80 percent of maximum for 4–6 minutes. Alternatively, the patient may simply undertake the task that previously caused the symptoms. A 15-percent decrease in PEF or FEV₁ (with measurements taken before and after exercise at 5-minute intervals for 20–30 minutes) is compatible with EIB.

MANAGEMENT STRATEGIES

The Expert Panel recommends that an important dimension of adequate asthma control is a patient's ability to participate in any activity he or she chooses without experiencing asthma symptoms. EIB should not limit either participation or success in vigorous activities. Recommended treatments include:

- **Long-term control therapy, if appropriate (Evidence A).** There is evidence that appropriate long-term control of asthma with anti-inflammatory medication will reduce airway responsiveness, and this is associated with a reduction in the frequency and severity of EIB (Vathenen et al. 1991; Vidal et al. 2001). Frequent, severe EIB may indicate poorly controlled asthma and thus a need to initiate or increase daily long-term control therapy.
- **Pretreatment before exercise:**
 - **Inhaled beta₂-agonists** will prevent EIB in more than 80 percent of patients (Evidence A).
 - ◆ **SABA** used shortly before exercise (or as close to exercise as possible) may be helpful for 2–3 hours.
 - ◆ **LABAs** can be protective up to 12 hours (Ferrari et al. 2002; Newnham et al. 1993; Richter et al. 2002; Shapiro et al. 2002). When LABAs are administered on a daily basis, however, there is some shortening of the duration of protection, even in patients using ICSs (Simons et al. 1997). Frequent and chronic use of LABAs for EIB should be discouraged. Such use may disguise poorly controlled persistent asthma, which should be managed with daily anti-inflammatory therapy.
 - **LTRAs** can attenuate EIB in up to 50 percent of patients (Evidence B). The onset of action is generally hours after administration. Few comparisons with other protective agents are currently available (Mastalerz et al. 2002; Moraes and Selvadurai 2004; Steinshamn et al. 2002).
 - **Cromolyn or nedocromil** taken shortly before exercise is an alternative treatment to prevent EIB, but it is not as effective as SABAs (Spooner et al. 2003) (Evidence B). The addition of cromolyn to a SABA is helpful in some individuals who have EIB (Spooner et al. 2003). These studies (Spooner et al. 2003) indicate that anticholinergics may also attenuate EIB, but they are less likely to be protective than either mast cell stabilizers or SABAs.
 - **A warmup period before exercise** may reduce the degree of EIB (de Bisschop et al. 1999) (Evidence C).
 - **A mask or scarf over the mouth may attenuate cold-induced EIB (Beuther and Martin 2006) (Evidence C).**

The Expert Panel recommends that teachers and coaches be notified that a child has EIB, that the child should be able to participate in activities, and that the child may need inhaled medication before activity (Evidence D). Individuals involved in

competitive athletics need to be aware that their medication use should be disclosed, and they should adhere to standards set by the sports-governing bodies (Anderson et al. 2003). The U.S. Anti-Doping Agency Drug Reference Line is 1–800–233–0393.

Surgery and Asthma

The Expert Panel recommends consideration that patients who have asthma are at risk for specific complications during and after surgery (EPR—2 1997). These complications include acute bronchoconstriction triggered by intubation, hypoxemia and possible hypercapnia, impaired effectiveness of cough, atelectasis, and respiratory infection (Kingston and Hirshman 1984); latex exposure (Slater 1994; Sussman and Beezhold 1995); and even some anesthetic agents (Nishiyama and Hanaoka 2001). The likelihood of these complications depends on the severity of the patient's airway hyperresponsiveness, airflow obstruction, mucus hypersecretions, latex sensitivity, and history of prior surgeries, because the latter is a risk factor for both latex and anesthetic agent sensitivities.

The Expert Panel recommends the following actions to reduce risk of complications during surgery (EPR—2 1997):

- **Patients who have asthma should have an evaluation before surgery that includes a review of symptoms, medication use (particularly the use of oral systemic corticosteroids for longer than 2 weeks in the past 6 months), and measurement of pulmonary function.**
- **If possible, attempts should be made to improve lung function preoperatively (FEV₁ or peak expiratory flow rate [PEFR]) to either their predicted values or their personal best level. A short course of oral systemic corticosteroids may be necessary to optimize lung function.**
- **For patients who have received oral systemic corticosteroids during the past 6 months and for selected patients on a long-term high dose of an ICS, give 100 mg hydrocortisone every 8 hours intravenously during the surgical period and reduce the dose rapidly within 24 hours after surgery. Stress doses of corticosteroids may be considered for select patients treated with prior high-dose ICS therapy as well, because clinically important adrenal suppression has been reported in such patients, particularly children (Todd et al. 2002a, b).**

Pregnancy and Asthma

The NAEP “Working Group Report on Managing Asthma During Pregnancy: Recommendations for Pharmacologic Treatment—Update 2004” (NAEPP 2005) emphasizes that maintaining adequate control of asthma during pregnancy is important for the health and well-being of both the mother and her baby. Maternal asthma increases the risk of perinatal mortality, preeclampsia, preterm birth, and low-birth-weight infants. More severe asthma is associated with increased risks, while better-controlled asthma is associated with decreased risks. It is safer for pregnant women who have asthma to be treated with asthma medications than to have asthma symptoms and exacerbations. Monitoring and making appropriate adjustments in

therapy may be required to maintain lung function and, hence, blood oxygenation that ensures oxygen supply to the fetus.

The following is a summary of the recommendations made in the 2004 update. See that report for evidence reviews.

- **Monitoring of asthma status during prenatal visits is encouraged.** Because the course of asthma improves for about one-third of women and worsens for about one-third of women during pregnancy, monthly evaluations of asthma history and pulmonary function (spirometry is preferred, but measurement with a peak flow meter is generally sufficient) are recommended. This evaluation will allow the opportunity to step down treatment, if possible, or to increase treatment if necessary.
- **Albuterol is the preferred SABA** because it has an excellent safety profile and the most data related to safety during human pregnancy are available for this medication.
- **ICSs are the preferred treatment for long-term control medication. Budesonide is the preferred ICS because more data are available on using budesonide in pregnant women than are available on other ICSs, and the data are reassuring.** Preference for ICSs is based on strong data on effectiveness in nonpregnant women as well as effectiveness and safety data in pregnant women; the data show no increased risk of adverse perinatal outcomes. Although budesonide is the preferred ICS, it is important to note that no data indicate that the other ICS preparations are unsafe during pregnancy. Cromolyn has an excellent safety profile but has limited effectiveness compared with ICSs. Minimal published data are available on the use of LTRAs during pregnancy; however, animal safety data submitted to the FDA are reassuring. Data are limited describing the effectiveness and/or safety of LABAs during pregnancy, although there is justification for expecting LABAs to have a safety profile similar to that of albuterol, for which there are data related to safety during pregnancy.
- **For the treatment of comorbid conditions, intranasal corticosteroids are recommended for treatment of allergic rhinitis because they have a low risk of systemic effect. LTRAs can also be used, but minimal data are available on their use during pregnancy. The current second-generation antihistamines of choice are loratadine or cetirizine.**

For more information, see the NAEPP “Working Group Report on Managing Asthma During Pregnancy: Recommendations for Pharmacologic Treatment—Update 2004” (NAEPP 2005).

Racial and Ethnic Disparity in Asthma

The Expert Panel recommends heightened awareness of cultural barriers between the clinician and patient that may influence asthma management as well as modification of educational/communication strategies to address these barriers (Evidence D) (See “Component 3: Education for a Partnership in Asthma Care.”).

Aggressive efforts have been made to understand better the growing problem of racial and ethnic disparity in asthma. It has been documented that racial and ethnic minorities

tend to receive lower quality health care than whites even when insurance status, age, income, and severity of conditions are comparable (Institute of Medicine 2002). The paradox is that, despite our increased understanding of asthma and the availability of highly effective drugs for controlling asthma, no substantial improvement in asthma morbidity and mortality has occurred among certain racial and ethnic minority populations. Multiple initiatives have been launched recently to develop strategies to eliminate disparities in asthma care that are based on race and culture (AHRQ 2003; NIH 2004). Assessment of asthma status, health care use, and processes of asthma care among children in managed Medicaid programs demonstrated that Black and Hispanic children had worse asthma than white children, but the minorities used less anti-inflammatory medication (Lieu et al. 2002). This study and other studies suggest that underutilization of preventive therapy, especially ICSs, contributes to disparities in asthma and care for asthma (Haltermann et al. 2000, 2002; Ortega et al. 2002; Warman et al. 2001). These studies suggest that lack of adherence—due to cost, inadequate literacy, or multiple competing priorities for the patient—may contribute to underuse of medication, but other factors are equally important.

Less than optimal use of preventive asthma medications may be due to nonfinancial barriers to optimal asthma care. A study of Medicaid pediatric patients who have asthma showed that black and hispanic children were much less likely than whites to receive followup care in a timely fashion after being seen in the ED for asthma (Shields et al. 2004), demonstrating important differences in the process of care. A prospective cohort study of Medicaid-insured children who had asthma found that practice-site policies predicted higher quality care for these children; policies included presence of ethnically diverse or bilingual clinicians, cross-cultural or diversity training, continuity in care, and use of feedback to clinicians about prescribing of medication (Lieu et al. 2004). Such observations have stimulated great interest in the study of culturally influenced health beliefs and attitudes, demonstrated the importance of cultural competency for health care providers, and shown the need for improved communication between provider and patient or family regarding use of asthma medication.

A large proportion of ethnic and racial minorities live in urban areas where exposure to indoor allergens (e.g., cockroach and mold) can be high; efforts to mitigate these allergens can reduce symptoms successfully and significantly for urban children who have asthma (Morgan et al. 2004).

Multivariate analysis models have been used in an attempt to disentangle the effects of race, ethnicity, income, and other individual-level risk factors that influence the expression of asthma in various populations. The influence of race versus socioeconomic status on asthma morbidity and mortality remains controversial. Some studies suggest that differences in patterns of asthma-related health care are driven largely by ethnicity and only partially by financial barriers (Boudreaux et al. 2003; Grant et al. 2000; Higgins et al. 2005; Miller 2000; Zoratti et al. 1998). On the other hand, some studies suggest that low socioeconomic status, not race, is largely responsible for poor asthma health outcomes and health care-seeking behavior (Apter et al. 1997; Haas et al. 1994).

Accumulating evidence suggests that biological and pathophysiological differences between ethnic groups may contribute to racial and ethnic disparities in the expression of asthma, and these differences may be independent of socioeconomic and educational influences. For example, there appears to be a significant racial difference between total

serum IgE and airway hyperresponsiveness, and a significant positive relationship between total serum IgE and reactivity to methacholine has been demonstrated in White children but not in Black children (Joseph et al. 2000). This difference supports the hypothesis that Black children may be predisposed to more severe asthma or that racial differences may predispose to more severe asthma.

While biological and pathophysiological differences between population groups may contribute to the heterogeneity of asthma and its variable expression, gene by environmental influences are not exclusive variables that affect the expression of this disease. The significance of social and geographical environmental differences and the significance of ethnocultural influences on the expression of asthma warrant additional investigations, especially with regard to their effect on asthma outcomes and asthma disparities.

Hispanic populations are characterized by diverse racial, ethnic, national, and cultural expressions. Among Hispanics, the highest mortality rates from asthma occur among Puerto Ricans, followed by Cuban Americans and Mexican Americans (Homa et al. 2000; Sly 2006). These differences cannot be explained by geographic location; neither can they be explained by other demographic variables (Ledogar et al. 2000). Our evolving understanding of the natural history of asthma may eventually confirm or challenge some current notions about how asthma is expressed in various populations.

References

- Agency for Healthcare Research and Quality (AHRQ). *National Healthcare Disparities Report* (AHRQ 2003). Rockville, MD, Agency for Healthcare Research and Quality (AHRQ), July 2003.
- Anderson SD. Single-dose agents in the prevention of exercise-induced asthma: a descriptive review. *Treat Respir Med* 2004;3(6):365–79.
- Anderson SD, Brannan JD. Long-acting beta₂-adrenoceptor agonists and exercise-induced asthma: lessons to guide us in the future. *Paediatr Drugs* 2004;6(3):161–75.
- Anderson SD, Fitch K, Perry CP, Sue-Chu M, Crapo R, McKenzie D, Magnussen H. Responses to bronchial challenge submitted for approval to use inhaled beta₂-agonists before an event at the 2002 Winter Olympics. *J Allergy Clin Immunol* 2003;111(1):45–50.
- Apter AJ, Reisine ST, Kennedy DG, Cromley EK, Keener J, ZuWallack RL. Demographic predictors of asthma treatment site: outpatient, inpatient, or emergency department. *Ann Allergy Asthma Immunol* 1997;79(4):353–61.
- Beuther DA, Martin RJ. Efficacy of a heat exchanger mask in cold exercise-induced asthma. *Chest* 2006;129(5):1188–93.
- Boudreaux ED, Emond SD, Clark S, Camargo CA Jr. Acute asthma among adults presenting to the emergency department: the role of race/ethnicity and socioeconomic status. *Chest* 2003;124(3):803–12.

- Carlsen KH, Carlsen KC. Exercise-induced asthma. *Paediatr Respir Rev* 2002;3(2):154–60.
- Chhabra SK, Ojha UC. Late asthmatic response in exercise-induced asthma. *Ann Allergy Asthma Immunol* 1998;80(4):323–7.
- de Bisschop C, Guenard H, Desnot P, Vergeret J. Reduction of exercise-induced asthma in children by short, repeated warm ups. *Br J Sports Med* 1999;33(2):100–4.
- Edmunds AT, Tooley M, Godfrey S. The refractory period after exercise-induced asthma: its duration and relation to the severity of exercise. *Am Rev Respir Dis* 1978;117(2):247–54.
- EPR—2. Expert panel report 2: guidelines for the diagnosis and management of asthma (EPR—2 1997). NIH Publication No. 97-4051. Bethesda, MD: U.S. Department of Health and Human Services; National Institutes of Health; National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program, 1997.
- Ferrari M, Segattini C, Zanon R, Bertaiola M, Balestreri F, Brotto E, Lo Cascio V. Comparison of the protective effect of formoterol and of salmeterol against exercise-induced bronchospasm when given immediately before a cycloergometric test. *Respiration* 2002;69(6):509–12.
- Grant EN, Lyttle CS, Weiss KB. The relation of socioeconomic factors and racial/ethnic differences in US asthma mortality. *Am J Public Health* 2000;90(12):1923–5.
- Haas JS, Cleary PD, Guadagnoli E, Fanta C, Epstein AM. The impact of socioeconomic status on the intensity of ambulatory treatment and health outcomes after hospital discharge for adults with asthma. *J Gen Intern Med* 1994;9(3):121–126.
- Halterman JS, Aligne CA, Auinger P, McBride JT, Szilagyi PG. Inadequate therapy for asthma among children in the United States. *Pediatrics* 2000;105(1 Pt 3):272–6.
- Halterman JS, Yoos HL, Kaczorowski JM, McConnochie K, Holzhauer RJ, Conn KM, Lauver S, Szilagyi PG. Providers underestimate symptom severity among urban children with asthma. *Arch Pediatr Adolesc Med* 2002;156(2):141–6.
- Higgins PS, Wakefield D, Cloutier MM. Risk factors for asthma and asthma severity in nonurban children in Connecticut. *Chest* 2005;128(6):3846–53.
- Homa DM, Mannino DM, Lara M. Asthma mortality in U.S. Hispanics of Mexican, Puerto Rican, and Cuban heritage, 1990–1995. *Am J Respir Crit Care Med* 2000;161(2 Pt 1):504–9.
- Huggins JT, Kaplan A, Martin-Harris B, Sahn SA. Eucalyptus as a specific irritant causing vocal cord dysfunction. *Ann Allergy Asthma Immunol* 2004;93(3):299–303.

- Institute of Medicine. *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care*. Smedley BD, Stith AY, Nelson AR (eds.). Washington, DC: National Academies Press, 2002.
- Jarjour NN, Calhoun WJ. Exercise-induced asthma is not associated with mast cell activation or airway inflammation. *J Allergy Clin Immunol* 1992;89(1 Pt 1):60–8.
- Joseph CL, Ownby DR, Peterson EL, Johnson CC. Racial differences in physiologic parameters related to asthma among middle-class children. *Chest* 2000;117(5):1336–44.
- Kingston HG, Hirshman CA. Perioperative management of the patient with asthma. *Anesth Analg* 1984;63(9):844–55. Review.
- Ledogar RJ, Penchaszadeh A, Garden CC, Iglesias G. Asthma and Latino cultures: different prevalence reported among groups sharing the same environment. *Am J Public Health* 2000;90(6):929–35.
- Lieu TA, Finkelstein JA, Lozano P, Capra AM, Chi FW, Jensvold N, Quesenberry CP, Farber HJ. Cultural competence policies and other predictors of asthma care quality for Medicaid-insured children. *Pediatrics* 2004;114(1):e102–10.
- Lieu TA, Lozano P, Finkelstein JA, Chi FW, Jensvold NG, Capra AM, Quesenberry CP, Selby JV, Farber HJ. Racial/ethnic variation in asthma status and management practices among children in managed Medicaid. *Pediatrics* 2002;109(5):857–65.
- Mastalerz L, Gawlewicz-Mrocicka A, Nizankowska E, Cmiel A, Szczeklik A. Protection against exercise-induced bronchoconstriction by montelukast in aspirin-sensitive and aspirin-tolerant patients with asthma. *Clin Exp Allergy* 2002;32(9):1360–5.
- McFadden ER Jr, Gilbert IA. Exercise-induced asthma. *N Engl J Med* 1994;330(19):1362–7.
- McKenzie DC, Stewart IB, Fitch KD. The asthmatic athlete, inhaled beta agonists, and performance. *Clin J Sport Med* 2002;12(4):225–8.
- Miller JE. The effects of race/ethnicity and income on early childhood asthma prevalence and health care use. *Am J Public Health* 2000;90(3):428–30.
- Moraes TJ, Selvadurai H. Management of exercise-induced bronchospasm in children: the role of leukotriene antagonists. *Treat Respir Med* 2004;3(1):9–15. Review.
- Morgan WJ, Crain EF, Gruchalla RS, O'Connor GT, Kattan M, Evans R III, Stout J, Malindzak G, Smartt E, Plaut M, et al.; Inner-City Asthma Study Group. Results of a home-based environmental intervention among urban children with asthma. *N Engl J Med* 2004;351(11):1068–80.

- National Asthma Education Prevention Program (NAEPP). *Working Group Report on Managing Asthma During Pregnancy: Recommendations for Pharmacologic Treatment—Update 2004* (NAEPP 2005). NIH Publication No. 05-5236. Rockville, MD, U.S. Department of Health and Human Services, National Institutes of Health, National Heart, Lung, and Blood Institute, March 2005. Available at <http://www.nhlbi.nih.gov/health/prof/lung/asthma/astpreg.htm>.
- National Institutes of Health (NIH). *Strategic Plan and Budget To Reduce and Ultimately Eliminate Health Disparities, Vol. I: Fiscal Years 2002–2006* (NIH 2004). Bethesda, MD, National Institutes of Health, 2004. Available at http://ncmhd.nih.gov/our_programs/strategic/pubs/Volumel_031003EDrev.pdf.
- Newnham DM, Ingram CG, Earnshaw J, Palmer JB, Dhillon DP. Salmeterol provides prolonged protection against exercise-induced bronchoconstriction in a majority of subjects with mild, stable asthma. *Respir Med* 1993;87(6):439–44.
- Nishiyama T, Hanaoka K. Propofol-induced bronchoconstriction: two case reports. *Anesth Analg* 2001;93(3):645–6.
- Ortega AN, Gergen PJ, Paltiel AD, Bauchner H, Belanger KD, Leaderer BP. Impact of site of care, race, and Hispanic ethnicity on medication use for childhood asthma. *Pediatrics* 2002;109(1):E1.
- Richter K, Janicki S, Jorres RA, Magnussen H. Acute protection against exercise-induced bronchoconstriction by formoterol, salmeterol and terbutaline. *Eur Respir J* 2002;19(5):865–71.
- Shapiro GS, Yegen U, Xiang J, Kottakis J, Della Cioppa G. A randomized, double-blind, single-dose, crossover clinical trial of the onset and duration of protection from exercise-induced bronchoconstriction by formoterol and albuterol. *Clin Ther* 2002;24(12):2077–87.
- Shields AE, Comstock C, Weiss KB. Variations in asthma care by race/ethnicity among children enrolled in a state Medicaid program. *Pediatrics* 2004;113(3 Pt 1):496–504.
- Simons FE, Gerstner TV, Cheang MS. Tolerance to the bronchoprotective effect of salmeterol in adolescents with exercise-induced asthma using concurrent inhaled glucocorticoid treatment. *Pediatrics* 1997;99(5):655–9.
- Slater JE. Latex allergy. *J Allergy Clin Immunol* 1994;94(2 Pt 1):139–49; quiz 150.
- Sly RM. Decreases in Hispanic and non-Hispanic asthma mortality. *Ann Allergy Asthma Immunol* 2006;96(1):76–9.
- Spooner CH, Spooner GR, Rowe BH. Mast-cell stabilising agents to prevent exercise-induced bronchoconstriction. *Cochrane Database Syst Rev* 2003;(4):CD002307.
- Steinshamn S, Sandsund M, Sue-Chu M, Bjermer L. Effects of montelukast on physical performance and exercise economy in adult asthmatics with exercise-induced bronchoconstriction. *Scand J Med Sci Sports* 2002;12(4):211–7.

- Sullivan MD, Heywood BM, Beukelman DR. A treatment for vocal cord dysfunction in female athletes: an outcome study. *Laryngoscope* 2001;111(10):1751–5.
- Sussman GL, Beezhold DH. Allergy to latex rubber. *Ann Intern Med* 1995;122(1):43–6. Review.
- Tan RA, Spector SL. Exercise-induced asthma: diagnosis and management. *Ann Allergy Asthma Immunol* 2002;89(3):226–35; quiz 235–7, 297.
- Todd GR, Acerini CL, Buck JJ, Murphy NP, Ross-Russell R, Warner JT, McCance DR. Acute adrenal crisis in asthmatics treated with high-dose fluticasone propionate. *Eur Respir J* 2002a;19(6):1207–9.
- Todd GR, Acerini CL, Ross-Russell R, Zahra S, Warner JT, McCance D. Survey of adrenal crisis associated with inhaled corticosteroids in the United Kingdom. *Arch Dis Child* 2002b;87(6):457–61.
- Vathenen AS, Knox AJ, Wisniewski A, Tattersfield AE. Effect of inhaled budesonide on bronchial reactivity to histamine, exercise, and eucapnic dry air hyperventilation in patients with asthma. *Thorax* 1991;46(11):811–6.
- Vidal C, Fernandez-Ovide E, Pineiro J, Nunez R, Gonzalez-Quintela A. Comparison of montelukast versus budesonide in the treatment of exercise-induced bronchoconstriction. *Ann Allergy Asthma Immunol* 2001;86(6):655–8.
- Warman KL, Silver EJ, Stein RE. Asthma symptoms, morbidity, and antiinflammatory use in inner-city children. *Pediatrics* 2001;108(2):277–82.
- Zoratti EM, Havstad S, Rodriguez J, Robens-Paradise Y, Lafata JE, McCarthy B. Health service use by African Americans and Caucasians with asthma in a managed care setting. *Am J Respir Crit Care Med* 1998;158(2):371–7.