World Journal of Clinical Cases

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.12998/wjcc.v3.i6.499

World J Clin Cases 2015 June 16; 3(6): 499-503
ISSN 2307-8960 (online)

MINIREVIEWS

Nasobronchial interaction

Cemal Cingi, Nuray Bayar Muluk, Bengu Cobanoglu, Tolgahan Çatli, Oğuzhan Dikici

Cemal Cingi, Department of Otorhinolaryngology, Medical Faculty, Eskisehir Osmangazi University, 26020 Eskisehir, Turkey
Nuray Bayar Muluk, Department of Otorhinolaryngology, Medical Faculty, Kirikkale University, 71450 Kirikkale, Turkey
Bengu Cobanoglu, Department of Otorhinolaryngology, Trabzon Research and Training Hospital, 61040 Trabzon, Turkey
Tolgahan Çatli, Department of Otorhinolaryngology, Bozyaka Research and Training Hospital, 35170 İzmir, Turkey
Oğuzhan Dikici, Department of Otorhinolaryngology, Şevket Yılmaz Training and Research Hospital, 16000 Bursa, Turkey

Author contributions: All the authors solely contributed to this paper.

Conflict-of-interest: The authors declare that there is no conflict of interest.

Correspondence to: Dr. Nuray Bayar Muluk, Professor, Department of Otorhinolaryngology, Medical Faculty, Kirikkale University, Zirvekent 2, Etap Sitesi, C-3 blok, No: 62/43, 71450 Kirikkale, Turkey. nurayb@hotmail.com
Telephone: +90-312-4964073
Fax: +90-312-4964073

Received: October 30, 2014
Peer-review started: October 31, 2014
First decision: November 14, 2014
Revised: January 31, 2015
Accepted: March 18, 2015
Article in press: March 20, 2015
Published online: June 16, 2015

Abstract

Upper and lower airways can be considered as a unified morphofunctional unit. In this paper, nasobronchial interactions are evaluated based on literature.To discuss nasobronchial interactions, literature review from PubMed since 1982 is evaluated. Data base was including the terms "nasobronchial interaction, nasal and bronchial". Asthma and rhinosinusitis may be associated with environmental factors and immunological predisposition. Treatment of rhinosinusitis may decrease asthma exacerbations. It was concluded that "one airway, one disease"-concept may be accepted when considering naso-bronchial interaction. Asthma treatment should also mean treating the nose as good as treating patients with nasal symptoms. To reach the succesful results ıt should be associated with evaluation of lung functions.

Key words: Nasal; Bronchial; Nasobronchial interaction; Reflex; Airway

Core tip: Upper and lower airways may be accepted as unified morphofunctional unit. This concept is defined as nasobronchial interaction.

Cingi C, Muluk NB, Cobanoglu B, Çatli T, Dikici O. Nasobronchial interaction. *World J Clin Cases* 2015; 3(6): 499-503 Available from: URL: http://www.wjgnet.com/2307-8960/full/v3/i6/499.htm DOI: http://dx.doi.org/10.12998/wjcc.v3.i6.499

INTRODUCTION

Upper and lower airways may be accepted as unified morphofunctional unit. Likewise rhinosinusal disorders and lower airway diseases have interrelation. Inflammatory cytokines may play a role for the interaction between cells[1].

During infections of upper respiratory tract such as rhinosinusiitis, asthma development may occur[2,3]. Atopic dermatitis in children, and also allergies to the

food may be the first sign for developing of allergic rhinitis (AR) and astma[4].

In this paper, nasobronchial interactions were evaluated thoroughly by the means of literature review from PubMed since 1982. Data base was depended on the terms of nasobronchial interaction, nasal and bronchial.

NASAL FUNCTON

Nose works as "air-conditioner". Cold air through induces bronchospasm in asthmatic patients. Nose humidifies the air which inhaled nasally. In allergic rhinitis patients, exposure to allergens increase bronchial hyper-reactivity[5-8].

MECHANISMS FOR NASO-BRONCHIAL INTERACTION

Impaired nasal function, pulmonary aspiration of nasal contents, the nasal-bronchial reflex and increased absorption of inflammatory mediators in the blood stream maybe responsible for lower airway dysfunction in AR[7]. They also cause the interaction between the nose and the lung. After nasal allergen application, no allergen deposition was shown in the lungs by radiolabeled allergen[6]. Cold and dry air exposure may cause immediate bronchoconstriction[8]. Nasal provocation with methacholine also increase lower airway resistance in asthma and AR patients[9].

Mast cells and eosinophils are the major effector cells in AR and asthma[10,11]. Eosinophils migrate to the tissues from the blood and this process is depend on the expression of cytokines and adhesion molecules[12]. Vascular cell adhesion molecule-1 and E-selectin increased after nasal provocation[13]. After bronchial provocation, mast cell degranulation and increase of of basophils occur in the nasal mucosa[14].

Impaired nasal function

In AR, mouth breathing was observed related to the nasal obstruction. Therefore, with the lower nasal filter function, increased allergen exposure develops. This process is resulted in hyperresponsivity of the airway. If additional chronic rhino-sinusitis and/or nasal polyposis were present, surgery help to improve nasal functions. In these patients, asthma control could be done better[15]. When nose blocked with a clip, response to cat-allergen was not detected in patients with cat allergy[16].

Aspiration of nasal contents

Inhale particles may be removed by the help of the mucociliary clearance. With this function and beat of the cilia, particles were carried toward the pharynx. In AR patients, secretions contain inflammatory mediators and cells[7,17]. When allergens inhaled, there was swelling of the nasal mucosa[18].

Nasobronchial reflex

The trigeminal nevre is responsible for afferent sensory innervation of the nose. Efferent parasympathetic fibers are carried in the Vidian nevre. Vagal nevre supports afferent and efferent innervation of the lower airways[19]. Sneezing, coughing or bronchoconstriction occur with the help of reflex mechanisms. The receptors were present in the nose, trachea, larynx and respiratory tract. The are sensitive to the mechanical or chemical factors. Cold dry exposure of nasal mucosa can cause immediate bronchoconstriction in asthmatic patients[6,20,21].

Nasobronchial reflex is another mechanism for interaction between upper and lower airways. Receptors are localize in the nose, sinuses and pharynx. The signals were transferred to the medulla by trigeminal, facial and glossopharyngeal nerves[22]. In the medulla, connections with vagal nevre were performed and bronchoconstriction occur[23].

Triggers of the reflex

In infectious conditions of the nose and lungs, virus and bacteria may trigger the reflex system. Smoking, pollutant agents in the work places and environment may cause chronic inflammation[24]. Beta-blockers or aspirin, cold dry air exposure, and physical exercise may also trigger the AR and asthma[25].

Increased absorption of inflammatory mediators in the blood stream

Increase in the eosinophil count is detected in AR and asthma patients in the blood[26]. Nasal provocation, performed with methacholine, also increases the lower airway resistance. It may be said that systemic mediators may induce lower airway resistance[9]. In AR and asthma, inflammatory cells and progenitors may play a role[27-29].

RHINOSINUSITIS AND ASTHMA

Symptoms of rhinosinusitis

Syptoms of rhinosinusitis are known as nasal congestion, discharge, purulence and postnasal drip; hyposmia, facial pressure, fever, halitosis, dental pain and headache. Chronic rhinosinusitis (CRS) may damage to the mucociliary clearance. CRS is an independent risk factor for asthma[2,3,30,31].

Epidemiology

Rhinosinusitis and asthma were coexistently detected in 34%-50% of patients. In asthmatic patients, concomitant rhinosinusitis were present up to 84%[24].

Clinical appearence

In rhinosinusitis patients, there is the possibility of having asthma. When nasal disease was treated, asthma control maybe easier due to the reducing of

bronchial hyperresponsiveness. Therefore, therapeutic approach to asthma and rhinosinusitis should be planned together[32].

Treatment

Medical treatments or surgery for rhinosinusitis help the reduce of respiratory symptoms and impove the asthma. Cold air inhalation causes the decrease FEV1 in asthmatic patients[5].

AR AND ASTHMA

AR is a risk factor for asthma development[33]. Whereas, in same cases, asthma starts first. Exercise induces bronchoconstriction in most asthmatic patients. It may be related to to alterations in the osmolarity of the liquid covering the epithelial layer. This process may be resulted release of chemical mediators originating in mast cells[34].

Epidemiology

In 19%-38% of AR patients, there are concomitant asthma. Moreover, 30%-80% of asthmatic patients also have AR. Rhinitis symptoms were reported in 98.9% of allergic asthmatics and in 78.4% of non-allergic asthmatics[35]. Bronchial hyperreactivity was observed in most of the AR patients[36]. In AR petients, 40% have involvement of the lower airways. Additionally, allergic asthma patients have concomitant rhinitis symptoms as a 80%[37,38].

Potential mechanisms

The allergic response starts with the uptake of the antigen by antigen presenting cells, in particular dendritic cells[39,40]. Dendritic cells present the antigen to T lymphocytes in the regional lymph nodes[41,42]. B cells recognize antigen with surface immunoglobulin (sIg) receptors. The T cell receptor recognizes antigens and activation of the it stimulates the naive T helper cell, a ThO cell. It differentiates to either a Th1 or a Th2 subset[43,44].

Activation of Thl cell causes the release of IL-2 and lNF-y. Additionally IL-4, IL-5, IL-1O and IL-13 are also produced by Th2 cells. Th2 cytokines are also involved in IgE synthesis (IL-4)[45,46].

Nerve growth factor (NGF) and NGF receptors are expressed in the nasal mucosa[47]. In patients with AR and allergic asthma, serum levels[48-50]; and nasal and bronchial fluid levels of NGF increase[51-53].

Microbial stimuli

Exposure to endotoxins reduces the risk of developing allergic rhinitis and asthma during the first years of life. Chlamydia pneumoniae infection has been suggested as a possible causative factor for asthma[54]. It was also reported as protective against the development of asthma in children[55]. In infancy, bacterial infection is associated with a reduced prevalence of atopic eczema, allergic rhinitis and asthma[56]. Viral respiratory infections stimulate nasal allergic inflammation in atopic patients; and virus-induced airway hyperresponsiveness develops[57].

Treatment

The medical treatment of AR reduces the risk of asthma-related events in asthmatic patients[58]. Nasal corticosteroids stabilize bronchial hyperreactivity in allergic rhinitis patients with seasonal asthma[37,59]. The leukotriene receptor antagonists are less effective than antihistamines and nasal steroids in upper airway disease[60,61].

Allergen immunotherapy reduces asthma symptoms. This therapy also improves nasal disease[62,63]. By immunotherapy, progression of allergic rhinitis to bronchial asthma may be prevented. Specific immuno-therapy with seasonal allergic rhinitis significantly reduced the asthma development risk[64,65].

UPPER AIRWAYS AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

The correlation between chronic obstructive pulmonary disease and upper airway inflammation are reported. The relation between nasal and bronchial inflammation by estimating the IL-8 concentration were reported[66].

CONCLUSION

Upper and lower airways are thought as one functional entity. Local allergen exposure of the respiratory system induces mucosal inflammation. A "unified airway" concept suggests that the upper and lower airways function as a single unit[67]. The nasobronchial interaction may be suggested as present in airway. Trigger agents for naso-bronchial reflex are important to initiate the symptoms.

REFERENCES

1 **Passali D**, Benedetto de F, Benedetto de M, Chiaravalloti F, Damiani V, Passali FM, Bellussi LM. Rhino-Bronchial Syndrome. The SIO-AIMAR (Italian Society of Otorhinolaryngology, Head Neck Surgery-Interdisciplinary Scientific Association for the Study of the Respiratory Diseases) survey. *Acta Otorhinolaryngol Ital* 2011; **31**: 27-34 [PMID: 21808460]

2 **Bousquet J**, Van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001; **108**: S147-S334 [PMID: 11707753 DOI: 10.1067/mai.2001.118891]

3 Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. *Lancet* 1998; **351**: 1225-1232 [PMID: 9643741 DOI: 10.1016/S0140-6736(97)07302-9]

4 **Ciprandi G**, De Amici M, Giunta V, Marseglia A, Marseglia G. Serum interleukin-9 levels are associated with clinical severity in children with atopic dermatitis. *Pediatr Dermatol* 2013; **30**: 222-225 [PMID: 22612419 DOI: 10.1111/j.1525-1470.2012.01766]

5 **McLane ML**, Nelson JA, Lenner KA, Hejal R, Kotaru C, Skowronski M, Coreno A, Lane E, McFadden ER. Integrated response of the upper and lower respiratory tract of asthmatic subjects to frigid air. *J Appl Physiol* (1985) 2000; **88**: 1043-1050

[PMID: 10710402]
6 **Corren J**, Adinoff AD, Irvin CG. Changes in bronchial responsiveness following nasal provocation with allergen. *J Allergy Clin Immunol* 1992; **89**: 611-618 [PMID: 1740589 DOI: 10.1016/0091-6749(92)90329-Z]
7 **Corren J**. Allergic rhinitis and asthma: how important is the link? *J Allergy Clin Immunol* 1997; **99**: S781-S786 [PMID: 9042071 DOI: 10.1016/S0091-6749(97)70127-1]
8 **Nolte D**, Berger D. On vagal bronchoconstriction in asthmatic patients by nasal irritation. *Eur J Respir Dis Suppl* 1983; **128** (Pt 1): 110-115 [PMID: 6578061]
9 **Littell NT**, Carlisle CC, Millman RP, Braman SS. Changes in airway resistance following nasal provocation. *Am Rev Respir Dis* 1990; **141**: 580-583 [PMID: 2178523 DOI: 10.1164/ajrccm/141.3.580]
10 **Bousquet J**, Vignola AM, Campbell AM, Michel FB. Pathophysiology of allergic rhinitis. *Int Arch Allergy Immunol* 1996; **110**: 207-218 [PMID: 8688666 DOI: 10.1159/000237289]
11 **Busse WW**, Calhoun WF, Sedgwick JD. Mechanism of airway inflammation in asthma. *Am Rev Respir Dis* 1993; **147**: S20-S24 [PMID: 8494196 DOI: 10.1164/ajrccm/147.6_Pt_2.S20]
12 **Djukanović R**, Roche WR, Wilson JW, Beasley CR, Twentyman OP, Howarth RH, Holgate ST. Mucosal inflammation in asthma. *Am Rev Respir Dis* 1990; **142**: 434-457 [PMID: 2200318 DOI: 10.1164/ajrccm/142.2.434]
13 **Braunstahl GJ**, Overbeek SE, Kleinjan A, Prins JB, Hoogsteden HC, Fokkens WJ. Nasal allergen provocation induces adhesion molecule expression and tissue eosinophilia in upper and lower airways. *J Allergy Clin Immunol* 2001; **107**: 469-476 [PMID: 11240947 DOI: 10.1067/mai.2001.113046]
14 **Braunstahl GJ**, Overbeek SE, Fokkens WJ, Kleinjan A, McEuen AR, Walls AF, Hoogsteden HC, Prins JB. Segmental bronchoprovocation in allergic rhinitis patients affects mast cell and basophil numbers in nasal and bronchial mucosa. *Am J Respir Crit Care Med* 2001; **164**: 858-865 [PMID: 11549546 DOI: 10.1164/ajrccm.164.5.2006082]
15 **Dunlop G**, Scadding GK, Lund VJ. The effect of endoscopic sinus surgery on asthma: management of patients with chronic rhinosinusitis, nasal polyposis, and asthma. *Am J Rhinol* 1999; **13**: 261-265 [PMID: 10485011 DOI: 10.2500/105065899782102809]
16 **Wood RA**, Eggleston PA. The effects of intranasal steroids on nasal and pulmonary responses to cat exposure. *Am J Respir Crit Care Med* 1995; **151**: 315-320 [PMID: 7842184 DOI: 10.1164/ajrccm.151.2.7842184]
17 **Samoliński B**, Szczesnowicz-Dabrowska P. Relationship between inflammation of upper and lower respiratory airways. *Otolaryngol Pol* 2002; **56**: 49-55 [PMID: 12053668]
18 **Hellings PW**, Hessel EM, Van Den Oord JJ, Kasran A, Van Hecke P, Ceuppens JL. Eosinophilic rhinitis accompanies the development of lower airway inflammation and hyper-reactivity in sensitized mice exposed to aerosolized allergen. *Clin Exp Allergy* 2001; **31**: 782-790 [PMID: 11422139 DOI: 10.1046/j.1365-2222.2001.01081.x]
19 **Undem BJ**, McAlexander M, Hunter DD. Neurobiology of the upper and lower airways. *Allergy* 1999; **54** Suppl 57: 81-93 [PMID: 10565483 DOI: 10.1111/j.1398-9995.1999.tb04409.x]
20 **Rosenberg GL**, Rosenthal RR, Norman PS. Inhalation challenge with ragweed pollen in ragweed-sensitive asthmatics. *J Allergy Clin Immunol* 1983; **71**: 302-310 [PMID: 6826990]
21 **Schumacher MJ**, Cota KA, Taussig LM. Pulmonary response to nasal-challenge testing of atopic subjects with stable asthma. *J Allergy Clin Immunol* 1986; **78**: 30-35 [PMID: 3722633 DOI: 10.1016/0091-6749(86)90111-9]
22 **Sluder G**. Asthma as a nasal reflex. *JAMA* 1919; **73**: 589-591 [DOI: 10.1001/jama.1919.02610340021006]
23 **Settipane GA**. Allergic rhinitis--update. *Otolaryngol Head Neck Surg* 1986; **94**: 470-475 [PMID: 3086809]
24 **Bresciani M**, Paradis L, Des Roches A, Vernhet H, Vachier I, Godard P, Bousquet J, Chanez P. Rhinosinusitis in severe asthma. *J Allergy Clin Immunol* 2001; **107**: 73-80 [PMID: 11149994 DOI: 10.1067/mai.2001.111593]
25 **Fontanari P**, Zattara-Hartmann MC, Burnet H, Jammes Y. Nasal eupnoeic inhalation of cold, dry air increases airway resistance in asthmatic patients. *Eur Respir J* 1997; **10**: 2250-2254 [PMID: 9387948 DOI: 10.1183/09031936.97.10102250]
26 **Alvarez MJ**, Olaguibel JM, García BE, Rodríquez A, Tabar AI, Urbiola E. Airway inflammation in asthma and perennial allergic rhinitis. Relationship with nonspecific bronchial responsiveness and maximal airway narrowing. *Allergy* 2000; **55**: 355-362 [PMID: 10782520 DOI: 10.1034/j.1398-9995.2000.00312.x]
27 **Inman MD**, Ellis R, Wattie J, Denburg JA, O'Byrne PM. Allergen-induced increase in airway responsiveness, airway eosinophilia, and bone-marrow eosinophil progenitors in mice. *Am J Respir Cell Mol Biol* 1999; **21**: 473-479 [PMID: 10502557 DOI: 10.1165/ajrcmb.21.4.3622]
28 **Palframan RT**, Collins PD, Williams TJ, Rankin SM. Eotaxin induces a rapid release of eosinophils and their progenitors from the bone marrow. *Blood* 1998; **91**: 2240-2248 [PMID: 9516121]
29 **Denburg JA**, Inman MD, Sehmi R, Uno M, O'Byrne PM. Hemopoietic mechanisms in allergic airway inflammation. *Int Arch Allergy Immunol* 1998; **117**: 155-159 [PMID: 9831802 DOI: 10.1159/000024004]
30 **Jarvis D**, Newson R, Lotvall J, Hastan D, Tomassen P, Keil T, Gjomarkaj M, Forsberg B, Gunnbjornsdottir M, Minov J, Brozek G, Dahlen SE, Toskala E, Kowalski ML, Olze H, Howarth P, Krämer U, Baelum J, Loureiro C, Kasper L, Bousquet PJ, Bousquet J, Bachert C, Fokkens W, Burney P. Asthma in adults and its association with chronic rhinosinusitis: the GA2LEN survey in Europe. *Allergy* 2012; **67**: 91-98 [PMID: 22050239]
31 **Jani AL**, Hamilos DL. Current thinking on the relationship between rhinosinusitis and asthma. *J Asthma* 2005; **42**: 1-7 [PMID: 15801321 DOI: 10.1081/JAS-200044744]
32 **Caimmi D**, Marseglia A, Pieri G, Benzo S, Bosa L, Caimmi S. Nose and lungs: one way, one disease. *Ital J Pediatr* 2012; **38**: 60 [PMID: 23098057]
33 **Compalati E**, Ridolo E, Passalacqua G, Braido F, Villa E, Canonica GW. The link between allergic rhinitis and asthma: the united airways disease. *Expert Rev Clin Immunol* 2010; **6**: 413-423 [PMID: 20441427 DOI: 10.1586/eci.10.15]
34 **Valero A**, Serrano C, Valera JL, Barberá A, Torrego A, Mullol J, Picado C. Nasal and bronchial response to exercise in patients with asthma and rhinitis: the role of nitric oxide. *Allergy* 2005; **60**: 1126-1131 [PMID: 16076296]
35 **Simons FE**. Allergic rhinobronchitis: the asthma-allergic rhinitis link. *J Allergy Clin Immunol* 1999; **104**: 534-540 [PMID: 10482824 DOI: 10.1016/S0091-6749(99)70320-9]
36 **Ciprandi G**, Cirillo I. The lower airway pathology of rhinitis. *J Allergy Clin Immunol* 2006; **118**: 1105-1109 [PMID: 17088136]
37 **Jarjour NN**, Peters SP, Djukanović R, Calhoun WJ. Investigative use of bronchoscopy in asthma. *Am J Respir Crit Care Med* 1998; **157**: 692-697 [PMID: 9517577 DOI: 10.1164/ajrccm.157.3.9705020]
38 **Bardin PG**, Van Heerden BB, Joubert JR. Absence of pulmonary aspiration of sinus contents in patients with asthma and sinusitis. *J Allergy Clin Immunol* 1990; **86**: 82-88 [PMID: 2370390]
39 **Fokkens WJ**, Bruijnzeel-Koomen CA, Vroom TM, Rijntjes E, Hoefsmit EC, Mudde GC, Bruijnzeel PL. The Langerhans cell: an underestimated cell in atopic disease. *Clin Exp Allergy* 1990; **20**: 627-638 [PMID: 2083402 DOI: 10.1111/j.1365-2222.1990.tb02701.x]
40 **Hoogsteden HC**, Verhoeven GT, Lambrecht BN, Prins JB. Airway inflammation in asthma and chronic obstructive pulmonary disease with special emphasis on the antigen-presenting dendritic cell: influence of treatment with fluticasone propionate. *Clin Exp Allergy* 1999; **29** Suppl 2: 116-124 [PMID: 10421834 DOI: 10.1046/j.1365-2222.1999.00020.x]
41 **Cella M**, Sallusto F, Lanzavecchia A. Origin, maturation and antigen presenting function of dendritic cells. *Curr Opin Immunol* 1997; **9**: 10-16 [PMID: 9039784 DOI: 10.1016/S0952-7915(97)80153-7]
42 **Lanzavecchia A**. Mechanisms of antigen uptake for presentation. *Curr Opin Immunol* 1996; **8**: 348-354 [PMID: 8794000 DOI: 10.1016/S0952-7915(96)80124-5]
43 **Banchereau J**, Briere F, Caux C, Davoust J, Lebecque S, Liu YJ, Pulendran B, Palucka K. Immunobiology of dendritic cells. *Annu*

Rev Immunol 2000; **18**: 767-811 [PMID: 10837075]
44 **Coyle AJ**, Gutierrez-Ramos JC. The expanding B7 superfamily: increasing complexity in costimulatory signals regulating T cell function. *Nat Immunol* 2001; **2**: 203-209 [PMID: 11224518]
45 **Romagnani S**. The Th1/Th2 paradigm and allergic disorders. *Allergy* 1998; **53**: 12-15 [PMID: 9825989]
46 **Del Prete GF**, De Carli M, D'Elios MM, Maestrelli P, Ricci M, Fabbri L, Romagnani S. Allergen exposure induces the activation of allergen-specific Th2 cells in the airway mucosa of patients with allergic respiratory disorders. *Eur J Immunol* 1993; **23**: 1445-1449 [PMID: 8100770 DOI: 10.1002/eji.1830230707]
47 **Piotrowska VM**, Piotrowski WJ, Kurmanowska Z, Marczak J, Górski P, Antczak A. Rhinosinusitis in COPD: symptoms, mucosal changes, nasal lavage cells and eicosanoids. *Int J Chron Obstruct Pulmon Dis* 2010; **5**: 107-117 [PMID: 20631813]
48 **Raap U**, Goltz C, Deneka N, Bruder M, Renz H, Kapp A, Wedi B. Brain-derived neurotrophic factor is increased in atopic dermatitis and modulates eosinophil functions compared with that seen in nonatopic subjects. *J Allergy Clin Immunol* 2005; **115**: 1268-1275 [PMID: 15940146 DOI: 10.1016/j.jaci.2005.02.007]
49 **Raap U**, Werfel T, Goltz C, Deneka N, Langer K, Bruder M, Kapp A, Schmid-Ott G, Wedi B. Circulating levels of brain-derived neurotrophic factor correlate with disease severity in the intrinsic type of atopic dermatitis. *Allergy* 2006; **61**: 1416-1418 [PMID: 17073871 DOI: 10.1111/j.1398-9995.2006.01210.x]
50 **Bonini S**, Lambiase A, Bonini S, Angelucci F, Magrini L, Manni L, Aloe L. Circulating nerve growth factor levels are increased in humans with allergic diseases and asthma. *Proc Natl Acad Sci USA* 1996; **93**: 10955-10960 [PMID: 8855290 DOI: 10.1073/pnas.93.20.10955]
51 **Sanico AM**, Stanisz AM, Gleeson TD, Bora S, Proud D, Bienenstock J, Koliatsos VE, Togias A. Nerve growth factor expression and release in allergic inflammatory disease of the upper airways. *Am J Respir Crit Care Med* 2000; **161**: 1631-1635 [PMID: 10806167]
52 **Virchow JC**, Julius P, Lommatzsch M, Luttmann W, Renz H, Braun A. Neurotrophins are increased in bronchoalveolar lavage fluid after segmental allergen provocation. *Am J Respir Crit Care Med* 1998; **158**: 2002-2005 [PMID: 9847299 DOI: 10.1164/ajrccm.158.6.9803023]
53 **Olgart Höglund C**, de Blay F, Oster JP, Duvernelle C, Kassel O, Pauli G, Frossard N. Nerve growth factor levels and localisation in human asthmatic bronchi. *Eur Respir J* 2002; **20**: 1110-1116 [PMID: 12449162 DOI: 10.1183/09031936.02.00205402]
54 **Hahn DL**, Dodge RW, Golubjatnikov R. Association of Chlamydia pneumoniae (strain TWAR) infection with wheezing, asthmatic bronchitis, and adult-onset asthma. *JAMA* 1991; **266**: 225-230 [PMID: 2056624 DOI: 10.1001/jama.1991.03470020051031]
55 **Schmidt SM**, Müller CE, Wiersbitzky SK. Inverse association between Chlamydia pneumoniae respiratory tract infection and initiation of asthma or allergic rhinitis in children. *Pediatr Allergy Immunol* 2005; **16**: 137-144 [PMID: 15787871 DOI: 10.1111/j.1399-3038.2005.00229.x]
56 **Resch A**, Schlipköter U, Crispin A, Behrendt H, Heinrich J, Wichmann HE, Ring J, Schäfer T; KORA study group. Atopic disease and its determinants -- a focus on the potential role of childhood infection. *Clin Exp Allergy* 2004; **34**: 1184-1191 [PMID: 15298557 DOI: 10.1111/j.1365-2222.2004.02016.x]
57 **Alho OP**, Karttunen R, Karttunen TJ. Nasal mucosa in natural colds: effects of allergic rhinitis and susceptibility to recurrent sinusitis. *Clin Exp Immunol* 2004; **137**: 366-372 [PMID: 15270854 DOI: 10.1111/j.1365-2249.2004.02530.x]
58 **Crystal-Peters J**, Neslusan C, Crown WH, Torres A. Treating allergic rhinitis in patients with comorbid asthma: the risk of asthma-related hospitalizations and emergency department visits. *J Allergy Clin Immunol* 2002; **109**: 57-62 [PMID: 11799366 DOI: 10.1067/mai.2002.120554]
59 **Corren J**, Manning BE, Thompson SF, Hennessy S, Strom BL. Rhinitis therapy and the prevention of hospital care for asthma: a case-control study. *J Allergy Clin Immunol* 2004; **113**: 415-419 [PMID: 15007339 DOI: 10.1016/j.jaci.2003.11.034]
60 **Pullerits T**, Praks L, Skoogh BE, Ani R, Lötvall J. Randomized placebo-controlled study comparing a leukotriene receptor antagonist and a nasal glucocorticoid in seasonal allergic rhinitis. *Am J Respir Crit Care Med* 1999; **159**: 1814-1818 [PMID: 10351924 DOI: 10.1164/ajrccm.159.6.9810016]
61 **Nathan RA**, Yancey SW, Waitkus-Edwards K, Prillaman BA, Stauffer JL, Philpot E, Dorinsky PM, Nelson HS. Fluticasone propionate nasal spray is superior to montelukast for allergic rhinitis while neither affects overall asthma control. *Chest* 2005; **128**: 1910-1920 [PMID: 16236835]
62 **La Rosa M**, Lionetti E, Leonardi S, Salpietro A, Bianchi L, Salpietro C, Miraglia Del Giudice M, Ciprandi G, Marseglia GL. Specific immunotherapy in children: the evidence. *Int J Immunopathol Pharmacol* 2011; **24**: 69-78 [PMID: 22032790]
63 **Caffarelli C**, Cardinale F, Povesi C, Chinellato I, Sterpeto Loffredo M. Optimal duration of SLIT. *Int J Immunopathol Pharmacol* 2009; **22**: 17-22 [PMID: 19944005]
64 **Möller C**, Dreborg S, Ferdousi HA, Halken S, Høst A, Jacobsen L, Koivikko A, Koller DY, Niggemann B, Norberg LA, Urbanek R, Valovirta E, Wahn U. Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-study). *J Allergy Clin Immunol* 2002; **109**: 251-256 [PMID: 11842293 DOI: 10.1067/mai.2002.121317]
65 **Polosa R**, Li Gotti F, Mangano G, Paolino G, Mastruzzo C, Vancheri C, Lisitano N, Crimi N. Effect of immunotherapy on asthma progression, BHR and sputum eosinophils in allergic rhinitis. *Allergy* 2004; **59**: 1224-1228 [PMID: 15461606 DOI: 10.1111/j.1398-9995.2004.00537.x]
66 **Hurst JR**, Wilkinson TM, Perera WR, Donaldson GC, Wedzicha JA. Relationships among bacteria, upper airway, lower airway, and systemic inflammation in COPD. *Chest* 2005; **127**: 1219-1226 [PMID: 15821198 DOI: 10.1378/chest.127.4.1219]
67 **Lohia S**, Schlosser RJ, Soler ZM. Impact of intranasal corticosteroids on asthma outcomes in allergic rhinitis: a meta-analysis. *Allergy* 2013; **68**: 569-579 [PMID: 23590215 DOI: 10.1111/all.12124]

P- Reviewer: Coskun A, Eweiss A, Saedi B, Unal M
S- Editor: Song XX **L- Editor**: A **E- Editor**: Wu HL

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com