

# References

1. Grupo de trabajo sobre GPC. Elaboracion de Guías de Práctica Clínica en el Sistema Nacional de Salud. Manual Metodológico. Madrid: Plan Nacional para el SNS del MSC. Instituto Aragonés de Ciencias de la Salud-I+CS; 2007. Guías de Práctica Clínica en el SNS: I+CS N.o 2006/OI.
2. GINA 2006. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention NHLBI/WHO Workshop Report. 2006. <http://www.ginasthma.com>.
3. NAEPP-EP3 2007. National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the diagnosis and management of asthma. Bethesda: National Institutes of Health, National Heart, Lung, and Blood Institute, 2007.
4. BTS 2007. British Thoracic Society, Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma. 2007. [http://www.sign.ac.uk/guidelines.Thorax.2008;63\(Suppl4\):iv1-121](http://www.sign.ac.uk/guidelines.Thorax.2008;63(Suppl4):iv1-121).
5. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coeillo P, et al: GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008; 336(7650): 924-6.
6. ECRHHS. The European Community Respiratory Health Survey II. *Eur Respir J*. 2002; 20: 1071-9.
7. ISAAC. ISAAC STEERING COMMITTEE. Variations in the prevalence of respiratory symptoms, self-reported asthma attacks, and use of asthma medication in the European Community Respiratory Health Survey (ECRHS). *Eur Respir*. 1996; 9:687-95.
8. Grupo Español del Estudio Europeo en Asma. Estudio europeo del asma Prevalencia de hiperreactividad bronquial y asma en jóvenes en 5 regiones de España. Grupo español del estudio europeo del asma. *Med Clin (Barc)*. 1996; 106: 761-7.
9. Martínez Moratalla J, Alma E, Sunyer J, Ramos J, Pereira A, Payo F, et al. Grupo Español de Estudio Europeo del Asma. Identificación y tratamiento de individuos con criterios epidemiológicos de asma en adultos jóvenes de cinco áreas españolas. *Arch Bronconeumol*. 1999; 35: 223-8.
10. Sobradillo V, Miravittles M, Jimenez CA, Gabriel R, Viejo JL, Masa JF, et al. Estudio IBERPOC en España: prevalencia de síntomas respiratorios habituales y de limitación crónica al flujo aéreo. *Arch bronconeumol*. 1999; 35: 159-66.
11. ISAAC, Carvajal-Urena I, García-Marcos L, Busquets-Monge R, Morales Sánchez-Varela M, García De Andoain N, et al. Variaciones geográficas de la prevalencia de síntomas de asma en los niños y adolescentes españoles. International Study of Asthma and Allergies in Childhood (ISAAC) Fase III España. *Arch Bronconeumol*. 2005; 41: 659-66.
12. Cohn L, Elias JA, Chupp GL. Asthma mechanisms of disease persistence and progression. *Annu Rev Immunol*. 2004; 22: 789-815.
13. Douwes J, Gibson P, Pekkanen J, Pearce N. Non eosinophilic asthma: importance and possible mechanisms. *Thorax*. 2002; 57: 643-8.
14. Murray CS, Woodcock A, Langley SJ, Morris J, Custovic A. Secondary prevention of asthma by the use of Inhaled Fluticasone propionate in Wheezy Infants (IFWIN): double-blind, randomised, controlled study. *Lancet*. 2006; 368: 754-62.
15. Hirst SJ, Martin JG, Bonacci JV, Chan V, Fixman ED, Hamid QA, et al. Proliferative aspects of airway smooth muscle. *J Allergy Clin Immunol*. 2004; 114(Suppl 2): S2-17.
16. Hoshino M, Nakamura Y, Hamid Q. Gene expression of vascular endothelial growth factor and its receptors and angiogenesis in bronchial asthma. *J Allergy Clin Immunol*. 2001; 107: 1034-8.
17. Brightling CE, Bradding P, Symon FA, Holgate ST, Wardlaw AJ, Pavord ID. Mast cell infiltration of airway smooth muscle in asthma. *N Engl J Med*. 2002; 346(22): 1699-705.
18. Gleich GJ. Mechanisms of eosinophil-associated inflammation. *J Allergy Clin Immunol*. 2000; 105: 651-63.
19. Fahy JV, Kim KW, Liu J, Boushey HA. Prominent neutrophilic inflammation in sputum from subjects with asthma exacerbation. *J Allergy Clin Immunol*. 1995; 95(4): 843-52.
20. Peters-Golden M. The alveolar macrophage: the forgotten cell in asthma. *Am J Respir Cell Mol Biol*. 2004; 31(1): 3-7.
21. Polito AJ, Proud D. Epithelial cells as regulators of airway inflammation. *J Allergy Clin Immunol*. 1998; 102(5): 714-8. V. Plaza et al / *Arch Bronconeumol*. 2009;45(Supl 7):2-35
22. Groneberg DA, Quarcoo D, Frossard N, Fischer A. Neurogenic mechanisms in bronchial inflammatory diseases. *Allergy*. 2004; 59: 1139-52.
23. Murray CS. Can inhaled corticosteroids influence the natural history of asthma? *Curr Opin Allergy Clin Immunol*. 2008; 8(1): 77-8.
24. Holgate ST, Polosa R. The mechanisms, diagnosis, and management of severe asthma in adults. *Lancet*. 2006; 368(9537): 780-93.
25. O'Byrne PM, Inman MD. Airway hyperresponsiveness. *Chest*. 2003; 123: 411S6S.
26. Holloway JW, Keith TP, Davies DE, Powell R, Haitchi HM, Holgate ST. The discovery and role of ADAM 33, a new candidate gene for asthma. *Expert Rev Mol Med*. 2004; 6: 1-12.
27. Brusasco V, Crimi E, Pellegrino R. Airway hyperresponsiveness in asthma: not just a matter of airway inflammation. *Thorax*. 1998; 53: 992-8.
28. Warner JO, Naspitz CK. Third International Pediatric Consensus statement on the management of childhood asthma. International Pediatric Asthma Consensus Group. *Pediatr Pulmonol*. 1998; 25: 1-17.
29. Castillo Laita JA, De Benito Fernandez J, Escribano Montaner A, Fernandez Benitez M, Garcia de la Rubia S, Garde Garde J, et al. Consenso sobre tratamiento del asma en pediatría. *An Pediatr (Barc)*. 2007; 67(3): 253-73.
30. Martínez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ. Asthma and wheezing in the first six years of life. The Group Health Medical Associates. *N Engl J Med*. 1995; 332: 133-8.

31. Castro-Rodriguez JA, Holberg CJ, Wright AL, Martinez FD. A clinical index to define risk of asthma in young children with recurrent wheezing. *Am J Respir Crit Care Med*. 2000; 162: 1403-6.
32. Gilbert TW, Morgan WJ, Zeiger RS. Atopic characteristics of children with recurrent wheezing at high risk for the development of childhood asthma. *J Allergy Clin Immunol*. 2004; 114: 1282-7.
33. BTS 2004. British guideline on the management of asthma. A national clinic guideline. Revised edition. 2004; Edinburg.
34. Buke W, Fesinmeyer M, Reed K, Hampson L, Carlsten C. Family history as a predictor of asthma risk. *Am J Prev Med*. 2003; 24(2): 160-9.
35. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. *Eur Respir J*. 2005; 26(5): 948-68.
36. Kitch BT, Paltiel AD, Kuntz KM, Dockery DW, Schouten JP, Weiss ST, et al. A single measure of FEV1 is associated with risk of asthma attacks in long-term follow up. *Chest*. 2004; 126: 1875-82.
37. Dekker FW, Schrier AC, Sterk PJ, Dijkman JH. Validity of peak expiratory flow measurement in assessing reversibility of airflow obstruction. *Thorax*. 1992; 47:162-6.
38. Phillips K, Osborne J, Lewis S, Harrison TW, Tattersfield AE. Time course of action of two inhaled corticosteroids, fluticasone propionate and budesonide. *Thorax*. 2004; 59: 26-30.
39. Reddel HK, Salome CM, Peat JK, Woolcock AJ. Which index of peak expiratory flow is most useful in the management of stable asthma? *Am J Respir Crit Care Med*. 1995; 151: 1320-5.
40. Boezen HM, Schouten JP, Postma DS, Rijcken B. Distribution of peak expiratory flow variability by age, gender and smoking habits in a random population sample aged 20-70 yrs. *Eur Respir J*. 1994; 7: 1814-20.
41. Cockcroft DW. Bronchoprovocation methods: direct challenges. *Clin Rev Allergy Immunol*. 2003; 24: 19-26.
42. Van den Berge M, Meijer RJ, Kerstjens HA, de Reus DM, Koeter GH, Kauffman HF, Postma DS. PC20 adenosine 5'-monophosphate is more closely associated with airway inflammation in asthma than PC20 methacholine. *Am J Respir Crit Care Med*. 2001; 163: 1546-50.
43. Anderson SD, Brannan J, Spring J, et al. A new method for bronchial provocation testing in asthmatic subjects using a dry powder of mannitol. *Am J Respir Crit Care Med*. 1997; 156: 758-65.
44. Crapo RO, Casaburi R, Coates AL, Enright PL, Hankinson JL, Irvin CG, et al. Guidelines for methacholine and exercise challenge testing. *Am J Respir Crit Care Med*. 2000; 161: 309-29.
45. Cockcroft DW, Murdock KY, Berscheid BA, Gore BP. Sensitivity and specificity of histamine PC20 determination in a random selection of young college students. *J Allergy Clin Immunol*. 1992; 89: 23-30.
46. ATS/ERS2005. American Thoracic Society/European Respiratory Society. Recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide. *Am J Respir Crit Care Med*. 2005; 171: 912-30.
47. Taylor DR, Pijnenburg MW, Smith AD, De Jongste JC. Exhaled nitric oxide measurements: clinical application and interpretation. *Thorax*. 2006; 61: 817-27.
48. Dupont LJ, Demedts MG, Verleden GM. Prospective evaluation of the validity of exhaled nitric oxide for the diagnosis of asthma. *Chest*. 2003; 123: 751-6.
49. Smith AD, Cowan JO, Filsell S, McLachlan C, Monti-Sheehan G, Jackson P, et al. Diagnosing asthma: comparisons between exhaled nitric oxide measurements and conventional tests. *Am J Respir Crit Care Med*. 2004; 169: 473-8.
50. Bacharier LB, Strunk RC, Mauger D, White D, Lemanske RF, Sorkness CA. Classifying Asthma Severity in Children: Mismatch Between Symptoms, Medication Use, and Lung Function. *Am J Respir Crit Care Med*. 2004; 170(4): 426-32.
51. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A. ATS/ERS TASK force: standardisation of lung function testing. Standardisation of spirometry. *Eur Respir J*. 2005; 26: 319-38.
52. Ownby D, Peterson E, Johnson C. Factors Related to Methacholine Airway Responsiveness in Children. *Am J Respir Crit Care Med*. 2000; 161(5): 1578-83.
53. Parker AL, Abu-Hijleh M, McCool FD. Ratio Between Forced Expiratory Flow Between 25% and 75% of Vital Capacity and FVC Is a Determinant of Airway Reactivity and Sensitivity to Methacholine. *Chest*. 2003; 124(1): 63-9.
54. Faul JL, Demers EA, Burke CM, Poulter LW. The reproducibility of repeat measures of airway inflammation in stable atopic asthma. *Am J Respir Crit Care Med*. 1999; 160: 1457-61.
55. Asensio de la Cruz O, Cordon Martinez A, Elorz Lambarri J, Moreno Galdo A, Villa Asensi JR, Grupo de Tecnicas de la Sociedad Española de Neumología Pediátrica. Estudio de la función pulmonar en el paciente colaborador. Parte II. *An Pediatr (Barc)*. 2007; 66(5): 518-30.
56. Perez-Yarza EG, Villa JR, Cobos N, Navarro M, Salcedo A, Martin C, et al. Espirometría forzada en preescolares sanos bajo las recomendaciones de la ATS/ ERS: estudio CANDELA. *An Pediatr (Barc)*. 2009; 70(1): 3-11.
57. Stanojevic S, Wade A, Lum S, Stocks J. Reference equations for pulmonary function tests in preschool children: A review. *Pediatric Pulmonology*. 2007; 42(10): 9625-72.
58. Beydon N, Davis SD, Lombardi E, Allen JL, Arets H, Aurora P, et al. On behalf of the American Thoracic Society/European Respiratory Society Working Group on Infant and Young Children Pulmonary Function Testing. An Official American Thoracic Society/European Respiratory Society Statement: Pulmonary Function Testing in Preschool Children. *Am J Respir Crit Care Med*. 2007; 175: 1304-45.
59. Cobos Barroso N, Perez-Yarza EG, Sardon Prado O, Reverte Bover C, Gartner S, Korta Murua J. Oxido nítrico exhalado en niños: un indicador no invasivo de la inflamación de las vías aéreas. *Arch Bronconeumol*. 2008; 44(1): 41-51.
60. Warke TJ, Fitch PS, Brown V, Taylor R, Lyons JD, Ennis M, et al. Exhaled nitric oxide correlates with airway eosinophils in childhood asthma. *Thorax*. 2002; 57: 383-7.
61. Pijnenburg MW, Hofhuis W, Hop WC, De Jonste JC. Exhaled nitric oxide predicts asthma relapse in children with clinical asthma remission. *Thorax*. 2005; 60: 215-8.
62. Heinzerling L, Frew AJ, Bindsløv-Jensen C, Bonini S, Bousquet J, Bresciani M, et al. Standard skin prick testing and sensitization to inhalant allergens across Europe – a survey from GA2LEN network. *Allergy*. 2005; 60: 1287-300.
63. Chan EY, Dundas I, Bridge PD, Healy MJ, McKenzie SA. Skin-prick testing as a diagnostic aid for childhood asthma. *Pediatr Pulmonol*. 2005; 39: 558-62.
64. Oppenheimer J, Nelson HS. Skin testing. *Ann Allergy Asthma Immunol*. 2006; 96: S6-12.
65. Choi IS, Koh YI, Koh JS, Lee MG. Sensitivity of the skin prick test and specificity of the serum-specific IgE test for airway responsiveness to house dust mites in asthma. *J Asthma*. 2005; 42: 197-202.
66. Simpson A, Soderstrom L, Ahlstedt S, Murray CS, Woodcock A, Custovic A. IgE antibody quantification and the probability of wheeze in preschool children. *J Allergy Clin Immunol*. 2005; 116: 744-9.
67. Tschopp JM, Sistek D, Schindler C, Leuenberger P, Perruchoud AP, Wuthrich B, et al. Current allergic asthma and rhinitis:

- diagnostic efficiency of three commonly used atopic markers (IgE, skin prick tests, and Phadiatop). Results from 8329 randomized adults from the SAPALDIA Study. *Swiss Study on Air Pollution and Lung Diseases in Adults. Allergy.* 1998; 53: 608-13.
68. Beach J, Russell K, Blitz S, Hooton N, Spooner C, Lemiere C, et al. A systematic review of the diagnosis of occupational asthma. *Chest.* 2007; 131: 569-78.
  69. GINA 2002. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention: NHLBI/WHO Report. Bethesda: National Institutes of Health, National Heart, Lung, and Blood Institute, 2002. Publication 02-3659.
  70. NAEPP 2002. National Asthma Education and Prevention Program. Guidelines for the diagnosis and management of asthma: Expert Panel Report 2. Bethesda: National Institutes of Health, National Heart, Lung, and Blood Institute, 2002. Publication 97-4051.
  71. Plaza V, Alvarez FJ, Casan P, Cobos N, Lopez Vina A, et al. En calidad de Comité Ejecutivo de la GEMA y en representación del grupo de redactores. Guía Española para el Manejo del Asma (GEMA 2003). *Arch Bronconeumol.* 2003; 39(Suppl 5): 1-42.
  72. Bateman ED. Severity and control of severe asthma. *J Allergy Clin Immunol.* 2006; 117: 519-21.
  73. Stoloff SW, Boushey HA. Severity, control, and responsiveness in asthma. *J Allergy Clin Immunol.* 2006; 117: 544-8.
  74. Cockcroft DW, Swystun VA. Asthma control versus asthma severity. *J Allergy Clin Immunol.* 1996; 98: 1016-8.
  75. Taylor DR, Bateman ED, Boulet LP, Boushey HA, Busse WW, Casale TB, et al. A new perspective on concepts of asthma severity and control. *Eur Respir J.* 2008; 32: 545-54.
  76. Osborne ML, Vollmer WM, Pedula KL, Wilkins J, Buist AS, O'Hollaren M. Lack of correlation of symptoms with specialist-assessed long-term asthma severity. *Chest.* 1999; 115: 85-91.
  77. Bateman ED, Boushey HA, Bousquet J, Busse WW, Clark TJ, Pauwels RA, et al. Can guideline-defined asthma control be achieved? The Gaining Optimal Asthma Control study. *Am J Respir Crit Care Med.* 2004; 170: 836-44.
  78. Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, et al. Development of the asthma control test: a survey for assessing asthma control test. *J Allergy Clin Immunol.* 2004; 113: 59-65.
  79. Vega JM, Badia X, Badiola C, Lopez-Vina A, Olaguibel JM, Picado C, et al. Covalair Investigator Group. Validation of the Spanish version of the Asthma Control Test (ACT). *J Asthma.* 2007; 44:867-72.
  80. Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *Eur Respir J.* 1999; 14: 902-7.
  81. Picado C, Badiola C, Perulero N, Sastre J, Olaguibel JM, Lopez Vina A, Vega JM; Covalair Investigator Group. Validation of the Spanish version of the Asthma Control Questionnaire. *Clin Ther* 2008; 30: 1918-31.
  82. Juniper EF, Wisniewski ME, Cox FM, Emmett AH, Nielsen KE, O'Byrne PM. Relationship between quality of life and clinical status in asthma: a factor analysis. *Eur Respir J.* 2004; 23(2): 287-91. V. Plaza et al / *Arch Bronconeumol.* 2009;45(Supl 7):2-35.
  83. Juniper EF, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring quality of life in children with asthma. *Qual Life Res.* 1996; 5(1): 35-46.
  84. Juniper EF, Guyatt GH, Cox FM, Ferrie PJ, King DR. Development and validation of the Mini Asthma Quality of Life Questionnaire. *Eur Respir J* 1999; 14(1): 32-8.
  85. Fuhlbrigge AL, Kitch BT, Paltiel AD, et al. FEV1 is associated with risk of asthma attacks in a pediatric population. *J Allergy Clin Immunol.* 2001; 107: 61-7.
  86. Petsky HL, Cates CJ, Li AM, Kynaston JA, Turner C, Chang AB. Tailored interventions based on exhaled nitric oxide versus clinical symptoms for asthma in children and adults. *Cochrane Database Syst Rev.* 2008(2): CD006340.
  87. Szefer SJ, Mitchell H, Sorkness CA, Gergen PJ, O'Connor GT, Morgan WJ, et al. Management of asthma based on exhaled nitric oxide in addition to guideline-based treatment for inner-city adolescents and young adults: a randomised controlled trial. *Lancet.* 2008; 372(9643): 1065-72.
  88. Petsky H, Kynaston J, Turner C, Li A, Cates C, Lasserson T, et al. Tailored interventions based on sputum eosinophils versus clinical symptoms for asthma in children and adults. *Cochrane Database Syst Rev.* 2007(2): CD005603.
  89. Perez-Yarza EG, Badia X, Badiola C, Cobos N, Garde J, Ibero M, et al. On behalf of the CAN Investigator Group. Development and validation of a questionnaire to assess asthma control in pediatrics. *Pediatr Pulmonol.* 2009; 44: 54-63.
  90. Boulet LP, Becker A, Berube D, Beveridge R, Ernst P, on behalf of the Canadian Asthma Consensus Group. Summary of recommendations from the Canadian Asthma Consensus report. *CMAJ.* 1999; 161(Suppl 11): S1-S12.
  91. Gibson PG, Powell H, Ducharme FM. Differential effects of maintenance longacting betaagonist and inhaled corticosteroid on asthma control and asthma exacerbations. *J Allergy Clin Immunol.* 2007; 119: 344-50.
  92. Bateman ED, Jacques L, Goldfrad C, Atienza T, Mihaescu T, Duggan M. Asthma control can be maintained when fluticasone propionate/salmeterol in a single inhaler is stepped down. *J Allergy Clin Immunol.* 2006; 117(3): 563-70.
  93. Cockcroft DW. As-needed inhaled beta2-adrenoceptor agonists in moderate-to-severe asthma: current recommendations. *Treat Respir Med.* 2005; 4: 169-74.
  94. Tan RA, Spector SL. Exercise-induced asthma: diagnosis and management. *Ann Allergy Asthma Immunol.* 2002; 89: 226-35.
  95. Adams NP, Bestall JB, Malouf R, Lasserson TJ, Jones PW. Inhaled beclomethasone versus placebo for chronic asthma. *Cochrane Database Syst Rev.* 2005; (1): CD002738.
  96. Adams NP, Bestall JC, Lasserson TJ, Jones PW, Cates C. Fluticasone versus placebo for chronic asthma in adults and children. *Cochrane Database Syst Rev.* 2005; (4): CD003135.
  97. Koh MS, Irving LB. Evidence-based pharmacologic treatment for mild asthma. *Int J Clin Pract.* 2007; 61: 1375-9.
  98. Reddel HK, Belousova EG, Marks GB, Jenkins CR. Does continuous use of inhaled corticosteroids improve outcomes in mild asthma? A double-blind randomised controlled trial. *Prim Care Respir J.* 2008; 17: 39-45.
  99. Boushey HA, Sorkness CA, King TS, Sullivan SD, Fahy JV, et al. Daily versus as-needed corticosteroids for mild persistent asthma. *N Engl J Med.* 2005; 352: 1519-28.
  100. Zeiger RS, Bird SR, Kaplan MS, Schatz M, Pearlman DS, Orav EJ, et al. Short-term and long-term asthma control in patients with mild persistent asthma receiving montelukast or fluticasone: a randomized controlled trial. *Am J Med.* 2005; 118: 649-57.
  101. Barnes NC, Miller CJ. Effect of leukotriene receptor antagonist therapy on the risk of asthma exacerbations in patients with mild to moderate asthma: an integrated analysis of zafirlucast trials. *Thorax.* 2000; 55: 478-83.
  102. Peters SP, Anthonisen N, Castro M, Holbrook JT, Irvin CG, et al. ALA. American Lung Association Asthma Clinical Research Centers. Randomized comparison of strategies for reducing treatment in mild persistent asthma. *N Engl J Med.* 2007; 356: 2027-39.
  103. Busse WW, Casale TB, Dykewicz MS, Meltzer EO, Bird SR, Hustad CM, et al. Efficacy of montelukast during the allergy

- season in patients with chronic asthma and seasonal aeroallergen sensitivity. *Ann Allergy Asthma Immunol*. 2006; 96: 60-8.
104. Price DB, Swern A, Tozzi CA, Philip G, Polos P. Effect of montelukast on lung function in asthma patients with allergic rhinitis: analysis from the COMPACT trial. *Allergy*. 2006; 61: 737-42.
  105. O'Byrne PM, Barnes PJ, Rodriguez Roisin R, Runnerstrom E, Sandstrom T, Svensson K, et al. Low dose inhaled budesonide and formoterol in mild persistent asthma: the OPTIMA randomized trial. *Am J Respir Crit Care Med*. 2001; 164: 1392-7.
  106. Dahl R, Larsen BB, Venge P. Effect of long-term treatment with inhaled budesonide or theophylline on lung function, airway reactivity and asthma symptoms. *Respir Med*. 2002; 96: 432-8.
  107. Sullivan P, Bekir S, Jaffar Z, Page C, Jeffery P, Costello J. Anti-inflammatory effects of low-dose oral theophylline in atopic asthma. *Lancet*. 1994; 343(8904): 10068.
  108. Dudley T, Parker S, Baldwin R. Clinical inquiries. Is nedocromil effective in preventing asthmatic attacks in patients with asthma? *J Fam Pract*. 2004; 53: 927-8.
  109. Woolcock A, Lundback B, Ringdal N, Jacques LA. Comparison of addition of salmeterol to inhaled steroids with doubling of the dose of inhaled steroids. *Am J Respir Crit Care Med*. 1996; 153: 1481-8.
  110. Pauwels RA, Lofdahl CG, Postma DS, Tattersfield AE, O'Byrne P, Barnes PJ, et al. Effect of inhaled formoterol and budesonide on exacerbations of asthma. Formoterol and Corticosteroids Establishing Therapy (FACET) International Study Group. *N Engl J Med*. 1997; 337: 1405-11.
  111. Shrewsbury S, Pyke S, Britton M. Meta-analysis of increased dose of inhaled steroid or addition of salmeterol in symptomatic asthma (MIASMA). *BMJ*. 2000; 320: 1368-73.
  112. Greenstone IR, Ni Chroinin MN, Masse V, Danish A, Magdalinos H, Zhang X, et al. Combination of inhaled long-acting beta2-agonists and inhaled steroids versus higher dose of inhaled steroids in children and adults with persistent asthma. *Cochrane Database Syst Rev*. 2005; (4): CD005533.
  113. Masoli M, Weatherall M, Holt S, Beasley R. Moderate dose inhaled corticosteroids plus salmeterol versus higher doses of inhaled corticosteroids in symptomatic asthma. *Thorax*. 2005; 60: 730-4.
  114. Scicchitano R, Aalbers R, Ukena D, Manjra A, Fouquert L, Centanni S, et al. Efficacy and safety of budesonide/formoterol single inhaler therapy versus a higher dose of budesonide in moderate to severe asthma. *Curr Med Res Opin*. 2004; 20: 1403-18.
  115. O'Byrne PM, Bisgaard H, Godard PP, Pistolesi M, Palmqvist M, Zhu Y, et al. Budesonide/formoterol combination therapy as both maintenance and reliever medication in asthma. *Am J Respir Crit Care Med*. 2005; 171: 129-36.
  116. Rabe KF, Atienza T, Magyar P, Larsson P, Jorup C, Laloo UG. Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations: a randomized controlled, double-blind study. *Lancet*. 2006; 368(9537): 744-53.
  117. Rabe KF, Pizzichini E, Stallberg B, Romero S, Balanzat AM, Atienza T, et al. Budesonide/formoterol in a single inhaler for maintenance and relief in mild-to-moderate asthma: a randomized, double-blind trial. *Chest*. 2006; 129: 246-56.
  118. Vogelmeier C, D'Urzo A, Pauwels R, Merino JM, Jaspal M, Boutet S, et al. Budesonide/formoterol maintenance and reliever therapy: an effective asthma treatment option? *Eur Respir J*. 2005; 26: 819-28.
  119. Bousquet J, Boulet LP, Peters MJ, Magnussen H, Quirarte J, Martinez-Aguilar NE, et al. Budesonide/formoterol for maintenance and relief in uncontrolled asthma vs. high-dose salmeterol/fluticasone. *Respir Med*. 2007; 101: 2437-46.
  120. Kuna P, Peters MJ, Manjra AI, Jorup C, Naya IP, Martinez-Jimenez NE, et al. Effect of budesonide/formoterol maintenance and reliever therapy on asthma exacerbations. *Int J Clin Pract*. 2007; 61: 725-36.
  121. Szefler SJ, Martin RJ, King TS, Boushey HA, Cherniack RM, Chinchilli VM, et al. Significant variability in response to inhaled corticosteroids for persistent asthma. *J Allergy Clin Immunol*. 2002; 109: 410-8.
  122. Powell H, Gibson PG. Initial starting dose of inhaled corticosteroids in adults with asthma: a systematic review. *Thorax*. 2004; 59: 1041-5.
  123. Pieters WR, Wilson KK, Smith HC, Tamminga JJ, Sondhi S. Salmeterol/fluticasone propionate versus fluticasone propionate plus montelukast: a cost-effective comparison for asthma. *Treat Respir Med*. 2005; 4: 129-38.
  124. Joos S, Miksch A, Szecsenyi J, Wieseler B, Grouven U, Kaiser T, et al. Montelukast as add-on therapy to inhaled corticosteroids in the treatment of mild to moderate asthma: a systematic review. *Thorax*. 2008; 63: 453-62.
  125. Ram FS, Cates CJ, Ducharme FM. Long-acting beta2-agonists versus antileukotrienes as add-on therapy to inhaled corticosteroids for chronic asthma. *Cochrane Database Syst Rev*. 2005; 25(1): CD003137. Update in: *Cochrane Database Syst Rev*. 2006; (4): CD003137.
  126. Ni Chroinin M, Greenstone IR, Danish A, Magdalinos H, Masse V, Zhang X, et al. Long-acting beta2-agonists versus placebo in addition to inhaled corticosteroids in children and adults with chronic asthma. *Cochrane Database Syst Rev*. 2005; (4): CD005535.
  127. Toogood JH, Baskerville JC, Jennings B, Lefcoe NM, Johanson SA. Influence of dosing frequency and schedule on the response of chronic asthmatics to the aerosol steroid, budesonide. *J Allergy Clin Immunol*. 1982; 70: 288-98.
  128. Tonelli M, Zingoni M, Bacci E, Dente FL, Di Franco A, Giannini D, et al. Short-term effect of the addition of leukotriene receptor antagonists to the current therapy in severe asthmatics. *Pulm Pharmacol Ther*. 2003; 16: 237-40.
  129. Inoue H, Komori M, Matsumoto T, Fukuyama S, Matsumura M, Nakano T, et al. Effects of salmeterol in patients with persistent asthma receiving inhaled corticosteroid plus theophylline. *Respiration*. 2007; 74: 611-6.
  130. Humbert M, Berger W, Rapatz G, Turk F. Add-on omalizumab improves day-to-day symptoms in inadequately controlled severe persistent allergic asthma. *Allergy*. 2008; 63: 592-6.
  131. Humbert M, Beasley R, Ayres J, Slavov R, Hebert J, Bousquet J, et al. Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy (GINA 2002 step 4 treatment): INNOVATE. *Allergy*. 2005; 60: 309-16.
  132. Busse W, Corren J, Lanier BQ, McAlary M, Fowler-Taylor A, Cioppa GD, et al. Gupta N. Omalizumab, anti-IgE recombinant humanized monoclonal antibody, for the treatment of severe allergic asthma. *J Allergy Clin Immunol*. 2001; 108(2): 184-90.
  133. Busse WW, Massanari M, Kianifard F, Geba GP. Effect of omalizumab on the need for rescue systemic corticosteroid treatment in patients with moderate-to-severe persistent IgE-mediated allergic asthma: a pooled analysis. *Curr Med Res Opin*. 2007; 23: 2379-86.
  134. Mash B, Bheekie A, Jones PW. Inhaled vs oral steroids for adults with chronic asthma. *Cochrane Database Syst Rev*. 2000. p. 2.
  135. Polosa R. An overview of chronic severe asthma. *Intern Med J*. 2008; 38: 190-8.
  136. Newman SP, Clarke SW. Therapeutic aerosols 1—physical and practical considerations. *Thorax*. 1983; 38: 881-6.

137. Clarke SW, Newman SP. Therapeutic aerosols 2—Drugs available by the inhaled route. *Thorax*. 1984; 39: 1-7.
138. Giner J, Basualdo LV, Casan P, Hernandez C, Macian V, Martinez I, et al. Normativa sobre la utilizacion de farmacos inhalados. Recomendaciones SEPAR. *Arch Bronconeumol*. 2000; 36: 34-43.
139. Hess DR. Aerosol delivery devices in the treatment of asthma. *Respir Care*. 2008; 53: 699-723.
140. Cheng YS, Fu CS, Yazzie D, Zhou Y. Respiratory deposition patterns of salbutamol pMDI with CFC and HFA-134a formulations in a human airway replica. *J Aerosol Med*. 2001; 14: 255-66. V. Plaza et al / *Arch Bronconeumol*. 2009;45(Supl 7):2-35.
141. Brown PH, Greening AP, Crompton GK. Large volume spacer devices and the influence of high dose beclomethasone dipropionate on hypothalamopituitaryadrenaxis function. *Thorax*. 1993; 48: 233-8.
142. Newman SP, Newhouse MT. Effect of add-on devices for aerosol drug delivery: deposition studies and clinical aspects. *J Aerosol Med*. 1996; 9: 55-70.
143. Newman SP. Spacer devices for metered dose inhalers. *Clin Pharmacokinet*. 2004; 43: 349-60.
144. Plaza V, Sanchis J. Medical personnel and patient skill in the use of metered dose inhalers: a multicentric study. CESEA Group. *Respiration*. 1998; 65: 195-8.
145. Giner J, Macian V, Hernandez C, Grupo EDEN, et al. Multi-center prospective study of respiratory patient education and instruction in the use of inhalers (EDEN study). *Arch Bronconeumol*. 2002; 38: 300-5.
146. Lange P, Parner J, Vestbo J, Schnohr P, Jensen G. A 15-year followup study of ventilatory function in adults with asthma. *N Engl J Med*. 1998; 339: 1194-200.
147. James AL, Palmer LJ, Kicic E, Maxwell PS, Lagan SE, Ryan GF, et al. Decline in lung function in the Busseton Health Study: the effects of asthma and cigarette smoking. *Am J Respir Crit Care Med*. 2005; 171:109-14.
148. Jimenez Ruiz CA, Barrueco M, Solano S, Torrecilla M, Dominguez M, Diaz-Maroto, et al. Recomendaciones en el abordaje diagnostico y terapeutico del tabaquismo. Documento de consenso. *Arch Bronconeumol*. 2003; 39: 35-41.
149. Morgan WJ, Crain EF, Gruchalla RS, O'Connor GT, Kattan M, Evans R, et al. Results of a home-based environmental intervention among urban children with asthma. *N Engl J Med*. 2004; 351: 1068-80.
150. Phipatanakul W, Cronin B, Wood RA, Eggleston PA, Shih MC, Song L, et al. Effect of environmental intervention on mouse allergen levels in homes of inner-city Boston children with asthma. *Ann Allergy Asthma Immunol*. 2004; 92: 420-5.
151. Shirai T, Matsui T, Suzuki K, Chida K. Effect of pet removal on pet allergic asthma. *Chest*. 2005; 127: 1565-71.
152. Orriols R, Abu K, Alday E, Cruz MJ, Galdiz JB, Isidro I, et al. Normativa del asma ocupacional. *Arch Bronconeumol*. 2006; 42(9): 457-74.
153. Luczynska C, Tredwell E, Smeeton N, Burney P. A randomized controlled trial of mite allergen-impermeable bed covers in adult mite-sensitized asthmatics. *Clin Exp Allergy*. 2003; 33: 1648-53.
154. Woodcock A, Forster L, Matthews E, Martin J, Letley L, Vickers M, et al. Medical Research Council General Practice Research Framework. Control of exposure to mite allergen and allergen-impermeable bed covers for adults with asthma. *N Engl J Med*. 2003; 349: 225-36.
155. Gotzsche PC, Johansen HK. House dust mite control measures for asthma: systematic review. *Allergy*. 2008; 63:646-59.
156. Htut T, Higenbottam TW, Gill GW, Darwin R, Anderson PB, Syed N. Eradication of house dust mite from homes of atopic asthmatic subjects: a double-blind trial. *J Allergy Clin Immunol*. 2001; 107: 55-60.
157. Halken S, Host A, Niklassen U, Hansen LG, Nielsen F, Pedersen S, et al. Effect of mattress and pillow encasings on children with asthma and house dust mite allergy. *J Allergy Clin Immunol*. 2003; 111: 169-76.
158. Sheikh A, Hurwitz B, Shehata Y. House dust mite avoidance measures for perennial allergic rhinitis. *Cochrane Database of Systematic Reviews*. 2007, Issue
159. Platts-Mills TAE. Allergen avoidance in the treatment of asthma: Problems with the meta-analyses. *J Allergy Clin Immunol*. 2008; 122: 694-6.
160. Plaza V, Serrano J, Picado C, Sanchis J. High Risk Asthma Research Group. Frequency and clinical characteristics of rapid-onset fatal and near-fatal asthma. *Eur Respir J*. 2002; 19: 846-52.
161. Nizankowska-Mogilnicka E, Bochenek G, Mastalerz L, Swierczyfska M, Picado C, Scadding G, et al. EAACI/GA2LEN guideline: aspirin provocation tests for diagnosis of aspirin hypersensitivity. *Allergy*. 2007; 62: 1111-8.
162. Casadevall J, Ventura PJ, Mullol J, Picado C. Intranasal challenge with aspirin in the diagnosis of aspirin intolerant asthma: evaluation of nasal response by acoustic rhinometry. *Thorax*. 2000; 55: 921-4.
163. Valero A, Baltasar M, Enrique E, Pau L, Dordal MT, Cistero A, et al. NSAID-sensitive patients tolerate rofecoxib. *Allergy*. 2002; 57: 1214-5.
164. Abramson MJ, Puy RM, Weiner JM. Is allergen immunotherapy effective in asthma? A meta-analysis of randomized controlled trials. *Am J Respir Crit Care Med*. 1995; 151: 969-74.
165. Abramson MJ, Puy RM, Weiner JM. Allergen immunotherapy for asthma. *Cochrane Database Syst Rev*. 2003; (4): CD001186.
166. Adkinson NF Jr, Eggleston PA, Eney D, Goldstein EO, Schuberth KC, Bacon JR, et al. A controlled trial of immunotherapy for asthma in allergic children. *N Engl J Med*. 1997; 336: 324-31.
167. Bernstein DI, Wanner M, Borish L, Liss GM, Immunotherapy Committee, American Academy of Allergy, Asthma and Immunology. Twelve-year survey of fatal reactions to allergen injections and skin testing: 1990-2001. *J Allergy Clin Immunol*. 2004; 113: 1129-36.
168. Moreno C, Cuesta Herranz J, Fernandez Tavora L, Alvarez Cuesta E. Immunotherapy safety: a prospective multi-centric monitoring study of biologically standardized therapeutic vaccines for allergic diseases. *Clin Exp Allergy*. 2004; 34: 527-31.
169. Olaguibel JM, Alvarez Puebla MJ. Efficiency of sublingual allergen vaccination for respiratory allergy in children. Conclusions from one metaanalysis. *J Investig Allergol Clin Immunol*. 2005; 15: 9-16.
170. Penagos M, Passalacqua G, Compalati E, Baena-Cagnani CE, Orozco S, Pedroza A, et al. Metaanalysis of the efficiency of sublingual immunotherapy in the treatment of allergic asthma in pediatric patients, 3 to 18 years of age. *Chest*. 2008; 133: 599-609.
171. Durham SR, Walker SM, Varga EM, Jacobson MR, O'Brien F, Noble W, et al. Longterm clinical efficacy of grasspollen immunotherapy. *N Engl J Med*. 1999; 341: 468-75.
172. Jacobsen L, Niggemann B, Dreborg S, Ferdousi HA, Halken S, Host A, et al. The PAT investigator group. Specific immunotherapy has long-term preventive effect of seasonal and perennial asthma: 10-year follow-up on the PAT study. *Allergy*. 2007; 62: 943-8.
173. Pajno GB, Barberio G, De Luca F, Morabito L, Parmiani S. Prevention of new sensitizations in asthmatic children mono-sensitized to house dust mite by specific immunotherapy. A sixyear follow-up study. *Clin Exp Allergy*. 2001; 31: 1392-7.
174. Abadoglu O, Mungan D, Pasaoglu G, Celik G, Misirligil Z.

- Influenza vaccination in patients with asthma: effect on the frequency of upper respiratory tract infections and exacerbations. *J Asthma*. 2004; 41: 279-83.
175. Christy C, Aligne CA, Auinger P, Pulcino T, Weitzman M. Effectiveness of influenza vaccine for the prevention of asthma exacerbations. *Arch Dis Child*. 2004; 89: 734-5.
  176. Sheikh A, Alves A, Dhimi S. Pneumococcal vaccine for asthma. *Cochrane Database of Systematic Reviews* 2002, Issue 1. Art. N.o: CD002165. DOI: 10.1002/14651858.CD002165.
  177. Johnston NW, Sears MR. Asthma exacerbations. *Epidemiology. Thorax*. 2006; 61: 722-8.
  178. Hughes DM, McLeod M, Garner B, Goldbloom RB. Controlled trial of a home and ambulatory program for asthmatic children. *Pediatrics*. 1991; 87: 54-61.
  179. Colland VT. Learning to cope with asthma: a behavioural selfmanagement program for children. *Patient Educ Couns*. 1993; 22: 141-52.
  180. Van der Palen J, Klein JJ, Zielhuis GA, van Herwaarden CL, Seydel ER. Behavioural effect of self-treatment guidelines in a self-management program for adults with asthma. *Patient Educ Couns*. 2001; 43: 161-9.
  181. Gibson PG, Powell H, Coughlan J, Wilson AJ, Abramson M, Haywood Bauman A, et al. Educacion para el autocuidado y examen medico regular para adultos con asma (Revision Cochrane traducida). En: *La Biblioteca Cochrane Plus*, 2008 Numero 1. Oxford: Update Software Ltd. Disponible en: <http://www.updatesoftware.com>.
  182. Powell H, Gibson PG. Opciones para la educacion sobre el autocuidado para los adultos con asma (Revision Cochrane traducida). En: *La Biblioteca Cochrane Plus*, 2008, Numero 1. Oxford: Update.
  183. Partridge MR. Patient education. En: O'Byrne P, Thomsen NC, editores. *Manual of asthma management*. WB Saunders. 1995. p. 378-92.
  184. Haynes RB, McDonald H, Garg AX et al. Interventions for helping patients to follow prescriptions for medications (Cochrane Review). 2001; 3. Oxford: Update Software.
  185. Creer TL. Medication compliance and childhood asthma. En: Krasnegor NA, Epstein L, Johnson SB, Yaffe SJ, editores. *Developmental aspects of health compliance behavior*. Hittsdale, NS: Lawrence Associate. 1993; 303-33.
  186. Gibson PG, Coughlan J, Wilson AJ, Abramson M, Bauman A, Hensley MJ, et al. Self-management education and regular practitioner review for adults with asthma. *Cochrane Database Syst Rev*. 2000; (2):CD001117. *Cochrane Database Syst Rev*. 2003; (1): CD001117.
  187. Abramson MJ, Bailey MJ, Couper FJ, Drivers JS, Drummer OH, Forbes AB, et al. Are asthma medications and management related to deaths from asthma? *Am J Respir Crit Care Med*. 2001; 163: 12-8.
  188. Douglass J, Aroni R, Goeman D, Stewart K, Sawyer S, Thien F, et al. A qualitative study of action plans for asthma. *BMJ*. 2002; 324: 1003-5.
  189. Reddel HK, Marks GB, Jenkins CR. When can personal best peak flow be determined for asthma action plans? *Thorax*. 2004; 59: 922-4.
  190. Lahdensuo A. Guided self management of asthma-how to do it. *BMJ*. 1999; 319: 759-60.
  191. Cote J, Bowie DM, Robichaud P, Parent JG, Battisti L, Boulet LP. Evaluation of two different educational interventions for adult patients consulting with an acute asthma exacerbation. *Am J Respir Crit Care Med*. 2001; 163: 1415-9.
  192. Gibson PG, Powell H. Written action plans for asthma: an evidencebased review of the key components. *Thorax*. 2004; 59: 94-9.
  193. Castro M, Zimmermann NA, Crocker S, Bradley J, Leven C, Schechtman KB. Asthma intervention program prevents readmissions in high healthcare users. *Am J Respir Crit Care Med*. 2003; 168(9): 1095-9.
  194. Borgmeyer A, Gyr PM, Jamerson PA, Henry LD. Evaluation of the role of the pediatric nurse practitioner in an inpatient asthma program. *J Pediatr Health Care*. 2008; 22(5): 273-81.
  195. Woodruff PG, Emond SD, Singh AK, Camargo CA Jr. Sudden-onset severe acute asthma: clinical features and response to therapy. *Acad Emerg Med*. 1998; 5: 695-701.
  196. Turner MO, Noertjojo K, Vedal S, Bai T, Crump S, Fitzgerald JM. Risk factors for near-fatal asthma. A casecontrol study in hospitalized patients with asthma. *Am J Respir Crit Care Med*. 1998; 157: 1804-9.
  197. Mitchell I, Tough SC, Semple LK, Green FH, Hessel PA. Near-fatal asthma: a population-based study of risk factors. *Chest*. 2002; 121: 1407-13.
  198. Serrano J, Plaza V, Sureda B, De Pablo J, Picado C, Bardagi S, et al. Alexithymia: a relevant psychological variable in near-fatal asthma. *Eur Respir J*. 2006; 28: 296-302.
  199. ALERTA 2008. Guia ALAT-SEPAR ALERTA. America Latina y Espana: Recomendaciones para la Prevencion y el Tratamiento de la Exacerbacion Asmatica. Barcelona: Ed. Mayo. 2008.
  200. McFadden ER, Kisser R, De Groot WJ. Acute bronchial Asthma: relations between clinical and physiological manifestations. *Engl J Med*. 1973; 288:221-5.
  201. Rodrigo G, Rodrigo C. Early prediction of poor response in acute asthma patients in the emergency department. *Chest*. 1998; 114: 1016-21.
  202. Carruthers DM, Harrison BD. Arterial Blood gas analysis or oxygen saturation in the assessment of acute asthma? *Thorax*. 1995; 50: 186-8.
  203. Rodrigo GJ, Rodrigo C, Hall JB. Acute asthma in adults. A review. *Chest*. 2004; 125: 1081-2. V. Plaza et al / *Arch Bronconeumol*. 2009;45(Supl 7):2-35.
  204. Cowie RI, Revitt SG, Underwood MF. The effect of peak-flow based action plan in the prevention of exacerbation of asthma. *Chest*. 1997; 112: 1534-8.
  205. Reisner C, Kotch A, Dworkin G. Continuous versus frequent intermittent nebulization of albuterol in acute asthma: a randomized, prospective study. *Ann Allergy Asthma Immunol*. 1995; 75: 41-7.
  206. Cates CJ, Crilly JA, Rowe BH. Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma. *Cochrane Database of Systematic Reviews*. 2006; 2: CD000052. DOI: 10.1002/14651858.CD000052.pub2.
  207. Manser R, Reid D, Abramson M. Corticosteroids for acute severe asthma in hospitalised patients. *Cochrane Database Syst Rev*. 2000. p. 2.
  208. Hasegawa T, Ishihara K, Takakura S, Fujii H, Nishimura T, Okazaki M, et al. Duration of systemic corticosteroids in the treatment of asthma exacerbation: a randomized study. *Intern Med*. 2000; 39(10): 794-7.
  209. Rowe BH, Spooner C, Ducharme FM, Bretzlaff JA, Bota GW. Corticosteroids for preventing relapse following acute exacerbation of asthma (Cochrane Review). London: John Wiley & Sons Ltd. *The Cochrane Library*. 2001; 3.
  210. Rowe BH, Spooner CH, Ducharme FM, Bota GW. Corticosteroids for preventing relapse following acute exacerbations of asthma. *Cochrane Database of Systematic Reviews*. 2007; 3: CD000195. DOI: 10.1002/14651858.CD000195.
  211. Osman LM, Calder C, Godden DJ, Friend JA, McKenzie L, Legge JS, et al. A randomised trial of self-management planning for adult patients admitted to hospital with acute asthma. *Thorax*. 2002; 57: 869-74.

212. Rodrigo GJ, Rodriguez-Verde M, Peregalli V, Rodrigo C. effects of shortterm 28% and 100% oxygen in pACO<sub>2</sub> and peak expiratory flow rate in acute Asthma. A randomized trial. *Chest*. 2003; 124: 1312-7.
213. Rodrigo C, Rodrigo G. Therapeutic response patterns to high and cumulative doses of salbutamol in acute severe asthma. *Chest*. 1998; 113: 593-8.
214. Camargo CA, Spooner CH, Rowe BH. Continuous versus intermittent beta-agonists for acute asthma. *Cochrane Database of Systematic Reviews*. 2003; 4: CD001115. DOI: 10.1002/14651858.CD001115.
215. Travers A, Jones AP, Kelly K, Barker SJ, Camargo CA, Rowe BH. Intravenous beta2agonists for acute asthma in the emergency department. *Cochrane Database of Systematic Reviews*. 2001; 1: CD002988. DOI: 10.1002/14651858. CD002988.
216. Rubinfeld AR, Scicchitanow R, Hunt A, Thompson PJ, van Nooten A, Selroos O. Formoterol Turbuhaler as reliever medication in patients with acute asthma. *Eur Respir J*. 2006; 27:735-41.
217. Rodrigo GJ, Castro Rodriguez JA. Anticholinergics in the treatment of children and adults with acute asthma: a systematic review with meta-analysis *Thorax*. 2005; 60: 740-6.
218. Rowe BH, Spooner C, Ducharme FM, Bretzlaff JA, Bota GW. Early emergency department treatment of acute asthma with systemic corticosteroids. *Cochrane Database of Systematic Reviews*. 2001; 1: CD002178. DOI: 10.1002/14651858. CD002178.
219. Rodrigo GJ. Rapid effects of inhaled corticosteroids in acute asthma. An evidencebased evaluation. *Chest*. 2006; 130: 1301-11.
220. Rodrigo GJ, Nannini LJ. Is there a place for nebulized magnesium sulfate in the treatment of acute asthma? A systematic review. *Curr Ther*. 2006; 1: 181-5.
221. Rowe BH, Bretzlaff JA, Bourdon C, Bota GW, Camargo CA. Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. *Cochrane Database of Systematic Reviews* 2000, Issue 1. Art. N.o: CD001490. DOI: 10.1002/14651858.CD001490.
222. Parameswaran K, Belda J, Rowe BH. Addition of intravenous aminophylline to beta2-agonists in adults with acute asthma. *Cochrane Database of Systematic Reviews*. 2000; 4: CD002742. DOI: 10.1002/14651858. CD002742.
223. Rodrigo G, Pollack C, Rodrigo C, Rowe BH. Heliox for nonintubated acute asthma patients. *Cochrane Database of Systematic Reviews*. 2006; 4: CD002884. DOI: 10.1002/14651858. CD002884.pub2.
224. Tuxen DV. Permissive hypercapnic ventilation. *Am J Respir Crit Care Med*. 1994; 150: 870-4. 225. Strauss L, Hejal R, Galan G, Dixon L, McFadden ER. Observations of the effects of aerosolized albuterol in acute asthma. *Am J Respir Crit Care Med*. 1997; 155: 545-8. 226. Grunfeld A, Fitzgerald JM. Discharge considerations in acute asthma. *Can Respir J*. 1996; 3: 322-4.
227. Udwardia ZF, Harrison BD. An attempt to determine the optimal duration of hospital stay following a severe attack of asthma. *J R Coll Physicians Lond*. 1990; 24: 112-4.
228. Pearson MG, Ryland I, Harrison BD. National audit of acute severe asthma in adults admitted to hospital. Standards of Care Committee, British Thoracic Society. *Qual Health Care*. 1995; 4: 24-30.
229. Guilbert TW, Morgan WJ, Zeiger RS, Mauger DT, Boehmer SJ, Szeffler SJ, et al. Long-term inhaled corticosteroids in preschool children at high risk for asthma. *N. Engl. J Med*. 2006; 354: 1985-97. 230. McKean M, Ducharme F. Inhaled steroids for episodic viral wheeze of childhood. *Cochrane Database Syst Rev*. 2000; 1: CD001107.
231. Bisgaard H, Hermansen MN, Loland L, Halkjaer LB, Buchvald F. Intermittent inhaled corticosteroids in infants with episodic wheezing. *N Engl J Med*. 2006; 354: 1998-2005.
232. Teper AM, Kofman CD, Szulman GA, Vidaurreta SM, Maffey AF. Fluticasone improves pulmonary function in children under 2 years old with risk factors for asthma. *Am. J Respir Crit Care Med*. 2005; 171: 587-90.
233. Szeffler SJ, Phillips BR, Martinez FD, Chinchilli VM, Lemanske RF, Strunk RC, et al. Characterization of within-subject responses to fluticasone and montelukast in childhood asthma. *J Allergy Clin Immunol*. 2005; 115: 233-42.
234. Ducharme FM. Anti-leukotrienes as add-on therapy to inhaled glucocorticoids in patients with asthma: systematic review of current evidence. *BMJ*. 2002; 324: 1545.
235. Simons FE, Villa JR, Lee BW, Teper AM, Lyttle B, Aristizabal G, et al. Montelukast added to budesonide in children with persistent asthma: a randomized, doubleblind, crossover study. *J Pediatr*. 2001; 138: 694-8.
236. Bisgaard H, Zielen S, Garcia Garcia ML, Johnston SL, Gilles L, Menten J, et al. Montelukast reduces asthma exacerbations in 2- to 5-year-old children with intermittent asthma. *Am J Respir Crit Care Med*. 2005; 171: 315-22.
237. Straub DA, Moeller A, Minocchieri S, Hamacher J, Sennhauser FH, Hall GL. The effect of montelukast on lung function and exhaled nitric oxide in infants with early childhood asthma. *Eur Respir J*. 2005; 25: 289-94.
238. Van der Wouden JC, Tasche MJ, Bernsen RM, Uijen JH, De Jongste JC, Ducharme FM. Inhaled sodium cromoglycate for asthma in children. *Cochrane Database Syst Rev*. 2003; CD002173.
239. Bisgaard H. Effect of long-acting beta2 agonists on exacerbation rates of asthma in children. *Pediatr. Pulmonol*. 2003; 36: 391-8.
240. Bisgaard H, Le Roux P, Bjamer D, Dymek A, Vermeulen JH, Hultquist, C. Budesonide/Formoterol Maintenance Plus Reliever Therapy. A new strategy in pediatric asthma. *Chest*. 2006; 130: 1733-43.
241. Rodrigo GJ, Plaza V, Garcia-Marcos L, Castro Rodriguez JA. Safety of regular use of long-acting beta agonists as monotherapy or added to inhaled corticosteroids in asthma: a systematic review with meta-analysis. *Pulmonary Pharmacology and Therapeutics*. 2009; 22: 9-19.
242. Seddon P, Bara A, Ducharme FM, Lasserson TJ. Oral xanthines as maintenance treatment for asthma in children. *Cochrane Database Syst Rev*. 2006; CD002885.
243. Walker S, Monteil M, Phelan K, Lasserson TJ, Walters EH. Anti-IgE for chronic asthma in adults and children. *Cochrane Database Syst Rev*. 2006; CD003559.
244. Powell H, Gibson PG. High dose versus low dose inhaled corticosteroid as initial starting dose for asthma in adults and children. *Cochrane Database of Systematic Reviews*. 2003; 4: CD004109. DOI: 10.1002/14651858.CD004109.pub2.
245. Ni Chroinin M, Greenstone IIG, Ducharme F. Addition of inhaled longacting beta2-agonists to inhaled steroids as first line therapy for persistent asthma in steroid-naive adults. *Cochrane Database of Systematic Reviews*. 2004; 4: CD005307. DOI: 10.1002/14651858.CD005307.pub2.
246. Ducharme F, di Salvo F. Antileukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children. *Cochrane Database of Systematic Reviews*. 2004; 1: CD002314. DOI: 10.1002/14651858.CD002314.pub2.
247. Smith SR, Baty JD, Hodge D. Validation of the pulmonary score: An asthma severity score for children. *Acad Emerg Med*. 2002; 9: 99-104.

248. Wright RO, Santucci KA, Jay GD, Steele DW. Evaluation of pre- and posttreatment pulse oximetry in acute childhood asthma. *Acad Emerg Med.* 1997; 4(2): 114-7.
249. Robertson CF, Smith F, Beck R, Levison H. Response to frequent low doses of nebulized salbutamol in acute asthma. *J Pediatr.* 1985; 106(4): 672-4.
250. Castro-Rodriguez JA, Rodrigo GJ. Beta-agonist through metered-dose inhaler with valved holding chamber versus nebulizer for acute exacerbation of wheezing or asthma in children under 5 years of age: A systematic review with metaanalysis. *J Ped.* 2004; 145: 172-7.
251. Rubilar L, Castro-Rodriguez JA, Girardi G. Randomized trial of salbutamol via metered-dose inhaler with spacer versus nebulizer for acute wheezing in children less than 2 years of age. *Pediatr Pulmonol.* 2000; 29(4): 264-9.
252. Khine H, Fuchs SM, Saville AL. Continuous vs intermittent nebulized albuterol for emergency management of asthma. *Acad Emerg Med.* 1996; 3(11): 1019-24.
253. Plotnick LH, Ducharme FM. Combined inhaled anticholinergic agents and beta-2 agonists for initial treatment of acute asthma in children (Cochrane Review). London: John Wiley & Sons Ltd. The Cochrane Library. 2001; 3.
254. Everard ML, Bara A, Kurian M, Elliot TM, Ducharme F. Anticholinergic drugs for wheeze in children under the age of two years (Cochrane Review). London: John Wiley & Sons Ltd. The Cochrane Library. 2001; 3.
255. Becker JM, Arora A, Scarfone RJ, Spector ND, Fontana-Penn ME, Gracely E, et al. Oral versus intravenous corticosteroids in children hospitalized with asthma. *J Allergy Clin Immunol.* 1999; 103: 586-90.
256. Barnett PL, Caputo GL, Bassin M, Kuppermann N. Intravenous versus oral corticosteroids in the management of acute asthma in children. *Ann Emerg Med.* 1997; 29: 212-7.
257. Schuh S, Reisman J, Alshehri M, Dupuis A, Corey M, Arsenaault R, et al. A comparison of inhaled fluticasone and oral prednisone for children with severe acute asthma. *N Engl J Med.* 2000; 343: 689-94.
258. Schuh S, Dick PT, Stephens D, Hartley M, Khaikin S, Rodriguez L, et al. High-dose inhaled fluticasone does not replace oral prednisolone in children with mild to moderate acute asthma. *Pediatrics.* 2006; 118: 644-50.
259. Nakanishi AK, Klasner AK, Rubin BK. A randomized controlled trial of inhaled flunisolide in the management of acute asthma in children. *Chest.* 2003; 124: 790-4.
260. Geelhoed GC, Landau LI, Le Souef PN. Evaluation of SaO<sub>2</sub> as a predictor of outcome in 280 children presenting with acute asthma. *Ann Emerg Med.* 1994; 23(6): 1236-41.
261. Bradding P, Rushby I, Scullion J, Morgan MD. As-required versus regular nebulized salbutamol for the treatment of acute severe asthma. *Eur Respir J.* 1999; 13(2): 290-4.
262. Kayani S, Shannon DC. Adverse behavioral effects of treatment for acute exacerbation of asthma in children: a comparison of two doses of oral steroids. *Chest.* 2002; 122(2): 624-8.
263. International Rhinitis Management-Working Group. International Consensus Report on Diagnosis and Management of Rhinitis. *Allergy.* 1994; 49(19): 1-34.
264. Fokkens W, Lund V, Mullol J, EPPO. R. a. N. P. Group. European Position Paper on Rhinosinusitis and Nasal Polyps 2007. *Rhinology.* 2008; (Suppl 20): 1-111. V. Plaza et al / Arch Bronconeumol. 2009;45(Supl 7):2-35.
265. Johansson SG, Bieber T, Dahl R, Friedmann PS, Lanier BQ, Lockey RF, et al. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *J Allergy Clin Immunol.* 2004; 113(5): 832-6.
266. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 Update (in collaboration with the World Health Organization, GA2LEN\* and AllerGen\*\*). *Allergy.* 2008; 63(86): 8-160.
267. Bousquet J, van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol.* 2001; 108(Suppl 5): S147-334.
268. Ciprandi G, Cirillo I, Vizzaccaro A, Tosca M, Passalacqua G, Pallestrini E, et al. Seasonal and perennial allergic rhinitis: is this classification adherent to real life? *Allergy.* 2005; 60(7): 882-7.
269. Bauchau V, Durham SR. Epidemiological characterization of the intermittent and persistent types of allergic rhinitis. *Allergy.* 2005; 60(3): 350-3.
270. Valero A, Ferrer M, Sastre J, Navarro AM, Monclus L, Marti-Guadano E, et al. A new criterion by which to discriminate between patients with moderate allergic rhinitis and patients with severe allergic rhinitis based on the Allergic Rhinitis and its Impact on Asthma severity items. *J Allergy Clin Immunol.* 2007; 120: 359-65.
271. Bauchau V, Durham SR. Prevalence and rate of diagnosis of allergic rhinitis in Europe. *Eur Respir J.* 2004; 24(5): 758-64.
272. Pereira C, Valero A, Loureiro C, Davila I, Martinez-Cocera C, Murio C, et al. Iberian study of aeroallergens sensitisation in allergic rhinitis. *Eur Ann Allergy Clin Immunol.* 2006; 38(6): 186-94.
273. Navarro A. Rinitis. *Alergologica 2005. Factores epidemiologicos, clinicos y socioeconomicos de las enfermedades alergicas en Espana.* Madrid: Luzan 5 S.A. de ediciones. 2006. p. 107-32.
274. Bjorksten B, Clayton T, Ellwood P, Stewart A, Strachan D. Worldwide time trends for symptoms of rhinitis and conjunctivitis: Phase III of the International Study of Asthma and Allergies in Childhood. *Pediatr Allergy Immunol.* 2008; 19(2): 110-24.
275. Gendo K, Larson EB. Evidencebased diagnostic strategies for evaluating suspected allergic rhinitis. *Ann Intern Med.* 2004; 140(4): 278-89.
276. Crobach MJ, Hermans J, Kaptein AA, Ridderikhoff J, Petri H, Mulder JD. The diagnosis of allergic rhinitis: how to combine the medical history with the results of radioallergosorbent tests and skin prick tests. *Scand J Prim Health Care.* 1998; 16(1): 30-6.
277. Malm L, Gerth van Wijk R, Bachert C. Guidelines for nasal provocations with aspects on nasal patency, airflow, and airflow resistance. International Committee on Objective Assessment of the Nasal Airways, International Rhinologic Society. *Rhinology.* 2000; 38(1): 1-6.
278. Togias A. Rhinitis and asthma: evidence for respiratory system integration. *J Allergy Clin Immunol.* 2003; 111(6): 1171-83; quiz 1184.
279. Leynaert B, Neukirch C, Kony S, Guenegou A, Bousquet J, Aubier M, et al. Association between asthma and rhinitis according to atopic sensitization in a population-based study. *J Allergy Clin Immunol.* 2004; 113(1): 86-93.
280. Castillo JA, Mullol J. Comorbilidad de rinitis y asma en Espana. *Arch Bronconeumol.* 2008; 44: 593-9.
281. Navarro AM, Valero A, Julia B, Quirze S. Coexistence of asthma and allergic rhinitis in adult patients attending clinics: ONEAIR Study. *J Investig Allergol Clin Immunol.* 2008; 18(4): 233-8.
282. Arnedo-Pena A, Garcia-Marcos L, Garcia Hernandez G, Aguinagua Ontoso I, Gonzalez Diaz C, Morales Suarez-Varela M, et al. Time trends and geographical variations in the prevalence of symptoms of allergic rhinitis in 6-7-year-old children from eight areas of Spain according to the ISAAC. *An Pediatr (Barc.)* 2005; 62(3): 229-36.



283. Linneberg A, Henrik Nielsen N, Frolund L, Madsen F, Dirksen A, et al. The link between allergic rhinitis and allergic asthma: a prospective population-based study. *The Copenhagen Allergy Study. Allergy.* 2002; 57(11): 1048-52.
284. Guerra S, Sherrill DL, Martinez FD, Barbee RA. Rhinitis as an independent risk factor for adult-onset asthma. *J Allergy Clin Immunol.* 2002; 109(3): 419-25.
285. Bousquet J, Gaugris S, Kocevar VS, Zhang Q, Yin DD, Polos PG, et al. Increased risk of asthma attacks and emergency visits among asthma patients with allergic rhinitis: a subgroup analysis of the investigation of montelukast as a partner agent for complementary therapy [corrected]. *Clin Exp Allergy.* 2005; 35(6): 723-7.
286. Price D, Zhang Q, Kocevar VS, Yin DD, Thomas M. Effect of a concomitant diagnosis of allergic rhinitis on asthma-related health care use by adults. *Clin Exp Allergy.* 2005; 35(3): 282-7.
287. Sazonov Kocevar V, Thomas J, Jonsson L, Valovirta E, Kristensen F, Yin DD, et al. Association between allergic rhinitis and hospital resource use among asthmatic children in Norway. *Allergy.* 2005; 60(3): 338-42.
288. Boulay ME, Boulet LP. Lower airway inflammatory responses to repeated very low-dose allergen challenge in allergic rhinitis and asthma. *Clin Exp Allergy.* 2002; 32(10):1441-7.
289. Gaga M, Lambrou P, Papageorgiou N, Koulouris NG, Kosmas E, Fragakis S, et al. Eosinophils are a feature of upper and lower airway pathology in nonatopic asthma, irrespective of the presence of rhinitis. *Clin Exp Allergy.* 2000; 30(5): 663-9.
290. Taramaraz P, Gibson PG. Intranasal corticosteroids for asthma control in people with coexisting asthma and rhinitis. *Cochrane Database Syst Rev.* 2003; (4): CD003570.
291. Bousquet J, van Cauwenberge P, Ait Khaled N, Bachert C, Baena-Cagnani CE, Bouchard J, et al. Pharmacologic and anti-IgE treatment of allergic rhinitis ARIA update (in collaboration with GA2LEN). *Allergy.* 2006; 61(9): 1086-96.
292. Passalacqua G, Durham SR. Allergic rhinitis and its impact on asthma update: allergen immunotherapy. *J Allergy Clin Immunol.* 2007; 119(4): 881-91.
293. Simons FE. H1-antihistamines in children. *Clin Allergy Immunol.* 2002; 17: 437-64.
294. Pasquali M, Baiardini I, Rogkakou A, Riccio AM, Gamalero C, Descalzi D, et al. Canonica. Levocetirizine in persistent allergic rhinitis and asthma: effects on symptoms, quality of life and inflammatory parameters. *Clin Exp Allergy.* 2006; 36(9): 1161-7.
295. Canonica GW, Tarantini F, Compalati E, Penagos M. Efficacy of desloratadine in the treatment of allergic rhinitis: a meta-analysis of randomized, double-blind, controlled trials. *Allergy.* 2007; 62(4): 359-66.
296. Hore I, Georgalas C, Scadding G. Oral antihistamines for the symptom of nasal obstruction in persistent allergic rhinitis—a systematic review of randomized controlled trials. *Clin Exp Allergy.* 2005; 35(2): 207-12.
297. Simons FE. Advances in H1- antihistamines. *N Engl J Med.* 2004; 351(21): 2203-17.
298. Leurs R, Church MK, Tagliabata M. H1-antihistamines: inverse agonism, antiinflammatory actions and cardiac effects. *Clin Exp Allergy.* 2002; 32(4): 489-98.
299. Owen CG, Shahm A, Henshaw K, Smeeth L, Sheikh A. Topical treatments for seasonal allergic conjunctivitis: systematic review and meta-analysis of efficacy and effectiveness. *Br J Gen Pract.* 2004; 54(503): 451-6.
300. Weiner JM, Abramson MJ, Puy RM. Intranasal corticosteroids versus oral H1 receptor antagonists in allergic rhinitis: systematic review of randomised controlled trials. *BMJ.* 1998; 317(7173): 1624-9.
301. Yanez A, Rodrigo GJ. Intranasal corticosteroids versus topical H1 receptor antagonists for the treatment of allergic rhinitis: a systematic review with metaanalysis. *Ann Allergy Asthma Immunol.* 2002; 89(5): 479-84.
302. Barnes ML, Bialosterski BT, Gray RD, Fardon TC, Lipworth BJ. Decongestant effects of nasal xylometazoline and mometasone furoate in persistent allergic rhinitis. *Rhinology.* 2005; 43(4): 291-5.
303. Rodrigo GJ, Yanez A. The role of antileukotriene therapy in seasonal allergic rhinitis: a systematic review of randomized trials. *Ann Allergy Asthma Immunol.* 2006; 96(6): 779-86.
304. Borum P, Mygind N, Schultz Larsen F. Intranasal ipratropium: a new treatment for perennial rhinitis. *Clin Otolaryngol Allied Sci.* 1979; 4(6): 407-11.
305. Schuller DE, Selcow JE, Joos TH, Hannaway PJ, Hirsch SR, Schwartz HJ, et al. A multicenter trial of nedocromil sodium, 1% nasal solution, compared with cromolyn sodium and placebo in ragweed seasonal allergic rhinitis. *J Allergy Clin Immunol.* 1990; 86(4 Pt 1): 554-61.
306. Chervinsky P, Casale T, Townley R, Tripathy I, Hedgecock S, Fowler-Taylor A, et al. Omalizumab, an anti-IgE antibody, in the treatment of adults and adolescents with perennial allergic rhinitis. *Ann Allergy Asthma Immunol.* 2003; 91(2): 160-7.
307. Wilson DR, Lima MT, Durham SR. Sublingual immunotherapy for allergic rhinitis: systematic review and metaanalysis. *Allergy.* 2005; 60(1): 4-12.
308. Calderon MA, Alves B, Jacobson M, Hurwitz B, Sheikh A, Durham S. Allergen injection immunotherapy for seasonal allergic rhinitis. *Cochrane Database Syst Rev.* 2007: CD001936.
309. Custovic A, Wijk RG. The effectiveness of measures to change the indoor environment in the treatment of allergic rhinitis and asthma: ARIA update (in collaboration with GA(2) LEN). *Allergy.* 2005; 60(9): 1112-5.
310. Murphy VE, Clifton VL, Gibson PG. Asthma exacerbations during pregnancy: incidence and association with adverse pregnancy outcomes. *Thorax.* 2006; 61(2): 169-76. V. Plaza et al / *Arch Bronconeumol.* 2009;45(Supl 2):2-35 35.
311. Clifton V. Maternal asthma during pregnancy and fetal outcomes: potential mechanisms and possible solutions. *Curr Opin Allergy Clin Immunol.* 2006; 6(5): 307-11.
312. Kircher S, Schatz M, Long L. Variables affecting asthma course during pregnancy. *Ann Allergy Asthma Immunol.* 2002; 89(5): 437-8.
313. Demissie K, Breckenridge MB, Rhoads GG. Infant and maternal outcomes in the pregnancies of asthmatic women. *Am J Respir Crit Care Med.* 1998; 158(4): 1091-5.
314. Clifton VL, Giles WB, Smith R, Bisits AT, Hempenstall PA, Kessell CG, et al. Alterations of placental vascular function in asthmatic pregnancies. *Am J Respir Crit Care Med.* 2001; 164(4): 546-53.
315. Bakhireva LN, Schatz M, Jones KL, Tucker CM, Slymen DJ, Kloroff-Cohen HS, et al. OTIS Collaborative Research Group. Fetal sex and maternal asthma control in pregnancy. *J Asthma.* 2008; 45(5): 403-7.
316. Schatz M, Zeiger RS, Hoffman CP, Harden K, Forsythe A, Chilingar L, et al. Perinatal outcomes in the pregnancies of asthmatic women: a prospective controlled analysis. *Am J Respir Crit Care Med.* 1995; 151(4): 1170-4.
317. Wendel PJ, Ramin SM, Barnett-Hamm C, Rowe TF, Cunningham FG. Asthma treatment in pregnancy: a randomized controlled study. *Am J Obstet Gynecol.* 1996; 175(1): 150-4.
318. Schatz M, Zeiger RS, Harden K. The safety of asthma and allergy medications during pregnancy. *J Allergy Clin Immunology.* 1997; 100: 301-6.

319. NAEPP 2004. National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program Asthma and Pregnancy Working Group. NAEPP expert panel report. Managing asthma during pregnancy: recommendations for pharmacologic treatment-2004 update. *J Allergy Clin Immunol*. 2005; 115(1): 31-3.
320. Asthma in pregnancy. ACOG Practice Bulletin No. 90. American College of Obstetricians and Gynecologists. *Obstet Gynecol*. 2008; 111: 457-64. 321. Kallen B, Rydhstroem H, Aberg A. Congenital malformations after the use of inhaled budesonid in early pregnancy. *Obstet. Gynecol*. 1999; 93: 392-5. V. Plaza et al / *Arch Bronconeumol*. 2009;45(Supl 7):2-35.
322. Rayburn WF, Atkinson BD, Gilbert K. Short term effects of inhaled albuterol on maternal and fetal circulations. *Am J Obstet Gynecolog*. 1994; 170: 770-3.
323. Park-Wyllie L, Mazzotta P, Pastuszak A, Moretti ME, Beique L, Hunnisset L, et al. Birth defects after maternal exposure to corticosteroids: prospective cohort study and metaanalysis of epidemiological studies. *Teratology*. 2000; 62: 385.
324. Czeizel AE, Rockembauer M. Population based case-control study of teratogenic potential of corticosteroids. *Teratology*. 1997; 56:335-40.
325. Rey E, Boulet LP. Asthma in pregnancy. *BMJ*. 2007; 334: 582-5.
326. Barnes PJ, Woolcock AJ. Difficult asthma. *Eur Respir J*. 1998; 12: 1209-18.
327. Lopez Vina A, Agüero Balbin R, Aller Alvarez JL, Bazus Gonzalez T, Cosío BG, de Diego Damia A, et al. Normativa para el asma de control difícil. *Arch Bronconeumol*. 2005; 41: 513-23.
328. Robinson DS, Campbell DA, Durham SR, Pfeffer J, Barnes PJ, Chung KF. Asthma and Allergy Research Group of the National Heart and Lung Institute. Systematic assessment of difficult-to-treat asthma. *Eur Respir J*. 2003; 22: 478-83.
329. Wainwright NW, Surtees PG, Wareham NJ, Harrison BD. Psychosocial factors and incident asthma hospital admissions in the EPIC-Norfolk cohort study. *Allergy*. 2007; 62: 554-60.
330. Berry MA, Hargadon B, Shelley M, Parker D, Shaw DE, Green RH, et al. Evidence of a role of tumor necrosis factor alpha in refractory asthma. *N Engl J Med*. 2006; 354: 697-708.
331. Morjaria JB, Chauhan AJ, Babu KS, Polosa R, Davies DE, Holgate ST. The role of a soluble TNFalpha receptor fusion protein (etanercept) in corticosteroid refractory asthma: a double blind, randomised, placebo controlled trial. *Thorax*. 2008; 63: 584-91.
332. Wenzel S. Severe asthma in adults. *Am J Respir Crit Care Med*. 2005; 172: 149-60.
333. Miranda C, Busacker A, Balzar S, Trudeau J, Wenzel SE. Distinguishing severe asthma phenotypes: role of age at onset and eosinophilic inflammation. *J Allergy Clin Immunol*. 2004; 113: 101-8.
334. Bousquet J, Cabrera P, Berkman N, Buhl R, Holgate S, Wenzel S, et al. The effect of treatment with omalizumab, an anti-IgE antibody, on asthma exacerbations and emergency medical visits in patients with severe persistent asthma. *Allergy*. 2005; 60:302-8.
335. Bernstein IL, Bernstein DI, Chan-Yeung M, Malo JL. Definitions and classification of asthma in the workplace. En: Bernstein IL, Chan-Yeung M, Malo JL, Bernstein DI, editores. *Asthma in the workplace*. 3.a ed. New York: Marcel Dekker. 2006. p. 1-8.
336. Malo JL, Chan-Yeung M. *J Allergy Clin Immunol*. 2008. p. 23. Epub ahead of print.
337. Kogevinas M, Zock JP, Jarvis D, Kromhout H, Lillienberg L, Plana E, et al. Exposure to substances in the workplace and new-onset asthma: an international prospective population-based study (ECRHS-II). *Lancet*. 2007; 28: 370: 336-41.
338. Malo JL. Prevention of occupational asthma. Proceedings of the first Jack Pepys occupational asthma symposium. *Am J Respir Crit Care Med*. 2003; 167: 463-4.
339. Jeal H, Draper A, Jones M, Harris J, Welsh K, Taylor AN, et al. HLA associations with occupational sensitization to rat lipocalin allergens: a model for other animal allergies? *J Allergy Clin Immunol*. 2003; 111: 795-9.
340. Malo JL, Lemiere C, Desjardins A, Cartier A. Prevalence and intensity of rhinoconjunctivitis in subjects with occupational asthma. *Eur Respir J*. 1997; 10: 1513-5.
341. Karjalainen A, Mortikainen R, Khukka T, Saarinen K, Uitt T. Risk of asthma among Finnish patients with occupational rhinitis. *Chest*. 2003; 123: 283-88.
342. Pronk A, Preller L, Raulf-Heimsoth M, Jonkers IC, Lammers JW, Wouters IM, et al. Respiratory symptoms, sensitization, and exposure response relationships in spray painters exposed to isocyanates. *Am J Respir Crit Care Med*. 2007; 176(11): 1090-7.
343. Chan-Yeung M, Malo JL. Occupational asthma. *N Engl J Med*. 1995; 333: 107-12.
344. Vandenplas O, Cartier A, Malo JL. Occupational challenge test. En: Bernstein IL, Chan-Yeung M, Malo JL, Bernstein DI, editores. *Asthma in the workplace*. 3.a ed. New York: Marcel Dekker; 2006. p. 227-52.
345. Rachiotis G, Savani R, Brant A, MacNeill SJ, Newman-Taylor A, Cullinan P. The outcome of occupational asthma after cessation of exposure: a systematic review. *Thorax*. 2007; 62: 147-52.
346. Padoan M, Pozzato V, Simoni M, Zedda L, Milan G, Bononi L, et al. Longterm followup of toluene diisocyanate-induced asthma. *Eur Respir J*. 2003; 21: 637-40.
347. Cullinan P, Tarlo S, Nemery B. The prevention of occupational asthma. *Eur Respir J*. 2003; 22: 853-60.
348. Brooks SM, Weiss MR, Bernstein IL. Reactive airways dysfunction syndrome (RADS): persistent asthma syndrome after high level irritant exposures. *Chest*. 1985; 88: 376-84.
349. Tarlo SM, Boulet LP, Cartier A, Cockcroft D, Cote J, Hargreave FE, et al. Canadian Thoracic Society guidelines for occupational asthma. *Can Respir J*. 1998; 5: 289-300.
350. Brooks SM, Hammad Y, Richards I, Giovinco-Barbas J, Jenkins K. The spectrum of irritant-induced asthma. Sudden and not-so-sudden onset and the role of allergy. *Chest*. 1998; 113: 42-9.
351. Tarlo SM, Balmes J, Balkissoon R, Beach J, Beckett W, Bernstein D, et al. Diagnosis and management of work-related asthma: American College Of Chest Physicians Consensus Statement. *Chest*. 2008; 134(Suppl 3): 1S-41S.
352. Henneberger PK. Work-exacerbated asthma. *Curr Opin Allergy Clin Immunol*. 2007; 7: 146-51.
353. Christopher KL, Wood RP, Eckert RC, Blager FB, Raney RA, Souhrada JF. Vocal cord dysfunction presenting as asthma. *N Engl J Med*. 1983; 308(26): 1566-70.
354. Wood RP, Milgrom H. Vocal cord dysfunction. *J Allergy Clin Immunol*. 1996; 98(3): 481-5.
355. Kayani, S, Shannon DC. Vocal cord dysfunction associated with exercise in adolescent girls. *Chest*. 1998; 113(2): 540-2.
356. McFadden ER, Zawadzki DK. Vocal cord dysfunction masquerading as exercise induced asthma. a physiologic cause for "choking" during athletic activities. *Am J Respir Crit Care Med*. 1996; 153(3): 942-7.
357. Newman, KB, Mason UG, Schmalzing KB. Clinical features of vocal cord dysfunction. *Am J Respir Crit Care Med*. 1995; 152: 1382-6. 358. Doshi DR, Weinberger MM. Longterm outcome of vocal cord dysfunction. *Ann Allergy Asthma Immunol*. 2006; 96(6): 794-9.