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Immunity debt and unseasonal childhood respiratory viruses

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Key points

- Non-pharmaceutical measures in response to the COVID-19 pandemic suppressed many other seasonal respiratory viruses
- Lack of exposure to seasonal respiratory viruses means that the proportion of the population with immunity to such viruses is lower than preceding years, creating an "immunity debt"
- This gap between current, and usual levels of population immunity can lead to higher incidence of respiratory viral infections than usual, resulting in strain on health systems
- Resumption of normal mixing patterns has temporally displaced normal seasonal waves of infection
- Recent patterns of different respiratory viral infections have been less unpredictable, but health systems should prepare for convergence of major pathogens such as COVID-19, Influenza and RSV during the coming Autumn and Winter months

Main Article

From early in the COVID-19 pandemic, non-pharmaceutical interventions were applied across the world to stem the transmission of SARS-CoV-2, including mask wearing, social distancing, increased frequency and intensity of cleaning and handwashing, and "lockdowns", where much of the population were confined to their homes for weeks or months at a time. These interventions not only affected rates of transmission of SARS-CoV-2, but of many other respiratory viruses. Autumn and winter months in less temperate climates are usually characterised by a significant increase in seasonal respiratory viral infections in children such as influenza and RSV, but for many countries, the winter of 2020/2021 saw little to no cases of these infections (UK Health Security Agency 2022; Williams et al. 2021).

As widespread vaccination against COVID-19 reduced the risk of serious illness, many societies began reopening and reducing the scale of non-pharmaceutical interventions. As a result, many of the respiratory viral illnesses which had been at very low levels during the COVID-19 pandemic, have had a resurgence. However, there has been a huge shift in the temporal dynamics of these previously predictable diseases.

A significant increase in RSV infections have been witnessed from as early as late 2020 in Australia (Foley et al. 2021), seeing upwards of three times as many RSV-associated hospital admissions to children's hospitals at their peak as would be seen on an average year. But most surprisingly, the peak of infection occurred in Australian summertime. This displacement of transmission has been seen across the world in countries such as Japan (Ujiie et al. 2021), the USA (Agha and Avner 2021), and Israel (Weinberger Opek et al. 2021). Whilst New Zealand experienced a surge in RSV infections within the typical RSV season, it was to an unprecedented extent and placed intolerable pressures on children's hospitals and intensive care capacity (Hatter et al. 2021). The UK experienced an unseasonal summer wave of RSV in 2021, although the peak was less sharp than would normally be experienced in winter, with a longer tail lasting for several months (UK Health Security Agency 2022). More recently, influenza has reappeared in Australia during their winter, but with a much earlier and more pronounced peak than would normally be expected (Australian Government Department of Health 2022).

The usual patterns of seasonal viruses are influenced by many factors including, but not limited to, international travel (Belderok et al. 2013), viral interference (where the infection or replication of one virus is affected by the presence of another) (Piret and Boivin 2022), changes in humidity (Li et al. 2022) and antigenic drift (Bouvier and Palese 2008), but one of the most important influences is of population immunity. Over time, following the previous winter peak of infections, immunity to seasonal respiratory viruses wanes in the population who have been previously infected; antibody levels decline and people with existing immunity die, and a new cohort of infants is being born who are immunologically naïve. This reduces levels of immunity within the population, which when combined with environmental conditions more conducive to respiratory virus transmission, is enough to raise the effective reproduction number above 1, and a new seasonal wave occurs. This then ends once enough immunity has been acquired through infections to drive the effective reproduction number below 1 again, meaning that herd immunity has been reached, and the cycle continues.

One theory which seeks to explain the disruption of normal seasonal patterns of respiratory viruses is that it is, in part, due to the suppression of non SARS-CoV-2 viral transmission as an unintended consequence pandemic response measures. During time periods where seasonal waves of infection would have occurred and additional population immunity would have been accrued, lack of

transmission meant that levels of immunity in the population decreased. Immunity in the population continued to wane in those previously infected and a larger than usual cohort of immunologically naïve children were born, and the population was not being exposed to the usual rates of infection which stimulate immune memory activation. The difference between previous levels of immunity to respiratory viruses within the population, and levels seen following interruption of transmission of such viruses during the COVID-19 pandemic, has been termed, “immunity debt” (Hatter et al. 2021), or “immunity gap” (Messacar et al. 2022). Upon release of pandemic control measures and resumption of increased mixing patterns, a larger proportion of the population is needed to have immunity to respiratory viruses to get the effective reproductive number below 1 again. Previously temporally predictable increases in the incidence of respiratory viral infections are now displaced and occurring out of season due to lower levels of population immunity, coupled with the relaxation of non-pharmaceutical measures during warmer times of the year – often as a deliberate strategy to prevent larger “exit waves” of Covid-19 which might be expected during the Autumn or Winter (Scientific Advisory Group for Emergencies 2021).

There are several theoretical reasons why we might be concerned about the accrual of “immunity debt”. One is that needing more infections to reach herd immunity could result in larger waves of infection, and this may put strain on healthcare systems which are not set up to cope with such volumes of cases. This was the experience of New Zealand, Japan and parts of Australia with RSV (Foley et al. 2021; Hatter et al. 2021; Ujiie et al. 2021). The UK was fortunate that the timing of the unseasonal RSV wave coincided with the cessation of schooling for the summer, with reduced mixing of children who, unlike with SARS-CoV-2, are the driving cohort for transmission (Hogan et al. 2016). This may have led to a “flattening of the curve”, with a longer, flatter increase of infections. Another theoretical concern is of “overshoot”. A wave of infections begins to decline once Rt is below 1. However, infections continue to accrue after this point because infected individuals continue to infect more people (just fewer than 1 new infection per infected individual). The number of infections at the peak is therefore important, as it directly influences how many more infections accrue after herd immunity has been reached. This is referred to as the “overshoot” (Handel et al. 2007). If the peak is taller, then more infections than usual will occur during the overshoot. This means that although infections may have been deferred during the season where infections were missed, it is possible to end up with more infections overall.

It is difficult to predict what will happen in the short to medium term future regarding the temporal patterns of these viruses. The pattern of RSV in New South Wales, Australia, appears to have settled back to a more usual winter patterns after 2 years of disruption (New South Wales Health 2022). Influenza has also returned, albeit slightly earlier than usual. The dynamics of different viruses can be expected to adjust differently as each have their own unique factors influencing transmission. One of the most important concerns for the UK is regarding the resurgence of influenza in the winter. Vaccines can be administered which can help to “repay” some of the “immunity debt” acquired over the past 2 years. A more extensive Influenza vaccination campaign has been announced for the Autumn. Health systems should be prepared for the potential convergence of Influenza, COVID-19 and RSV, which is likely to put increased pressures on already stretched systems.

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