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Immunity debt and unseasonal childhood respiratory viruses

In the wake of the COVID-19 pandemic, there has been a dramatic shift in the patterns of traditionally seasonal childhood respiratory viruses which may be the result of changes in population immunity.

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From early in the COVID-19 pandemic, non-pharmaceutical interventions were applied across the world to stem the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), including mask wearing, social distancing, increased frequency and intensity of cleaning and handwashing, and ‘lockdowns’, where much of the population was confined to their homes for weeks or months at a time. These interventions not only affected rates of transmission of SARS-CoV-2, but also 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 respiratory syncytial virus, but for many countries, the winter of 2020–21 saw few to no cases of these infections (Williams et al, 2021; UK Health Security Agency, 2022).

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 respiratory viral illnesses have had a resurgence. However, there has been a huge shift in the temporal dynamics of these previously predictable diseases.

Unseasonal peaks of infection

A significant increase in respiratory syncytial virus infections has been witnessed since late 2020 in Australia (Foley et al, 2021). There were upwards of three times as many respiratory syncytial virus-associated hospital admissions to children’s hospitals at their peak as would be seen in an average year and, most surprisingly, the peak of infection occurred in Australian summertime. This displacement of transmission has also been seen in countries such as Japan (Ujiie et al, 2021), the USA (Agha and Avner, 2021) and Israel (Weinberger et al, 2021). While New Zealand experienced a surge in respiratory syncytial virus infections within the typical respiratory syncytial virus season, it was to an unprecedented extent and placed intolerable pressures on children’s hospitals and intensive care capacity (Hatter et al, 2021). In 2021, the UK experienced an unseasonal summer wave of respiratory syncytial virus, although the peak was less sharp than would normally be experienced in winter, with a longer tail that lasted 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 and Aged Care, 2022).

The usual patterns of seasonal viruses are influenced by many factors including, but not limited to, international travel, 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, but one of the most important influences is 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, people with existing immunity die and a new cohort of infants is 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, leading to a new seasonal wave of infections. This 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.

Immunity debt

One theory which seeks to explain the disruption of normal seasonal patterns of respiratory viruses is that it is, in part, the result of the suppression of non-SARS-CoV-2 viral transmission as an unintended consequence of pandemic response measures. During 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. Population immunity continued to wane in those previously infected, 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 activate immune memory. The difference between previous levels of immunity to respiratory viruses within the population, and levels seen following interrupted 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 removal of pandemic control measures and resumption of increased mixing patterns, a larger proportion of the population needs 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 because of 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 respiratory syncytial virus (Foley et al, 2021; Hatter et al, 2021; Ujiie et al, 2021). The UK was fortunate that the unseasonal respiratory syncytial virus 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 in the number of infections.

Another theoretical concern is of 'overshoot'. A wave of infections begins to decline once the effective reproduction number 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.

What next?

It is difficult to predict what will happen in the short to medium term regarding the temporal patterns of these viruses. The pattern of respiratory syncytial virus infection in New South Wales, Australia, appears to have settled back to a more usual winter pattern 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 has its own unique factors influencing transmission. One of the most important concerns for the UK is 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, and 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 respiratory syncytial virus, which is likely to put increased pressure on already stretched systems.

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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 could lead to a higher incidence of respiratory viral infections than usual, putting 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 predictable, but health systems should prepare for convergence of major pathogens such as severe acute respiratory syndrome coronavirus 2, influenza and respiratory syncytial virus during the coming autumn and winter months.

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