Increase in respiratory resistance after exercise in conscious guinea pigs.

As a model for exercise-induced asthma.

HIROICHI NAGAI*, TAKEHISA IWAMA, HIROSHI MORI, HIROYUKI NISHIDA, KIYOSHI TAKATSU, YOJI Iikura

We have developed an experimental model for exercise-induced asthma (EIA) using conscious guinea pigs. Respiratory resistance (Rrs) was measured before and after exercise (running). An exercise-induced increase in Rrs occurred 24h after exercise in metyrapone-pretreated guinea pig given an inhalation of lipopolysaccharide or an intratracheal injection of interleukin-5. Present results suggest that the participation of certain kinds of inflammatory cells in bronchoalveolar lavage fluid and a decrease in serum glucocorticoid levels are necessary for the onset of EIA.

An immunopharmacological study of the biphasic allergic skin reaction in mice.

HIROICHI NAGAI*, TOSHIK SAKURAI, NAOKI INAGAKI, HIROSHI MORI

Biphasic skin reactions, with peaks at 1 and 24h after epicutaneous challenge with antigen (immediate phase response: IPR and late phase response: LPR, respectively), were induced ddY, ICR, Balb/c and Balb/c-nu/nu mice passively sensitized with monoclonal IgE antibody 24h before. In WBB6F1-W/W mice, which lack mast cells, only the LPR was observed. Histamine H1 receptor antagonists and the allergic histamine release inhibitors clearly inhibited the IPR, but not the LPR, although prednisolone and dexamethasone inhibited both. Prednisolone also inhibited the LPR in WBB6F1-W/W mice. These results indicate that IgE antibody-dependent biphasic skin reactions consist of a mast cell- and histamine-dependent IPR and a mast cell-independent LPR.

Studies on anti-allergic action of AH 21-132, a novel isozyme-selective phosphodiesterase inhibitor in airways.

HIROICHI NAGAI*, HIROSHI TAKEDA, TAKEHISA IWAMA, SHUJI YAMAGUCHI, HIROSHI MORI

The effects of AH 21-132, a type III and IV phosphodiesterase (PDE) inhibitor, on allergic reactions in the airway were studied by comparing them with the effects of rolipram, a type IV PDE inhibitor, and aminophylline, a non-selective PDE inhibitor. AH 21-132 inhibited the antigen-induced contraction of isolated guinea pig tracheal muscle in vitro, and also inhibited antigen-induced both immediate- and late-phase increase in the airway resistance in guinea pigs. These results suggest that AH 21-132 has an anti-allergic effect in the airway and that these actions may be beneficial for the treatment of allergic bronchial asthma.