

Infección por virus respiratorio sincitial (VRS) e hiperreactividad bronquial

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A number of studies have implicated severe infections early in life by respiratory syncytial virus (RSV) as a risk factor for the subsequent development of asthma. It has been suggested that RSV infection may enhance the development of "allergic" inflammatory responses when the host is exposed to allergens after an episode of bronchiolitis. It has also been suggested that neuronal mechanisms are important in RSV infection and subsequent airway hyperreactivity. Recently, we advanced the hypothesis that immune and neuronal mechanisms may be linked and that combined neuro-immune responses may be in play.

In the airways, a dense network of sensory nerve fibers is strategically placed just below the epithelial surface so that any change in the bronchial environment may stimulate the release of the proinflammatory neuropeptide substance P. During RSV infection, stimulation of these nerves causes a marked increase in airway vascular permeability when compared with pathogen-free rats, and results in an increase in overall inflammatory status. Our work has revealed that these changes are mediated by the high affinity receptor for substance P (NK1 receptor), whose expression is greatly increased by RSV. This up-regulation presumably occurs at the gene expression level, as NK1 mRNA levels increase substantially during and after RSV infection. More recent work from our group has shown that T-lymphocytes subpopulations within the bronchial-associated lymphoid tissue (BALT) in the lungs of RSV-infected rats express high levels of the NK1 receptor. As a consequence, stimulation of the sensory nerves by any airborne irritant may cause a cycle of inflammation mediated by NK1-expressing T-lymphocytes. We propose that this mechanism may es-

tablish important neuro-immune interactions, which undergo long-term dysregulation following RSV infection and predispose to airway inflammation and hyperreactivity.

Finally, the recent epidemiological evidence supporting the role of early RSV infection as an important risk factor for the subsequent development of childhood asthma has boosted interest in the longer-term consequences of RSV prophylaxis. In particular, data obtained in animal models of bronchiolitis suggest that monoclonal antibodies against the fusion (F) protein of RSV protect the respiratory tract from persistent virus-induced inflammation when given before or in the early phase of the infection. Thus, the administration of anti-RSV antibodies to high-risk infants may limit the severity of the acute airway inflammation as well as protecting against the respiratory sequelae associated with this virus.

SUGGESTED FURTHER READING

- Lemanske Jr RF, Piedimonte G, Wenzel S, Elliott GR. 2000. Asthma and RSV disease.
- Stein RT, Sherrill D, Morgan WJ, Holberg CJ, Halonen M, Taussig LM, Wright AL, Martinez FD. Respiratory syncytial virus in early life and risk of wheeze and allergy by age 13 years. *Lancet* 1999; 354: 541-545.
- Piedimonte G, Rodriguez MM, King KA, McLean S, Jiang X. Respiratory syncytial virus upregulates expression of the substance P receptor in rat lungs. *Am J Physiol* 1999; 277: L831-L840.
- Piedimonte G, King KA, Holmgren NL, Bertrand PJ, Rodriguez MM, Hirsch RL. A humanized monoclonal antibody against respiratory syncytial virus (palivizumab) inhibits RSV-induced neurogenic-mediated inflammation in rat airways. 2000; 47: 351-356.