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The Changing Epidemiology of Respiratory Viruses in Children During the COVID-19 Pandemic: A Canary in a COVID Time

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The Changing Epidemiology of Respiratory Viruses in Children During the COVID-19 Pandemic: A Canary in a COVID Time

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Key Words: bronchiolitis, COVID-19, influenza, respiratory syncytial virus (RSV), respiratory infection, SARS CoV-2

INTRODUCTION

The World Health Organization (WHO) has reported over 200 million cases of SARS-CoV-2 infection, and 4 million deaths since the declaration of the COVID-19 pandemic in March 2020.¹ Although children predominantly experience asymptomatic or mild infection, representing a minority of hospitalizations and deaths, children have been significantly impacted by the COVID-19 pandemic. There have been increasing concerns raised of “COVID-19 collateral damage” with lock-downs, school closures, and social isolation contributing to delayed presentation of serious illness, reduction in vaccination rates, impaired mental health and increased safeguarding concerns.² An additional effect of the nonpharmaceutical interventions (NPIs) implemented in response to COVID-19 has

included an unprecedented reduction in children presenting with respiratory illnesses, including those due to respiratory syncytial virus (RSV) and influenza. Here we review how COVID-19 has affected the epidemiology of respiratory infections in children.

REDUCTION IN PEDIATRIC PRESENTATIONS TO ED DURING COVID-19 PANDEMIC

In 2020, as the number of adult patients hospitalized with COVID-19 increased globally, an Italian paper reported a 73–88% reduction in children presenting to emergency departments with acute illness compared with the same time period in 2018–2019.³ In addition, a snapshot survey of 2433 pediatricians from the UK and Ireland reported that 32% of pediatricians working in acute care settings had witnessed delayed presentations of children with critical illnesses such as diabetic ketoacidosis, safeguarding concerns, and malignancy in the previous 14 days.² It rapidly became apparent that there were also fewer children presenting to emergency departments with common childhood infections such as gastroenteritis, chickenpox, acute otitis media, scarlet fever, and pertussis.⁴ The IRIS initiative (Invasive Respiratory Infection Surveillance) recently published prospective surveillance data from 26 countries demonstrating that in early 2020 there was also a significant and sustained reduction in hospital presentations with invasive bacterial diseases due to *Streptococcal pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis* when compared with 2018 and 2019.⁵ These reductions are felt to be due to interrupted person-to-person transmission of pathogens because

of nonpharmaceutical interventions (NPIs) for the containment of SARS-CoV-2, including physical distancing, handwashing, and face-masks. At the same time, there is emerging concern that the lack of immune stimulation from reduced exposure to common circulating pathogens may lead to a decline in population immunity and result in delayed and larger peaks when NPIs are lifted.⁴

INITIAL REDUCTION IN RESPIRATORY ILLNESSES DURING COVID-19 PANDEMIC

There is a predictable seasonality to pediatric medicine, with admissions peaking in winter due to respiratory illnesses such as bronchiolitis, pneumonia, and wheeze. Bronchiolitis is a leading cause of infant hospitalization, previously accounting for 18% of all pediatric admissions in the United States and 12% of all admissions to Pediatric Intensive Care Units (PICU) in England in 2011.⁶ Following the emergence of SARS-CoV-2, Australia and New Zealand went into lockdown in late March 2020, with international border closures. This period coincides with the southern hemisphere autumn, a time when local RSV, influenza, and bronchiolitis numbers typically begin to rise. However, in September 2020, data from the southern hemisphere emerged demonstrating large reductions in hospitalizations due to RSV, influenza, and bronchiolitis during the 2020 winter. In Western Australia, polymerase chain reaction (PCR) detection of RSV and Influenza in children <16 years of age was reduced by 98% and 94%, respectively, compared with the previous 8 years.⁷ This reduction was sustained throughout the Australian winter, despite relaxing of local

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restrictions including schools reopening, but with both international and state borders remaining closed. A similar reduction in RSV was reported in New South Wales, Australia.⁸ Comparison with the previous five years identified a 94.3% lower than expected frequency of RSV-positive PCR tests during April–June 2020 despite double the number of tests being performed during this period. There was a corresponding reduction in bronchiolitis hospitalizations (85.9%), ED attendance with acute respiratory illness (70.8%) and PICU admissions with bronchiolitis (89.1%).⁸ Similar reductions were reported from New Zealand.⁹ It appears that COVID-19 strategies including border control and implementation of NPIs halted the seasonal transmission of respiratory viruses, including influenza and RSV.

Subsequently, similar reductions in rates of RSV, influenza and bronchiolitis admissions were reported during the 2020 winter period in the northern hemisphere.⁴ Rhinovirus, however, continued to circulate at pre-COVID-19 pandemic levels during this period.⁸ There are a number of possible theories accounting for this including that rhinovirus is a nonenveloped virus and, therefore, not as susceptible to NPIs such as hand-washing as the enveloped viruses including SARS-CoV-2, RSV and influenza.⁸

SUBSEQUENT SOUTHERN HEMISPHERE RISE IN RESPIRATORY ILLNESSES

COVID-19 case numbers have remained low in both Australia and New Zealand, largely due to strict international border controls and mandatory 14-day quarantine for international arrivals.¹ However, this has not remained true for all respiratory viruses. On-going surveillance in Western Australia showed significant resurgence in positive RSV PCR tests in children <16 years of age during September–December 2020.¹⁰ RSV detections during this time exceeded the median seasonal peak of the average epidemic curves of 2012–2019.¹⁰ This occurred at a time when physical distancing recommendations were being relaxed but prior to the opening of interstate borders. Of note, the median age of the children during this peak was 18.4 months, significantly higher than the previous 2012–2019 upper range (7.3–12.5 months; $P < 0.001$).¹⁰

In April 2021, a trans-Tasman bubble opened between Australia and New Zealand allowing freedom of travel without a mandatory 14-day hotel quarantine period. In late May 2021, New Zealand case numbers of RSV began to rise, from a sporadic 20 cases (01 January to 22 May 2021) to over 100 cases per week.¹¹ On 03 October 2021, the NZ Environmental Science and Research (ESR) network had reported 6327 cases between weeks 18–39. This compares with an average

of 1743 cases reported during the typical winter peak (week 18–39) during 2016–2019.¹¹ New Zealand hospitals are subsequently seeing a significant rise in hospitalizations with bronchiolitis and RSV necessitating the delay of elective surgeries and re-purposing playrooms into clinical areas.

These southern hemisphere findings appear to be associated with the relaxation of COVID-19 related NPIs and the easing of travel restrictions. An older median age of cases suggests that those affected possibly represent an immunologically RSV-naïve population or those with waning population immunity due to reduced circulating viruses in 2020, NPIs, and physical distancing.¹⁰

NORTHERN HEMISPHERE RSV EXPERIENCE

This southern hemisphere experience raised early concern that there would be a significant surge in RSV case numbers in the northern hemisphere with the progressive easing of COVID-19 restrictions. This has subsequently been reported to have occurred in France and the United States.¹² In contrast to Western Australia, this delayed RSV surge affected a younger cohort than previous years (median 6 months; range 12 days to 9 years, vs. median 17 months; range 11 days to 18 years).¹² They also reported a higher proportion requiring PICU admission compared with previous years (81% vs. 45%).¹² The authors proposed that the more severe RSV disease in younger infants could represent a decline in infant and maternal immunity from a lack of RSV exposure in the previous season.

In the UK, laboratory surveillance data from the Respiratory DataMart System on the rate of RSV as of 05 August 2021 shows that RSV positivity has increased from 3.4% to 15.1% in the last 4 weeks, while Influenza case numbers remain low at 0.0% (0/2288 samples influenza-positive).¹³ At the time of writing, UK COVID-19 case numbers remain high with persistent circulation of the Delta variant in a highly vaccinated adult population.

DISCUSSION

On 19 July 2021, England moved to the final stage of relaxation of lockdown restrictions at a time where, unlike the Australian and NZ experience, both UK COVID-19 and RSV case numbers continued to rise. The southern hemisphere experience foreshadowed that an unprecedented and non-seasonal peak in RSV cases could occur in the northern hemisphere with the easing of NPIs. This places additional strain on already stretched healthcare systems. As pediatricians, it is important to be mindful that although a minority of children become significantly unwell with SARS-CoV-2, the pediatric

population has been significantly affected by the collateral damage of COVID-19 and we must ensure we minimize this damage in the face of rising RSV and bronchiolitis numbers. This includes maintaining pediatric access to primary and secondary care, adequate hospital bed spaces, staffing, oxygen and funding for at-risk infants to receive passive immunization against RSV.

It is important to reflect on the lessons learned from the first waves of the COVID-19 pandemic. The initial significant reduction in pediatric respiratory virus transmission with the introduction of population-wide NPIs is now well-described.^{7,8} Although it has not yet been possible to tease out which NPI has had the most significant impact, it is worth considering whether selected NPIs such as hand-hygiene, facemasks and improved respiratory etiquette should be encouraged in future winter seasons to protect vulnerable children and healthcare systems from the predictable seasonality of respiratory illnesses. Healthcare infection control precautions should reflect the potential impacts of pediatric respiratory viral infections, including childhood morbidity and mortality as well as transmission to staff and other patients. The widespread use of respiratory isolation precautions for all respiratory presentations in pediatrics may also help reduce nosocomial transmission and staff illness and have associated implications for improved patient care and safety.

Although with lockdowns and travel restrictions in place, the Pediatric Infectious Diseases community has never been more physically distanced, it has never been more tele-connected. Rapid communication through early publication of reports and online global meetings has allowed for early dialogue and planning amongst pediatricians. This has facilitated rapid mobilization of resources to develop surveillance studies such as the UK multicenter prospective observational cohort study “BronchStart” as well as advocacy for widening the Palivizumab UK criteria to include a larger number of at-risk-infants.

CONCLUSION

The epidemiology of COVID-19 and respiratory viruses in children is constantly evolving with the emergence of variants of concern, the introduction of vaccination and the easing of nonpharmaceutical interventions. Although the southern hemisphere experience has alluded to what can be expected in the weeks to come, the UK is in a unique situation with the recent lifting of restrictions in the face of ongoing COVID-19 transmission and increasing RSV case numbers. It is important to reflect on the lessons learned from the initial COVID-19 waves and southern hemisphere experience to minimize ongoing pediatric COVID-19 collateral damage.

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