SUMMARY

Acute exacerbations of asthma are the major cause of morbidity and mortality of the disease and are difficult to prevent and treat. Asthma exacerbations are associated with several factors, including allergen exposure, air pollution and stress, but the major cause of exacerbations is respiratory virus infection. Respiratory viral infections cause >80% of asthma exacerbations in children and >50% in adults. The most prevalent viruses detected during exacerbations are the rhinoviruses. Respiratory viruses may induce asthma exacerbations through direct effects on their main target, airway epithelium, as well as via systemic immune reaction.

Key words: asthma exacerbations, respiratory virus infections, rhinoviruses
INTRODUCTION

Asthma is a chronic inflammatory disorder of the airways in which many genetic and environmental factors contribute to the expression of phenotype. The natural history of asthma can be strongly influenced by allergens, irritants, or infections that promote inflammation of the smaller airways. Asthma exacerbations are associated with several factors, including allergen exposure, air pollution, and stress, but the major cause of exacerbations is respiratory virus infection. An association between colds and asthma exacerbations has long been recognised, but early studies yielded low virus detection rates of approximately 10%. These studies used virus detection methods that have low sensitivity for rhinoviruses (RV) and coronaviruses, which between them account for the majority of colds. The optimum method for virus detection is with polymerase chain reaction (PCR)-based methods, and studies using PCR have shown that respiratory viruses are responsible for a much higher proportion of asthma exacerbations than was previously suspected (1, 2). Respiratory viruses have also been detected in a high proportion of more severe exacerbations requiring hospitalization. Respiratory viruses can act synergistically with other factors that cause asthma exacerbations. Admission to the hospital with an acute asthma exacerbation is strongly associated with the combination of sensitization and exposure to an allergen, and concurrent viral infection. The presence of high ambient levels of nitrogen dioxide prior to a viral infection is more associated with lower respiratory tract symptoms and greater falls in peak expiratory flow during the exacerbation. Although many respiratory viruses can provoke acute asthma symptoms, RV are most often detected, especially during the spring and fall RV seasons. In fact, the spring and fall peaks in hospitalisations because of asthma closely coincide with patterns of RV isolation within the community. Influenza and respiratory syncytial viruses (RSVs) are somewhat more frequently detected in children over the age of two years in the wintertime, but seem to account for a smaller fraction of asthma flares (3). Furthermore, RV infections are frequently detected in children over the age of two years who present to emergency departments with acute wheezing, and in adults, are detected in approximately half of asthma-related acute care visits (4). In addition to provoking asthma, RV infections can also increase lower airway obstruction in individuals with other chronic airway diseases (e.g., chronic obstructive lung disease, cystic fibrosis), and in infants and the elderly. Thus, common cold viruses that produce relatively mild illnesses in most people can cause severe pulmonary problems in selected individuals.

INFLAMMATORY MEDIATORS

Viral infection in asthmatic patients induces more lower respiratory tract symptoms and falls in lung functi-
in sputum samples and both the peak cold symptoms and time to virus clearance from sputum samples in asthmatic patients infected with rhinovirus, suggesting that a stronger Th1 immune response is associated with less severe colds and faster viral clearance (15). There is also evidence that weak Th1 responses are associated with more severe disease in infections with another respiratory virus - respiratory syncytial virus. It has been suggested that this may be another mechanism through which virus infection can exacerbate a preexisting Th2-mediated lung disease (3, 10).

Most immunologic research into asthma has focused on the role of the adaptive immune response in disease pathogenesis, but evidence is emerging suggesting that innate immunity may be impaired in asthmatic patients (13). Wark et al. have shown that bronchial epithelial cells obtained from asthmatic patients support markedly increased rhinovirus replication compared to cells from nonasthmatic patients (16). This is accompanied by reduced apoptosis of epithelial cells in the asthmatic patients and impaired production of the antiviral cytokine IFN-β. Impaired IFN-β production and cells apoptosis result in greater virus replication, eventually leading to cytotoxic cells death with the release of inflammatory mediators and large numbers of intact viral particles. The administration of IFN-β restores the virus protection observed in epithelial cells from normal airways. If confirmed in vivo, it will be interesting to see whether these novel observations translate into new therapies aimed at augmenting or replacing deficient IFN-β production in asthma patients (17).

References

EGZACERBACIJE ASTME I VIRUSI

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Sažetak

Akutne egzacerbacije astme su glavni uzročnici morbiditeta i mortaliteta kod ove bolesti i veoma su teške za sprečavanje i lečenje. Egzacerbacije astme udružene su sa više faktora, uključujući ekspoziciju alergenima, aerozagađenje i stres, ali su glavni uzročnici egzacerbacije virusne respiratorne infekcije. One uzrokuju >80% egzacerbacija astme kod dece i >50% kod odraslih. Najprevalentniji virus detekovan tokom egzacerbacije astme je rinovirus. Egzacerbaciju astme respiratorni virusi indukuju direktnim dejstvom na epitel disajnih puteva ili posredstvom sistemskih imunih reakcija.

Ključne reči: egzacerbacija astme, respiratorne virusne infekcije, rinovirusi