For Everything, There Is a Season

Renewed interest in the seasonality of some infections should lead to better understanding of emerging infections and effects of climatic change

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Everyone is aware that they are more likely to get a common cold when they are themselves cold during the winter months. Up until the advent of mass immunization against measles, parents knew that this infection too tended to peak during the winter. And people of my generation recall parental anxieties about infantile paralysis (poliomyelitis) each year as summer approached.

Medical microbiologists, on the other hand, seem not to be as interested as their forebears were in the seasonality of communicable disease. Near the center of the stage a century or more ago, the subject has attracted less attention in most of the intervening decades. Could things now be changing, as we try to predict how global warming may influence our vulnerability to pathogens?

One of the outcomes of past research on seasonality was a recognition that the “obvious” reasons for patterns of infection were not as straightforward as they might seem. For example, many authors, many years ago, claimed that peaks of measles incidence in the winter were attributable to a combination of lower indoor humidity (which helps the virus to survive) and children congregating together in school. The idea was confirmed, surprisingly recently, by a detailed analysis of cases in England and Wales that documented a fall in transmission during school holidays (P. Fine and J. Clarkson, Int. J. Epidemiol. 11:5, 1982).

Yet this explanation appears to be valid only for temperate regions of the world. In the tropics, there is no association between measles outbreaks and school terms. Instead, the incidence of the infection peaks during the dry season. The crucial determinant of the peaks seems to be the greater survival of the virus in drier air.

One organism that has certainly rekindled interest in seasonality is respiratory syncytial virus (RSV), the leading cause of lower respiratory tract infections in young children throughout the world. In both northern and southern hemispheres, outbreaks of RSV infection among children in temperate countries tend to happen predominantly during the cold months of the year (C.B. Hall et al., J. Infect. Dis. 162:1283, 1990). In North America, the RSV season commences in southern coastal areas during the early autumn and then moves northwards (L.G. Stensballe et al., Pediatr. Infectious Dis. J. 22: S21, 2003). Epidemics also take place during the winter in subtropical countries.

However, as pointed out by Saad Omer and colleagues at the Johns Hopkins Bloomberg School of Health, Baltimore, Md., and centers in Indonesia and Europe (Epidemiol. Infect. 136: 1319, 2008), the situation is quite different in the tropical belt. There, the key factor linked with the cyclical predations of RSV is often not temperature but rainfall. In Hong Kong, RSV epidemics are more common during the rainy season, when the temperature is high. Yet again, this type of association is less pronounced in equatorial countries where there is rainfall throughout the year, despite evident seasonal variations in the transmission of the virus.

Omer and his associates were specially interested in learning more about the behavior of RSV in tropical equatorial regions. Previous data from Bandung (at an elevation of 750 m) in Java, Indonesia, had suggested that most infections are recorded during the rainy season (from February to May). Elsewhere there has been comparatively little information or analysis. In
particular, insight is required concerning the transmission of RSV among the populations of islands, where the dynamics of communicable diseases may differ considerably from those of nonisland populations.

The investigators took the opportunity to record the temporal and spatial aspects of childhood RSV disease, and to investigate any associations with climatic variables, in a defined island population at sea level in the equatorial tropics. The setting was Lombok Island, Indonesia, where they studied a large number of children referred to hospital with pneumonia.

During the three years of the research, hospitals on the island admitted just under 3,000 such children, and 741 of them were infected with RSV. Multivariate analysis showed that rainfall was associated with a 64% higher incidence of infection. An increase in mean relative humidity of 1% was linked with a 6% rise in RSV cases, while a 1°C rise in mean air temperature was linked with a 44% increase. There were also four significant local clusters of RSV pneumonia within the annual island-wide epidemics.

“This study provides evidence of an association between hospitalised RSV illness and several climatic variables in an equatorial island setting,” the authors conclude. “The local micro-epidemics suggest the effect of human behaviour within the annual epidemic. Prospective studies with more intense assessment of individual-level exposure are required to tease out the relative contributions of behavior and biology.”

From a practical standpoint, better understanding of climatological factors affecting the threat posed by RSV could lead to an improvement in preventive strategies for particularly vulnerable persons. At present, public health authorities in some parts of the world use virological surveillance data to determine when monoclonal antibodies should be made available to high-risk groups in the community. If the onset of the RSV season could be predicted from climatological changes, then prophylaxis might be initiated at the most propitious time even in regions where virological data are not available.

This reasoning has encouraged Daniel Noyola and Peter Mandeville of the Universidad Autonoma de San Luis Potosi in Mexico to study the relationship between RSV epidemiology and atmospheric conditions in the city of San Luis Potosi, S.L.P. They carried out their research during four consecutive epidemics between 2002 and 2006.

The results, published in *Epidemiology and Infection* (136:1328, 2008), are based on time-series and regression analysis and showed that weekly numbers of RSV detections were correlated with ambient temperature, barometric pressure, relative humidity, vapor tension, dew point, precipitation, and hours of light. These findings indicated that atmospheric conditions, particularly temperature, partly explain the year-to-year variability in RSV activity.

One specific environmental factor highlighted by the Mexico-based duo is ultraviolet B (UVB) radiation. This is at its highest in San Luis Potosi between March and August, the period showing the smallest amount of RSV activity in their study. “Lower UVB radiation during winter is associated with low vitamin D levels, particularly in infants that do not receive vitamin D supplementation,” Noyola and Mandeville write. “Low levels of vitamin D have been associated with increased susceptibility to respiratory tract infections in children. This association may be explained by the modulating effect of vitamin D on the immune system.”

What these and other recent studies have undoubtedly demonstrated is that seasonality, at one time considered to be a relatively simple phenomenon, is actually complex and only incompletely understood. One problem, as pointed out by Nicholas Grassly and Christopher Fraser of Imperial College, London (Proc. R. Soc. B 273:2541, 2006), is that peaks in disease incidence can occur at significantly different times of the year to peak transmission, depending on the characteristics of the infection. So infections with the same underlying cause of seasonal transmission can show different patterns of incidence.

“Furthermore, in many cases, the interaction of the nonlinear dynamics of the infection with seasonal forcing of transmission results in more complex dynamics, including multi-annual cycles with variable periodicity,” Grassly and Fraser point out. “These nonlinearities act to obscure correlation between climatic or behavioral factors and annual variation in disease incidence.”

Had more groundwork been done over past decades, our understanding of seasonality may well have provided more help in coping with today’s central issues of global warming and emerging infections.