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Safety and Efficacy of NPC 567 for the Treatment of Experimentally Induced Rhinovirus Infections. D.I. Bernstein, J.R. Sherwood, E.C. Young, G.M. Schiff. James N. Gamble Institute of Medical Research, Division of Clinical Virology, Cincinnati, Ohio USA.

NPC 567 is a bradykinin antagonist which inhibits *in vitro* responses to bradykinins by competitive blockade of the kinin receptor. Bradykinin has been detected in high concentrations in nasal fluids during rhinovirus infection and can induce many of the signs and symptoms of rhinitis when given intranasally. We therefore conducted a double blind placebo-controlled trial to determine if treatment with NPC 567 could prevent the symptoms of a rhinovirus infection. Forty-two healthy male volunteers, with serum neutralizing antibody titers of $\leq 2$ to the challenge virus were administered 275 pfu of rhinovirus 39 intranasally and were isolated for one week. Twenty-two subjects received NPC 567 and 20 received placebo beginning 32 hrs after viral challenge. Medication was dispensed in metered pump spray applied intranasally (approximately 1 mg per dose) six times daily. All volunteers shed rhinovirus and most (77% of NPC and 80% of placebo) seroconverted to rhinovirus type 39. Volunteers completed symptom questionnaires before each dose of medication and were examined by a physician daily. No significant differences were found in the distribution of subjects who experienced clinically significant colds (73% vs. 80% in NPC and placebo recipients respectively). Similarly no significant differences were found for any of the daily symptoms evaluated including physician and patient assessments or in the quantity of nasal discharge as measured by daily tissue weights. No apparent adverse effects were detected for NPC treatment. Treatment with NPC 567 at this dose appeared safe but was not effective for treating the signs and symptoms of rhinovirus infection.

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Development of an Adult Mouse Model for Studies on Protection Against Rotavirus. R.L. Ward[1], M.M. McNeal[1], J.F. Sheridan[2]. James N. Gamble Institute of Medical Research[1], Division of Clinical Virology, Cincinnati, Ohio; Ohio State University[2], College of Dentistry, Columbus, Ohio USA.

Although mice have been used as a model of rotavirus disease, pathogenesis studies in mice are limited by the short time period after birth in which they are susceptible to rotavius disease (i.e. approximately 15 days). To overcome this limitation, an adult mouse model was developed in which the end point was infection rather than illness. For this model to be useful, the rotavirus administered must consistently cause infection in adult animals. These mice, in turn, must be consistently protected against reinfection by the homotypic strain of rotavirus. The model developed utilized a strain of mouse rotavirus (EDIM) which was adapted to grow in culture by several passages in A104 cells. The unadapted parent virus caused severe diarrhea in newborn mice for a period of at least 7 days and no amelioration of disease was observed with the culture adapted preparation. Oral administration of $10^3$ plaque forming units of this preparation consistently caused infection of Balb C mice 4, 10, 15, 21, 30 and 60 days of age as determined by viral shedding and seroconversion. Reinoculation of these mice with the same virus preparation 2 months after the first inoculation produced no evidence of reinfection. In contrast, infection of infant mice with the heterotypic WC3 bovine rotavirus did not prevent reinfection upon inoculation with the culture adapted EDIM preparation 2 months later. This adult mouse model should be useful in studies of prophylactic and therapeutic treatments of rotavirus infection and disease.