CLINICAL INVESTIGATION

Transmission of respiratory viruses using a new viral challenge model

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Commentary

Interest in how respiratory viruses spread has been rekindled by the recent advent of Coronavirus Disease- 2019 (COVID-19), as well as the morbidity and mortality that it causes. Understanding the factors that influence transmission is essential for developing non-pharmaceutical therapies and halting spread. The Respiratory Syncytial Viruses (RSV-A and RSV-B), influenza A and B (Flu), Coronaviruses (CoV), Adenoviruses (AdV), Parainfluenza Viruses (PIV), Human Meta Pneumovirus (HMPV), and bocavirus are among the other common causes of Acute Respiratory Virus Infection (ARI), despite the current focus on infections caused by SARS-CoV-2. 1,2 ARIs have significant negative health and financial effects, resulting in 110 million primary care visits, 20 million missed school and work days, and an approximate 40 billion dollar yearly economic cost in the United States alone.

According to the most recent World Health Organization (WHO) report on the global burden of disease, respiratory infection complications caused three million deaths globally, making them one of the most common infectious causes of death in adults and the number one infectious cause of death in children under the age of five.

In the past, studies on the spread of colds used experimental infection of index cases with the lab-passaged virus. Challenge studies with respiratory viruses are still carried out, but they use virus strains that are produced in accordance with Good Manufacturing Practice (GMP) standards necessary for vaccine manufacture. This is primarily done to evaluate candidate vaccines, antivirals, and host-virus interactions. Comparatively few respiratory virus strains fulfil the necessary GMP requirements since the manufacturing procedure necessitates highly specialized knowledge, tools, and facilities, all of which are expensive. There hasn't been much investigation on how respiratory viruses spread naturally.

Studies that have tried to do this have mostly focused on studying transmission inside of homes or offices, used specialized aerosol collecting equipment, or were limited by difficulty controlling the interactions. These research flaws make it difficult to gauge the impact of interventions and develop tactics to stop transmission, and they draw attention to the need for an infection model that accurately represents the spread of human respiratory viruses in nature. Using controlled contacts between healthy adult volunteers and kids who were hospitalized with ARIs, we sought to assess the viability of a novel approach to identify human-to-human transmission of respiratory viruses.

In a 30-minute controlled experiment that simulated clinical encounters between children and medical professionals, we evaluated the rate of respiratory virus transmission in a hospital context. Because they experience ARIs more frequently than older age groups, have greater rates of respiratory virus positivity than older children and adults, and have higher hospitalization rates for respiratory illnesses, we chose young children with ARIs as our index patients. Because of their expertise, general interest, abilities, and potential acceptability to parents of children with ARIs, we used medical students as contacts. The interactions served as both a feasible platform for multicenter studies and a controlled assessment of the nosocomial spread of respiratory viruses in hospitals.

In our investigation, RT-PCR and sequencing were used to define virus transmission, while symptoms and symptom scores evaluated the interactions' safety and acceptability. According to non-significant variations in the symptom ratings of contacts in whom transmission did and did not occur, and a small number of reports of modified

Jackson scores of >6 and severity scores of 4, the aftereffects of the interactions were well tolerated by contacts. The accuracy of symptom scores in detecting virus transmission was quite low. Two contacts with symptom scores of greater than 6 had negative RT-PCR results. This could be because adults tend to shed smaller titers of respiratory viruses than young children do, or it could be caused by an infection with a virus that is not detected by the multiplex RT-PCR.

On the other hand, only two of the 14 encounters where RV transmission took place reported modified Jackson scores >6. The similarity of symptom scores between infected and uninfected contacts is consistent with other RT-PCR studies that found high rates (65%–97%) of asymptomatic ARIs in an ambulatory population and a four-fold higher incidence of asymptomatic RV infections than symptomatic RV infections among university students. The design and ventilation of facilities that provide care for vulnerable patients, as well as the usage of personal protective equipment (PPE), are all significantly impacted by these observations.

By employing brief, standardized encounters, this trial was successful in spreading respiratory viruses, primarily RV, from children to adults. However, there is an opportunity for improvement. First, rather than the method of transmission, we concentrated on the spread of viruses. For instance, participants could be vetted before or after encounters. Another option is air sampling. Second, no other viruses were found to be transmitted save RV and RSV-B. This may be due to the high rate of co-infection in children (45%), which raises the possibility that interference between co-infecting viruses could reduce the shedding of one or more viruses.

In addition, we found three instances of RV transfer using a 90% criterion for sequence homology. Sequencing helped us find more transmission events, but it's possible that we overestimated the number of them in this study. For that reason, in future work where we analyze the transmission rate as a major objective, we'll look to use a higher cut-off to confirm transmission. After a quick point-of-care screening test, the transmission of other viruses might have been detected if we had excluded kids with RV illnesses or co-infections. Third, some adult contacts engaged in several encounters, which could have skewed the findings.

A minimum of 28 days should pass between adult contacts to ensure their functional independence. Retrospective data analysis revealed that the distribution of transmission events between those who engaged in numerous interactions and those who engaged in a single interaction was equal, supporting our assumption that contacts were independent. Fourth, the disparity in RV transmission rates from all other viruses suggests that environmental, host and viral factors are key determinants of virus transmission. In conclusion, our investigation yielded three important conclusions. First, locally circulating RVs and RSV-B were naturally transmitted through relatively brief standardized contacts in a hospital setting. Second, we discovered that when children tested positive for RV, transmission events were more frequent when utilizing this methodology. Third, we demonstrated how sex affects the spread of viruses (higher among women). In comparison to virus challenge techniques, our technology has several significant advantages, and it might be applied in medical situations.