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Mystery of Seasonality: Getting the Rhythm of Nature

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Abstract

Seasonality, a systematic periodic occurrence of events over the course of a year, is a well-known phenomenon in life and health sciences. Understanding seasonal fluctuations in diseases patterns presents us with a major challenge. To develop efficient strategies for disease prevention and control, we need to grasp the main determinants of temporal variations and their interactions. This paper will introduce the notion of seasonality by outlining several of its factors, using as illustrations respiratory and enteric water- or food-borne infections.

Keywords

seasonality; water-borne infection; food-borne infection; respiratory infection

Introduction

> Now let us consider the seasons and the way we can predict whether it is going to be a healthy or an unhealthy year.
>
> (Hippocrates. *Air, Waters, Places*, 10)[1]

Seasonal fluctuations in birth and death, in sickness and health, are the haunting mysteries of mankind. People have made predictions from winds, tides, birds' migrations, spring blooms, sunsets, and constellations in hope of grasping the future. The complexity and uncertainty of ancient and modern means of prediction make us wonder to what extent we are able to understand the rhythm of nature. One might argue the future cannot be known, but from a practical point of view, a better understanding of changes in disease occurrences is essential for building efficient strategies for disease prevention and control.

Seasonality, a systematic periodic occurrence of events over the course of a year, is a well-known phenomenon in life and health sciences. Since Hippocrates, observers worldwide have noted and documented marked fluctuations in the incidence of many diseases. In the modern view, the main determinants of temporal variations in disease manifestation are evolving host susceptibility, periodicity in pathogen abundance and transmissibility, and the ever-changing environment that can support or repress a host or pathogen. Interactions among these factors responsible for seasonal variation are interwoven into the intricate fabric of life.

For many diseases, explanations for self-sustained oscillations still remain elusive. We lack adequate methods and sufficient analytical tools for comprehensive examination of seasonality in public health field studies. A dearth of observations, recorded over long periods at fine resolution, compounded by an enormous number of factors associated with periodic changes,

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[1]Hippocrates' citations are taken from: Lloyd, GER, editor. *Hippocratic Writings*. Trans. Chadwick J and Mann WN. London: Penguin; 1978.

obscure our ability to understand disease variation. Urgent need for effective strategies to prevent and control a spread of emerging infections in the rapidly changing world, however, demands a deeper insight into the cyclic nature of diseases.

This paper will introduce the notion of seasonality and outline several factors associated with seasonality using as illustrations enteric water- or food-borne infections and respiratory infections. Then I propose a framework for systematic evaluation of seasonal oscillations. In every part of this presentation, and most importantly, I wish to stimulate discussion on this challenging topic.

Notion of Seasonality

> Every disease occurs at any season of the year but some of them more frequently occur and are of greater severity at certain times.
>
> (Hippocrates. *Aphorisms*, III, 19)

Seasonality, as noted above, refers to the cyclic appearance of events over a period of time. A seasonal pattern may appear as a tight cluster of isolated outbreaks that occurred during a relatively short time period, then spreading over a wide geographic area.

For example, in a temporal curve of enteric infection cases (i.e. giardiasis, cryptosporidiosis, or rotavirus infections), a compact cluster of outbreaks is followed by a long interval of low incidence. Systematic recurrence of such sequences forms a seasonal pattern typical of a specific pathogen in a given population and in a given locality. A seasonal increase in enteric or respiratory infection often produces a well-defined oscillating curve that starts to rise in one season and declines over the next one.

The three main features characterize seasonality:

1. a point in time when a seasonal curve reaches its maximum,
2. an amplitude from peak to nadir, and
3. a duration of a seasonal increase defined by a shape of a curve.

   (The shape of a seasonal pattern reflects how fast a temporal curve reaches its peak and declines to nadir over a course of a full cycle. Depending on the length of a cycle whether it is one year or a half of a year, a seasonal curve would have one or two peaks.)

Seasonal patterns, described by these three characteristics, may vary for different diseases, different locations, or different subpopulations. Many viral and bacterial infections in humans show marked seasonal changes. In some diseases, like salmonellosis and influenza, annual oscillations explain up to 60% of variability. Such impact should not be ignored and deserves a proper examination.

Diseases Seasonal Patterns

> Diseases vary in their relationships one with another; some are opposed, some are mutually agreeable.
>
> (Hippocrates. *Aphorisms*, III, 3)

Differences in diseases peaks reflect different etiology, heterogeneity in host susceptibility, or route of transmission. In temperate climates, *Campylobacter* and *Salmonella* infections are known to rise in summer, giardiasis in early fall, and rotavirus infection in mid-winter, etc. Interestingly, for the same infectious agent, infections recorded in two different locations may present a different pattern of incidence. A seasonal pattern for cryptosporidiosis in the United

States exhibits one late summer peak (1); in contrast, in the United Kingdom, two seasonal peaks are seen (2). The UK picture reflects two dominant sources of exposure: one from animals in the late spring, and another from humans in the fall (3).

Close temporal clustering of seasonal peaks in diseases that share similar sources of exposure suggests dominant routes of transmissions. Peaks in water-borne cryptosporidiosis and giardiasis often cluster after a summer peak in ambient temperature. Such synchronization in disease manifestation can be governed by environmental and social factors. In some instances, periodicity of a given infection observed in a particular population may be not present in another. A seasonal peak in cryptosporidiosis cases observed in the general population is not apparent in the immunocompromized HIV-positive gay men, even though the incidence of cryptosporidiosis in HIV-positive population is very high. This suggests differences in dominant routes of transmission.

Seasonal patterns can change over time. After intense vaccination campaigns in the 1950s and 1970s in the United Kingdom, the patterns of measles and pertussis changed, with the high rates of disease usually seen when children were attending school diminishing for measles and practically disappearing for pertusis (4). Explanations for these phenomena remain elusive. A departure from a systematically observed pattern could reflect the evolution of a pathogen or a change in herd immunity. A simple rule to remember is that a discovery hides in outliers.

Faced with an abundance of causal agents, a bare observation of a rise in the incidence of non-specific enteritis should be interpreted with caution. A seasonal pattern can represent a mix of temporal curves. Imagine two periodic curves of similar intensity, but one peaks in a spring and another in a fall; the sum of these two curves might lose the appearance of seasonality, covering two distinctly seasonal phenomena.

Some infections are very rare. Their seasonal patterns are difficult to examine because the relevant data must be collected over a very long time and/or aggregated over large spatial units. Precision in evaluating seasonality can thus be jeopardized by time-dependent and/or space-dependent confounders.

Seasonal fluctuations can be found beyond infectious diseases; chronic somatic diseases also exhibit substantial temporal variations. Plausibly, exacerbations in chronic conditions are driven by infectious agents or environmental changes. Understanding the interplay of an infection and a chronic disease may lead to better control for both.

Seasonal Host Susceptibility

> When the weather is seasonable and the crops ripen at the regular times, diseases are regular in their appearance…
>
> (Hippocrates. *Aphorisms*, III, 8)

Poor nutrition directly affects host susceptibility. In places of food scarcity, researchers suspect that temporal patterns in birth weight and preterm delivery result from seasonal variations in food availability (5). In general, due to a less developed immune system, young children are susceptible to infection; their immune response may be further weakened by seasonal cutbacks in essential micronutrients and vitamins.

Anemnestic responses to an antigen determine whether an infection recurs. Short-lived immune memory together with seasonal changes in pathogen transmissibility contribute further to the complexity of seasonal patterns. Even a perfectly healthy person can experience a change in susceptibility to infection due to stress, injuries, or trauma. The probability of a marked impact of such factors on disease seasonality is virtually unknown.

Seasonality in Pathogens Survival and Transmissibility

> Some diseases are produced by the manner of life that is followed; others by the life-giving air we breathe.
>
> (Hippocrates. *The Nature of Man*, 9)

Temperature, humidity, and precipitation – the defining factors of seasons – are important determinants of pathogens' survival. Changes influence pathogens' potency and life expectancy, resulting in temporal fluctuations in pathogens' abundance. In many instances, seasonal changes in pathogen survival and transmission are inseparably related to both biological and social aspects of our lives. They are synchronized by weather. High ambient temperature, for example, provides a supportive environment for food-borne pathogens, favoring their multiplication in food and on food preparation surfaces (6). Food contamination is believed to be a significant mode of transmission for infections caused by *Salmonella* and *Campylobacter* (7); therefore, during warm weather, the risk for food-borne diseases increases (8).

Seasonal changes in level of contamination, availability of potable water, sanitation and hygiene practices, as well as crowding and person-to-person contacts, affect pathogens' transmissibility. Worldwide, water use differs from season to season (9). In temperate climates, warm weather leads to higher water consumption and encourages outdoor activities – swimming, camping, and recreational water use. In tropical regions, contamination of surface water increases during wet seasons. Although spread of pathogens via food is certainly possible, contaminated water is the dominant source of exposure for enteric infections caused by protozoa *Cryptosporidium* and *Giardia* (10–12). Depending on locality, outbreaks of cryptosporidiosis and giardiasis associated with drinking or recreational water frequently occur during warm or wet seasons (13,14).

With the onset of cooler weather, the “heating season” marks a change in indoor air quality. Inadequate and poorly designed ventilation in crowded public places and urban transit systems may boost exposure to air-borne pathogens by increasing their concentration in stagnant air and by re-circulating contaminated air. Higher relative humidity may also affect the stability of air-borne droplets in which viruses travel from person to person.

Disease Seasonality and Calendar Effects

> You will find, as a general rule, that the constitutions and the habits of a people follow the nature of the land where they live.
>
> (Hippocrates. *Air, Waters, Places*, 24)

Diseases do not watch calendars. Their incidence rises and falls because of changes in factors associated with the diseases. However, in every culture all social events are synchronized by calendars; and every calendar reflects the cyclic rhythm of nature.

Traditional celebrations and gatherings observed by communities according to calendars affect pathogen transmission. Holidays, social activities, and seasonal travel are often associated with changes in food consumption and preparation, and are therefore associated with changes in disease incidence. Preparing meat on a barbecue increases the risk of *Campylobacter* infection (15,16) and foreign travel increases the risk for enteric infections. Aggregation of children in schools, daycare centers, and summer camps, reflecting school calendars, facilitates rapid exchange of pathogens. There are marked seasonal variations in transmission, and thus the incidence of enteric and respiratory infections.

Climate Change, Extreme Weather Events, and Disease Seasonality

> The changes of the seasons are especially liable to beget diseases, as are great changes from heat to cold, or cold to heat in any season. Other changes in the weather have similarly severe effects.
>
> (Hippocrates. *Aphorisms*, III, 1)

As weather affects human health by creating favorable conditions for pathogen proliferation and transmission, severe weather can affect the timing and intensity of infectious outbreaks, and natural disasters lead to drastic changes in population structure and pathogen ecology. Catastrophic events like tsunamis, hurricanes, devastating floods, and heat waves that cause deaths, population displacement, and infrastructural damage may have dramatic effects on the incidence of infections and their seasonal patterns.

Recent work has shown highly significant associations between extreme precipitation and water-borne disease outbreaks (17). Heavy precipitation, rapid snowmelt, and floods flush animal wastes from the land into surface waters and may overwhelm drinking and wastewater treatment systems. The latter leads to discharges in watersheds of untreated human wastes. As a result, pathogens can appear in drinking and recreational water in very high concentrations (18,19). A rapid snowmelt, resultant runoff, and filtration system failure at the overloaded local drinking water treatment plant were implicated in the largest known water-borne outbreak of cryptosporidiosis, which occurred in Milwaukee, Wisconsin in 1993 (20). This outbreak happened in April, not within the usual seasonal peak for cryptosporidiosis cases. A flood, which also resulted from a rapid snowmelt, has been linked with a similar increased incidence of diarrhea (21).

Experts expect that global climate change will increase climate variability and the frequency of extreme precipitation events in temperate regions (22,23). “Global warming” may also increase the frequency and magnitude of other extreme weather events, such as heat waves and droughts, and thereby have profound effects on public health (24,25). In a comprehensive study conducted in the United Kingdom that described a short-term link between temperature and food poisoning, the authors also hypothesized that climate change could lead to changes in rates of food poisoning (26).

Integration of environmental parameters into disease forecasting and warning systems could allow public health officials to alert the populace when specific meteorological conditions pose predictable risks to health (27). Simple messages about proper food preparation and refrigeration and the risks of using contaminated recreational waters could, for example, be provided before, during, and after extreme events. Better understanding of disease seasonality would also help to predict outbreaks of infections triggered by climate variability.

Methodology in Studying Seasonality: Brining Mathematics and Philosophy to Public Health Thinking

> Desperate cases need the most desperate remedies.
>
> (Hippocrates. *Aphorisms*, I, 6)

At first, seasonal fluctuations should be systematically described. This requires a framework with sound definitions and analytic tools suitable for routine use by public health professionals. In public health sciences, the existing methodology currently lacks methods and tests for assessing complex interactions in the time-dependent factors responsible for disease seasonality.

Next, reliable data with fine temporal resolution are a must. The vast majority of epidemiological studies have examined seasonal patterns of infections using quarterly or monthly data. This coarse temporal aggregation can thwart an otherwise detailed, accurate, and comprehensive analysis of seasonal patterns and may even be misleading (28). Examination of daily or weekly rates can substantially improve evaluation of seasonal curves, but a systematic approach for using at least weekly aggregates is needed.

Finally, reluctance to apply sophisticated mathematical models in public health studies must be overcome. Underlying processes in disease manifestation and spread are complex and multifaceted. Causal pathways are often obscured. To disentangle causal effects of many factors within the circular processes of self-sustaining oscillations demands the careful building of sound conceptual models of seasonality; models that can be tested. The emerging fields of computational epidemiology and intelligent data mining will complement established work in philosophy of science and mathematical biology to become an essential part of thinking in public health and policy.

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