Beyond Our Pages

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Articles of note . . .

Thymic transplants for DiGeorge syndrome

The immunodeficiency associated with the complete DiGeorge syndrome is thought to result from failure to develop the thymus gland. Although a few cases of DiGeorge syndrome have been treated by transplantation of fetal thymus tissue, the immune reconstitution in these patients may have improved without therapy because some of these patients likely had partial DiGeorge syndrome. In a recent article in the *New England Journal of Medicine*, 5 patients with the complete DiGeorge syndrome were transplanted with cultured postnatal thymic tissue. Although 3 of the patients died from infections or abnormalities unrelated to the transplantation, an immunologic analysis was performed on all of the patients. Interestingly, 2 of the patients had restoration of normal T-cell function. Additionally, biopsy of the grafted thymus tissue showed normal morphologic features including active T-cell proliferation. Furthermore, donor T cells could be detected in some of the patients early after transplantation but there was no evidence of graft-versus-host disease. Thus cultured cells derived from postnatal thymic tissue, which can be readily obtained from children undergoing corrective heart surgery, can be successfully transplanted to restore normal immune function. It is interesting to consider the mechanism by which the partially MHC-mismatched thymic transplants are capable of positively selecting (educating) host T cells. In an accompanying editorial, it is discussed that the thymic epithelium as well as host stem cells that have repopulated the thymus are both responsible for this selection.
(Markert et al. N Engl J Med 1999;341:1180-9.)

Inhibitory role of gamma/delta T cells in airway hyperresponsiveness

Experimental modeling has led to the identification of a critical role for T cells in the development of allergic airway hyperresponsiveness. Most studies have concentrated on the role of T cells that bear the γ/δ T-cell receptor. In a recent report in *Nature Medicine* a new role for T cells expressing the γ/δ T cell receptor has been identified. Interestingly, mice deficient in γ/δ T cells had enhanced airway responsiveness indicating the important role of γ/δ T cells in negative regulation in the lung. Perhaps most interesting, the γ/δ T cell–deficient mice had enhanced airway responsiveness independent of antigen sensitization. In particular, exposure to only 3 doses of aerosolized antigen resulted in marked enhancement of airway responsiveness without any evidence of inflammatory cell infiltration or lymphocyte sensitization. These results identify γ/δ T cells as important cells in the regulation of pulmonary homeostasis and suggest that γ/δ T cells may have an interaction with innate systems in the lung. Further analysis of the importance of this pathway and the mechanisms by which γ/δ T cells negatively regulate airway hyperresponsiveness will likely be informative.
(Lahn M et al. Nat Med 1999;5:1150-6)

Aerobic training in asthmatics

Several previous studies have shown that asthmatics can improve their exercise performance after participating in an aerobic training program. Two recent controlled studies have investigated this further. (1) In one study swimming training of mild-moderate asthmatics for 6 weeks led to about about 50% less decrease in FEV_1 induced by cyclo ergometer exercise challenge. However, there was considerable variation among patients. Bronchial responsiveness to histamine was unaltered. (2) In the other study the effects of a supervised aerobic training program for 8 weeks were a reduction in medication score and the required dosages of inhaled and oral steroids. However, the occurrence of exercise-induced bronchospasm (EIB) did not change after training. Thus it appears that these approaches lead to improvement in some parameters, but EIB and bronchial hyperreactivity may be unaltered.
(1 Matsumoto et al. Thorax 1999;54:196-201)
(2 Neder et al. Thorax 1999;54:202-6)

Improving physician attitudes and practices in asthma care

In an International Drug Education Project, a new educational program for primary care physicians (PCP) was developed and then evaluated. In this program small peer groups of PCP in 4 countries (the Netherlands, Norway, Sweden, and Slovakia) met to discuss patterns of care for their asthma patients in comparison with national guidelines. As a result, there was subsequently significantly improved care (as per guidelines) in inhaled steroid use, treatment of exacerbations, and attitudes concerning overall asthma management. This improvement, although not striking, points out a possibly better way of teaching PCP about asthma management than reliance on handouts and lectures about this subject (which have

not been very effective in US trials).
(Veninga et al. Am J Respir Crit Care Med 1999;160:1254-62)

Emergency asthma treatment in pregnant women

Uncontrolled asthma in pregnancy is associated with many maternal and fetal complications. In a prospective study within the Multicenter Asthma Research Collaboration, 51 pregnant and 500 nonpregnant women seen in the emergency department (ED) with acute asthma flares were interviewed in the ED and 1 week later. Although the severity and duration of the flares before ED treatment were similar in both groups, the pregnant patients were less commonly treated with corticosteroids in the ED and in postdischarge management. The pregnant asthmatics were 2.9 more likely than nonpregnant asthmatics to report continuing symptoms 1 week later. The decreased use of corticosteroids in pregnant asthmatics may reflect exaggerated concerns among ED physicians about the adverse effects of such corticosteroid therapy in pregnant women.
(Cydulka et al. Am J Respir Crit Care Med 1999;160:887-92)

Other articles of interest

- **Vazquez-Torres A et al. Extraintestinal dissemination of *Salmonella* by CD18-expressing phagocytes. Nature 1999;804-8.**
  A new mechanism for the uptake of intestinal bacterial pathogens is described. In particular, CD18-expressing phagocytes in the intestinal tract are demonstrated to transfer intestinal bacterial pathogens into the systemic circulation, thereby promoting humoral immune responses.
- **Stein et al. RSV infection and atopic asthma. Lancet 1999;354:541-5.**
  This large, long-term, epidemiologic study of childhood respiratory diseases indicates that RSV infection in infancy predisposes to wheezing until age 10 years but not later. RSV infection does not correlate with later atopy.
- **Bachert et al. Nasal polyposis—a new concept in their formation. ACI Int 1999;11:130-5.**
  In the basis of their immunohistologic findings, the authors propose a new concept about the formation of nasal polyps.
- **Pearce. How much asthma is due to atopy? Thorax 1999;54:268-72.**
  This editorial reviews the evidence for the association of asthma and atopy with a conclusion that it may be overestimated.
- **Myou et al. Bronchodilator effect of inhaled olprinone in asthma. Am J Respir Crit Care Med 1999;160:817-20.**
  There has been great interest in the possible beneficial effects of inhibitors of phosphodiesterase (PDE) 3 in asthma treatment. Olprinone, a PDE3 inhibitor, induced increases in the FEV_1 of asthmatics to a degree similar to that induced by albuterol.
- **Harlan and Kirk. New concepts in the prevention of graft rejection. JAMA 1999;282:1076-82.**
  A nice brief review of immune concepts involved in graft rejection and its prevention/control, including possible modification of costimulatory receptor signaling.
- **Gorini et al. Chest wall hyperinflation during acute bronchoconstriction. Am J Respir Crit Care Med 1999;160:808-16.**
  Most of the hyperinflation during histamine-induced bronchoconstriction is associated with changes in rib cage volume, not depressed diaphragms. These changes are influenced by sustained postinspiratory activity of the inspiratory muscles.
- **Straub and Mannel. How the immune system puts the brain to sleep. Nat Med 1999;5:877-9.**
  A review of recent findings that may explain why we feel sleepy and lethargic during infections.

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