


Influenza and respiratory syncytial virus during the COVID-19 pandemic: Time for a new paradigm?

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Abstract

Seasonal epidemics of influenza and the respiratory syncytial virus (RSV) are the cause of substantial morbidity and mortality among children. During the global coronavirus disease 2019 (COVID-19) pandemic, the epidemiology of these viruses seems to have changed dramatically. In Australia and New Zealand, a significant decrease in both influenza and bronchiolitis have been noticed during usual peak seasons. Data from early months of winter seasons in Europe are showing similar trends. This current scenario imposes a reconsideration of the paradigm that toddlers and young school-children are the main drivers of seasonal RSV outbreaks and respiratory epidemics in general. In this article, we summarize current literature, address current knowledge or role of adults in the RSV epidemiology, describe the lessons learned from pertussis epidemics and call the international community to better understand the community

transmission dynamics of respiratory infections in all age groups. This can allow the establishment of better and more affordable preventive measures in the whole population level, which can ultimately save millions of child lives.

KEYWORDS

COVID-19, influenza, respiratory syncytial virus, SARS-COV-2

During the global course of Postgraduate Diploma in Pediatric Infectious Diseases at Oxford¹ the members of the course have reviewed the recent incidence of respiratory infections and the role of children and adults in transmission. The findings in 2020 have shown new epidemiology of respiratory infections.

While the coronavirus disease 2019 (COVID-19) pandemic has a lower clinical impact on children compared with adults,^{2,3} children have been significantly affected by its indirect consequences, due to restrictive measures that have potential implications on child's social, mental, and learning development.⁴ Nevertheless, a possible beneficial, unexpected effect of the pandemic on children's health has been recently described.

Seasonal epidemics of influenza and the respiratory syncytial virus (RSV) are the cause of substantial morbidity and mortality among children.⁵

During the global COVID-19 pandemic, the epidemiology of these viruses seems to have changed dramatically. In Western Australia, a decrease of 98.0%–99.4% in the detection of RSV and influenza infections, respectively, was reported compared with the previous winter seasons from 2012 to 2019.⁶ This dramatic decrease in respiratory infections was sustained over the subsequent 4-month period despite school reopenings. Similarly, in New South Wales, RSV detection between April and June 2020 was 94.3% lower than predicted based on comparison to 2015–2019.⁷ In New Zealand, where RSV season is from June to October and an aggressive elimination strategy effectively stamped out community transmission of COVID-19, a similar decline in seasonal respiratory infections was observed. Data from Kidz First Children's Hospital, Auckland, demonstrated only 268 admissions of respiratory infections from January to end of August, 2020, in comparison with 1486–2046 annually in previous years (2015–2019).⁸ In Europe, during the usual bronchiolitis/influenza seasons, the first months of winter showed a similar pattern.⁹ As of Week 53, 2020, there were 33 reported cases of influenza, compared with 10,616 reported cases at the same time last year.⁹ Similarly, there has been only 30 reported cases of RSV (both adults and children) at Week 53, compared with 3895 reported cases in the same week last year.⁹ Since laboratory testing is now mainly focused to detect severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections, it is possible that the real burden of RSV and influenza is

underestimated. However, reported hospitalizations of the more serious spectrum of disease (bronchiolitis) are equally reduced. This indicates that the reduction is not just a diagnostic bias. To confirm that this observation is not simply a bias, these early reports have been later confirmed in several settings in Northern and Southern Hemispheres. Nonpharmacological interventions led to reduced cases and admissions of pediatric RSV and influenza also in Chile and South Africa.¹⁰ Similarly, referral centers in Italy showed significant reductions of RSV cases and hospitalizations,¹¹ and Latin America registered a sharp decline in Pediatric Intensive Care Unit admissions for lower respiratory tract infections.¹² In the United States, Influenza viruses and human metapneumovirus circulated at historic lows through May 2021, and the weekly percentage of positive RSV results during January 4–April 4, 2020, decreased from 15.3% to 1.4%, then remained at historically low levels (<1.0% per week) for the next year.¹³ Importantly, other respiratory viruses of usual pediatric interest, such as the Rhinovirus, do not seem to have been similarly impacted. In the United Kingdom, for example, a typical annual spike in rhinovirus infections in children was observed with the return to schools in England in September 2020, and pediatric intensive care units saw ongoing admissions for rhinovirus induced wheeze and bronchiolitis in the autumn/winter of 2020 despite lockdown measures.^{14,15}

Historically, RSV has been directly linked with the pediatric population since its recognition as a human pathogen.¹⁶ As early as 1976, Hall et al.¹⁷ described that older siblings were the most likely index cases in household outbreaks, and subsequent studies over the years have also highlighted the role of older children in outbreaks.^{17–20} These studies historically informed control strategies.^{21,22} However, by the end of 2019, even before the COVID-19 pandemic, there was increased interest in the role of RSV in adults. A recent systematic review on RSV epidemiology in adults and elderlies in Latin America²³ found that RSV accounted for a considerable proportion of hospitalization in adults with influenza-like illness (69.9%) and community-acquired pneumonia (91.7%), suggesting that RSV may be a more significant cause of serious respiratory illness in adults than previously recognized. In Spain, Kestler et al. prospectively assessed 1200 patients admitted with an influenza-like respiratory infection, finding that 114 of the samples (9%) were positive for influenza and 95 (8%) were positive for RSV.²⁴

The epidemic control measures during COVID-19 pandemic have thus changed also the regular epidemics of RSV and influenza and the findings observed highlight a potential underestimated role of adults in the spread of RSV outbreaks and possibly other viral epidemics. Now, these findings need even more attention. During the first wave of the pandemic, almost all countries started complete lockdown with full school closures around March and April 2020⁴ suggesting that the reduced social life of children was the main reason for the reduced burden of respiratory infections in children. However, since September many countries have reopened schools. In particular, almost all countries fully reopened kindergartens and primary schools, while some implemented partial closures or distance learning for older children (>10–14 years of age). A constantly updated online data set is available on the Oxford COVID-19 Government Response Tracker (available at: <https://www.bsg.ox.ac.uk/research/research-projects/coronavirus-government-response-tracker>), which collects daily information on school closures and other preventive non-pharmacological interventions from >180 counties. Live heat maps show the gradual reopening of school closures in majority of countries worldwide at the end of local “SARS-CoV-2 waves.” In particular, since September 2020, most children came back to school, particularly the younger ones (<5 years of age), those that account for the majority of viral lower respiratory tract infections and bronchiolitis in particular. Conversely, masking have been kept, particularly in crowded and close environments, mostly mandatory for older children and adults, while for the youngest age-group masking is not compulsory and safe distance, as well as frequent hand hygiene is not easily achievable. Therefore, those children traditionally linked with the RSV epidemics, namely, kindergarteners and young schoolchildren, returned to almost normal life. Nevertheless, during the 2020/2021 European winter, the “acute respiratory infection” season has not started. This observation allows speculation that since adults are the ones who have mostly changed their daily habits, may be the ones mostly contributing to the current change in RSV and influenza epidemiology in the northern hemisphere. A paper by McNab et al.²⁵ described delayed re-emergence of RSV in Victoria compared with New South Wales and Western Australia. This happened in the context of Victoria having prolonged lock-down due to the highest rates of community transmission of any state or territory in Australia. The resurgence of RSV occurred after lock-down ended and interstate borders reopened. Childcares remained opened through most of the lock-down, further supporting the hypothesis of the potential role of adults in RSV transmission. A similar scenario has also been reported from New Zealand health authorities. New Zealand has had an optimal SARS-CoV-2 control and has lowered all restrictions, being at an “alert level 1” (low community transmission).²⁶ Interestingly, during the current respiratory season in New Zealand, the country is experiencing RSV case notifications higher than any seen in the past 10 years.^{27,28} Similarly in the United States, since April 2021 a rise, although less sharp, in RSV cases have been reported.¹³ Social circulation, reduction of nonpharmacological interventions, and an “immune-debt” of children that during the last year have not encountered RSV, are leading to an unprecedented surge of RSV and

pressure on local health systems. A new scenario that deserves appropriate investigation and understanding.

Although it may seem speculative, it is difficult to deny this statement since influenza and RSV cases in children seem to have significantly decreased since adults have started “keep distance,” “wearing masks,” and “washing their hands more regularly.” Stronger influenza vaccination campaigns and widely supported by governments are also contributing to lower numbers of lower respiratory tract infections. However, historically the adherence to influenza vaccination is much lower in children compared with adults even despite the health services distributing the influenza vaccines free of charge for children aged 2–12 years old in certain countries.

The depicted scenario imposes a reconsideration of the paradigm that toddlers and young schoolchildren are the main drivers of seasonal RSV outbreaks and respiratory epidemics in general. Considering the historical impact of the RSV and flu seasons on childhood morbidity and mortality, this new scenario must lead us to perform a comprehensive study to establish the role of the wider community in respiratory infection outbreaks, including those diseases that historically kill children. Current severe RSV outbreak in New Zealand is also another good reason to better understand dynamics of respiratory viruses in the community, to better plan preventive strategies and optimize health-care resources. Pertussis epidemiology is a well-known example of how extending surveillance to adults has increased understanding of pertussis epidemiology. It became clear around 2010 that focusing surveillance only on infants and children allowed to only detect the “tip of the iceberg” of the real pertussis epidemiology. Adults could act as a reservoir of infection toward young children. This concept derived from studies that estimated high incidence in adults based on serological assays and polymerase chain reaction (PCR), and from household contact studies, which identified adults and adolescents as frequent source of infection for infants.²⁹

Recent changes in RSV and epidemiological scenarios, apparently influenced by drastic changes in adults’ habits, allow to hypothesize that pertussis and RSV may share several epidemiological paradigms.

As a community of young pediatric infectious disease registrars and specialists, we call on current international leaders, experts and funding agencies to prioritize these issues in research. A better understanding of community transmission dynamics of respiratory infections in all age groups can allow the establishment of better and more affordable preventive measures in the whole population level. This may save millions of child lives, reduce morbidity and diminish the psychological burden on children during outbreaks or epidemics. These measures may also be easily introduced in low-to-middle income countries, where respiratory infections kill the most.³⁰

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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