- Cheung D, Timmers MC, Zwinderman AH, et al. Long-term effects of a long-acting beta 2-adrenoceptor agonist, salmeterol, on airway hyperresponsiveness in patients with mild asthma. N Engl J Med 1992;327:1198–203.
- Castle W, Fuller R, Hall J, et al. Serevent nationwide surveillance study: comparison of salmeterol with salbutamol in asthmatic patients who require regular bronchodilator treatment. BMJ 1993;306:1034

 –7.
- Nelson HS, Weiss ST, Bleecker ER, et al. The Salmeterol Multicenter Asthma Research Trial: a comparison of usual pharmacotherapy for asthma or usual pharmacotherapy plus salmeterol. Chest 2006;129:15–26.
- Sears MR, Ottosson A, Radner F, et al. Long-acting beta-agonists: a review of formoterol safety data from asthma clinical trials. Eur Respir J 2009;33:21–32.
- Huang EJ, Reichardt LF. Neurotrophins: roles in neuronal development and function. *Annu Rev Neurosci* 2001:24:677–736.
- Braun A, Lommatzsch M, Mannsfeldt A, et al. Cellular sources of enhanced brainderived neurotrophic factor production in a mouse model of allergic inflammation. Am J Respir Cell Mol Biol 1999;21:537–46.
- Lommatzsch M, Braun A, Renz H. Neurotrophins in allergic airway dysfunction: what the mouse model is teaching us. Ann NY Acad Sci 2003;992:241–9.
- Braun A, Lommatzsch M, Neuhaus-Steinmetz U, et al. Brain-derived neurotrophic factor (BDNF) contributes to neuronal dysfunction in a model of allergic airway inflammation. Br J Pharmacol 2004;141:431–40.
- Hahn C, Islamian AP, Renz H, et al. Airway epithelial cells produce neurotrophins and promote the survival of eosinophils during allergic airway inflammation. J Allergy Clin Immunol 2006;117:787–794.
- Lommatzsch M, Schloetcke K, Klotz J, et al. Brain-derived neurotrophic factor in platelets and airflow limitation in asthma. Am J Respir Crit Care Med 2005;171:115–20.
- Virchow JC, Julius P, Lommatzsch M, et al. Neurotrophins are increased in bronchoalveolar lavage fluid after segmental allergen provocation. Am J Respir Crit Care Med 1998;158:2002–5.
- Dolovich J, Hargreave FE, Jordana M, et al. Late-phase airway reaction and inflammation. J Allergy Clin Immunol 1989;83:521–4.
- Lommatzsch M, Klotz J, Virchow JC. Postnatal dexamethasone for lung disease of prematurity. N Engl J Med 2004;350:2715

 –8.
- Noga O, Hanf G, Schaper C, et al. The influence of inhalative corticosteroids on circulating nerve growth factor, brain-derived neurotrophic factor and neurotrophin-3 in allergic asthmatics. Clin Exp Allergy 2001;31:1906–12.
- Lommatzsch M, Zingler D, Schuhbaeck K, et al. The impact of age, weight and gender on BDNF levels in human platelets and plasma. Neurobiol Aging 2005;26:115–23.

- Pauwels RA, Lofdahl CG, Postma DS, 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.
- Bateman ED, Boushey HA, Bousquet J, 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
- Cockcroft DW, Davis BE. Mechanisms of airway hyperresponsiveness. J Allergy Clin Immunol 2006;118:551–9.
- Keir S, Page C, Spina D. Bronchial hyperresponsiveness induced by chronic treatment with albuterol: role of sensory nerves. J Allergy Clin Immunol 2002;110:388–94.
- Zaidi SI, Jafri A, Doggett T, et al. Airway-related vagal preganglionic neurons express brain-derived neurotrophic factor and TrkB receptors: implications for neuronal plasticity. Brain Res 2005;1044:133

 –43.
- Bennedich Kahn L, Gustafsson LE, Olgart Hoglund C. Brain-derived neurotrophic factor enhances histamine-induced airway responses and changes levels of exhaled nitric oxide in guinea pigs in vivo. Eur J Pharmacol 2008;595:78–83.
- Fujimura H, Altar CA, Chen R, et al. Brain-derived neurotrophic factor is stored in human platelets and released by agonist stimulation. Thromb Haemost 2002;87:728–34.
- Pitchford SC, Momi S, Baglioni S, et al. Allergen induces the migration of platelets to lung tissue in allergic asthma. Am J Respir Crit Care Med 2008;177:604—12.
- Pitchford SC, Riffo-Vasquez Y, Sousa A, et al. Platelets are necessary for airway wall remodeling in a murine model of chronic allergic inflammation. Blood 2004;103:639–47.
- Edwards MR, Haas J, Panettieri RA, et al. Corticosteroids and beta2 agonists differentially regulate rhinovirus-induced interleukin-6 via distinct cis-acting elements. J Biol Chem 2007:282:15366–75.
- Shieh PB, Ghosh A. Molecular mechanisms underlying activity-dependent regulation of BDNF expression. J Neurobiol 1999;41:127–34.
- Wechsler ME, Lehman E, Lazarus SC, et al. beta-Adrenergic receptor polymorphisms and response to salmeterol. Am J Respir Crit Care Med 2006;173:519–26.
- Hall IP, Blakey JD, Al Balushi KA, et al. Beta2-adrenoceptor polymorphisms and asthma from childhood to middle age in the British 1958 birth cohort: a genetic association study. Lancet 2006;368:771–9.
- Bleecker ER, Postma DS, Lawrance RM, et al. Effect of ADRB2 polymorphisms on response to longacting beta2-agonist therapy: a pharmacogenetic analysis of two randomised studies. Lancet 2007;370:2118–25.

Lung alert

Steroids do not improve RSV-related wheeze in children

Respiratory syncytial virus (RSV)-related lower respiratory tract infection is common in infants and is often followed by recurrent wheeze and morbidity. This double-blind placebo controlled trial investigated whether early glucocorticoids prevent recurrent wheeze.

The 243 participants were infants (aged <13 months) admitted to hospital with RSV (confirmed by immunofluorescence) from 19 clinical centres. They were randomised to receive beclometasone or placebo for 3 months and were followed up for 1 year. The primary outcome measure was number of days with wheeze.

No significant difference was found in the number of days or proportion of infants with wheeze. However, a temporary small relative reduction (32%) in wheeze was noted in the steroid group compared with the placebo group in the first 6 months in those infants who did not require mechanical ventilation (n = 221). Secondary outcome measures did not show evidence of side effects or a positive effect on health-related quality of life. The authors conclude that steroids have no major effect on recurrent wheeze post-RSV infection, and general early use is not advocated. They suggest that future studies investigate ventilated infants separately. Interestingly, this research supports other work which shows that inhaled steroids provide a partially effective strategy in children with postviral episodic wheezing; further research is warranted.

Ermers MJJ, Rovers MM, van Woensel JB, et al on behalf of the RSV Corticosteroid Study Group. The effect of high dose inhaled corticosteroids on wheeze in infants after respiratory syncytial virus infection: randomised double blind placebo controlled trial. BMJ 2009;338:b897.

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