TRANSMISSION AND CONTROL OF RHINOVIRUS Colds

L.C. JENNINGS and E.C. DICK

Department of Preventive Medicine, University of Wisconsin Medical School, Stovall Building, 465 Henry Mall, Madison, Wisconsin 53706.

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With the expanding knowledge of rhinovirus transmission and rhinovirus chemistry, the outlook for control of infections with these agents has brightened considerably. Although rhinoviruses are probably the world's leading cause of respiratory illness, they are surprisingly reluctant transmitters, infecting only about 50% of susceptibles in family-like settings. Current research suggests that rhinoviruses are spread chiefly by aerosol, rather than by fomites or personal contact. It has been possible to interrupt rhinovirus transmission completely by careful use of virucidal facial tissues, which, presumably, smothered aerosols generated by coughing, sneezing and nose blowing. Accordingly, it may be feasible to control rhinovirus (and perhaps other virus) dissemination by appropriate air handling and filtration systems in combination with careful nasal sanitation. Anti-rhinovirus drug development is also moving forward. Although there are over 1,00 rhinovirus serotypes, it has been found that most rhinoviruses attach to a single cell receptor by a single binding site on the virus. Also, the structure of the rhinovirus capsid is now known at the atomic level. These two pieces of knowledge about basic viral architecture appear to open new vistas for reasoned synthesis of antiviral drugs, and some promising compounds are now under investigation. Even interferon has been demonstrated useful in a family setting. On several research fronts, there are good grounds for optimism about control of rhinovirus colds.

TRANSMISSION

Introduction

Rhinoviruses are probably the most frequent cause of the common cold, accounting for 30 to 50 per cent of all acute respiratory illness (8). In children they may cause serious respiratory disease and exacerbations of asthma (19, 37, 40). Infections occur year-round with well defined periods of prevalence in the fall and spring, at least in the Northern Hemsphere (19, 24, 26, 42). Rhinoviral infections are spread from person to person by virus-containing respiratory secretions which may gain entry to a susceptible host's respiratory tract via small or large particle aerosols, by direct contact or by indirect contact involving contaminated environmental objects.

A major obstacle to understanding the importance of each of these possible routes of rhinovirus transmission has been the lack of a natural, reproducible experimental model. Experimental rhinovirus colds, like their natural counterparts (19), spread with surprising difficulty. Very low transmission rates (zero to 9%) have been reported for exposure periods extending from 45 minutes to 72 hours, whether exposure was by
aerosol alone (28) or by all routes (10, 39). Only when the duration of exposure was very substantially increased were appreciably higher attack rates attained. An 88-100% infection rate in eight recipients occurred over 17 days among residents of a small hut in Antarctica (34). The crowding, rather severe colds in the donors, and the long period of time together appear to have contributed to transmission efficiency. In our week-long experiments in childless married couples (11), a transmission rate of 38% (8/24) occurred between rhinovirus-infected donors and recipient spouses. Here, successful transmission was associated with donors who spent many hours with their spouses, had moderate or severe colds, and large amounts of virus in their nasal secretions (p = 0.025 by the two-sample Wilcoxon rank test). Transmission rates dropped sharply in these couples as the peak virus titer in nasal washings decreased: 71% (5/7) for donors with a peak titer of ≥5000 TCID₉₀, 33% (2/6) for those with a peak titer of 1000-5000 TCID₉₀, and 18% (2/11) for those shedding smaller amounts of virus.

**A Transmission Model**

In 1984, we described a human volunteer system in which natural rhinovirus transmission, theoretically by all possible routes, was achieved at predictable rates over time periods up to one week. This system, called the Miniature Field Trial or MFT (39) utilized experimentally-infected adult donors, selected from a pool of infected individuals for their moderate to severe colds, and susceptible (antibody-free to the donors’ virus) adult recipients. Interaction between donors and recipients took place in a single large room (figure 1). In a series of MFT experiments in which we observed recipient infection rates from zero to 100%, the rate of transmission correlated closely with the aggregate number of hours the recipients interacted with the donors (figure 2). About 200 hours of exposure to an individual with a moderately severe cold was needed for an antibody-free adult to have a 50% chance of infection.

Two hundred hours or eight days of exposure required, on average, for transmission to 50% of susceptibles in the MFT model is a long time. How does this time period relate to rhinovirus transmission in the natural setting? It is clear that virus is often shed by an individual for at least eight days. In volunteers, large amounts of rhinovirus (1000 to ≥3,200,000 TCID₉₀/ml of nasal wash specimen) (16, 21) may be shed during the first week of illness (11), and virus may continue to be produced for two to three weeks (21). Natural shedding has been demonstrated as late as 55 days after infection (24). It is also clear from intensive studies in natural settings that secondary attack rates of about 50% are usual over a week or more. In a nursery population in Chicago only three of 13 rhinovirus (RV) types spread at all; the secondary attack rates for those three types among the 22 susceptible children were: RV39, 77% over two weeks, RV36, 50% over one week and a non-typable RV, 42% over two weeks (3). In a second grade Wisconsin school room, attack rates observed over three semesters were: RV19, 18%; non-typable RV, 37%; and RV36, 55% (19). Within a group of 24 neighboring families in our Eagle Heights study, the intra-family attack rates of three spreading rhinovirus types were: RV51, 33%; RV43, 42%; and RV55, 59% (19). In a study of respiratory infection transmission within 48 families in Panama, intra-family secondary attack rates were: RV31, 10.5%; RV1A, 20.6%; RV1B, 26.3%; non-typable RV552, 40.5%; non-typable RV046, 47.3%; and RV39, 56% (41). The above evidence suggests that close exposure for a week to one or more individuals with nat-