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[Lab. of Pharmacology]

**Increase in respiratory resistance after exercise in conscious guinea pigs.**

**As a model for exercise-induced asthma.**

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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.

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[Lab. of Pharmacology]

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

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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 WBB6F<sub>1</sub>-W/W<sup>v</sup> mice, which lack mast cells, only the LPR was observed. Histamine H<sub>1</sub> 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 WBB6F<sub>1</sub>-W/W<sup>v</sup> 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.

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[Lab. of Pharmacology]

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

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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.