bias may occur with telephone surveys of patients and families after a surgical procedure. Finally, the diagnosis of obstructive sleep-disordered breathing on the basis of history findings, with similar assessments of improvement after surgery, does not have the quantitative accuracy of preoperative and postoperative polysomnographic evaluations. Despite these limitations, this study succeeded in showing that intracapsular tonsillar reduction (partial tonsillectomy) shows great promise as a safe effective treatment for children with obstructive sleep-disordered breathing and appears to cause less morbidity than standard tonsillectomy. Additional studies with more long-term follow-up monitoring are required to assess the recurrence rates for both obstructive and infectious tonsillar disease, after this procedure is performed among young children.

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Asthma

PATHOPHYSIOLOGY

EARLY THICKENING OF THE RETICULAR BASEMENT MEMBRANE IN CHILDREN WITH DIFFICULT ASTHMA


Purpose of the Study. To determine whether reticular basement membrane (RBM) thickening is present among children with difficult-to-control asthma and to compare the findings with those for adults with asthma.

Study Population. Subjects were 19 children (6–16 years of age) with difficult-to-control asthma. Control subjects were 10 children (7–16 years of age) without asthma, 10 adults with mild asthma, 6 adults with severe asthma, and 8 healthy adults.

Methods. The 19 asthmatic children underwent bronchoscopy and endobronchial biopsy as part of an asthma evaluation. Patients were treated with oral prednisolone therapy (40 mg/day) for 2 weeks before the biopsy. Exhaled nitric oxide levels were measured before and after the course of corticosteroids. Endobronchial samples were obtained from third-order or higher bronchi on either side of the lung. The control subjects were pediatric patients undergoing bronchoscopy because of other indications. The adults with mild asthma were corticosteroid-naive. Adults with severe asthma underwent biopsy while intubated because of a severe asthma attack. The 8 adult control subjects were nonsmokers. Three biopsy specimens for each patient were fixed immediately and stained for light-microscopic evaluation.

Results. Children with asthma had an average RBM thickness of 8.2 μm (range: 5.4–11.2 μm). Adults with mild asthma had a mean RBM thickness of 8.1 μm (range: 5.8–10.0 μm); adults with severe asthma had a mean RBM thickness of 7.2 μm (range: 2.8–10.0). Adult control subjects had an average RBM thickness of 4.4 μm (range: 3.2–6.3 μm; P < .01); pediatric control subjects had an average RBM thickness of 4.9 μm (range: 3.7–8.3 μm; P < .01). There was no correlation of RBM thickness with duration of asthma or age. The exhaled nitric oxide concentrations before and after prednisolone treatment were 16.9 ppb (range: 1.2–33.4 ppb) and 8.1 ppb (range: 1.3–24.5 ppb), respectively (normal values at the study center: <12.5 ppb). There was no correlation between RBM thickness and exhaled nitric oxide levels.

Conclusions. The authors concluded that RBM thickening is a feature of childhood asthma that is not present among normal control subjects. RBM thickness is a common feature of asthma among adults and children but is not correlated with age, severity, or duration.

Reviewers’ Comments. This study demonstrated that histologic changes in the airways of children with severe asthma, as evidenced by RBM thickening, are similar to those seen among adults. This is one of the few such studies among children and is novel for the inclusion of child and adult control subjects. The authors were unable to show a link between RBM thickness and severity of asthma or a marker of inflammation (exhaled nitric oxide). This information raises questions regarding the timing and appropriateness of antiinflammatory treatment delivered with the hope of preventing airway remodeling among children with asthma. Clinical trials are needed to establish whether it is possible to prevent these changes and whether such prevention is important.

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LIPOPOLYSACCHARIDE-ENHANCED, TOLL-LIKE RECEPTOR 4-DEPENDENT, T HELPER CELL TYPE 2 RESPONSES TO INHALED ANTIGEN


Purpose of the Study. To evaluate the dose-dependent effects of lipopolysaccharide (LPS) (endotoxin) inhalation and LPS-induced activation of toll-like receptor 4 (TLR4) on the generation of T helper (Th) cell type 2-dependent allergic inflammatory responses to an inhaled antigen, ovalbumin (OVA).

Study Population. Wild-type or TLR4-deficient, 6- to 10-week-old, female mice were studied.

Methods. Mice were sensitized with intranasal exposure to LPS-depleted OVA or OVA with either a low (0.1 μg) or high (100 μg) dose of LPS. After intranasal OVA challenge, pulmonary inflammatory responses were assessed through enumerating bronchoalveolar lavage cells, performing histopathologic analyses, measuring OVA-dependent cytokine production by lung-draining lymph node cells, and determining OVA-specific serum antibody levels. Dendritic cell responses to OVA with LPS were evaluated in cytokine production, activation marker expression, and cell migration studies.

Results. After antigen challenge, mice sensitized to OVA with low-dose LPS exhibited a Th2-associated response, with pulmonary eosinophilia, airway mucus secretion, Th2 cytokine (interleukin-5 and -13) production by lymph node cells, and production of high levels of OVA-specific immunoglobulin E and immunoglobulin G1. In contrast, mice sensitized to OVA with high-dose LPS developed a Th1-associated response, with a predominance of neutrophils, no airway mucus secretion, Th1 cytokine (interferon-γ) production by lymph node cells, and production of high levels of OVA-specific immunoglobulin G2a. No pulmonary inflammatory responses were observed with mice sensitized to LPS-depleted OVA. OVA sensitization of TLR4-deficient mice with either low- or high-dose LPS failed to generate inflammatory responses. However, treatment with tumor necrosis factor, which is secreted by LPS-stimulated dendritic cells, compensated.
EARLY THICKENING OF THE RETICULAR BASEMENT MEMBRANE IN CHILDREN WITH DIFFICULT ASTHMA

David W. Hauswirth and Larry W. Williams

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