To every disease there is a season? What our genes tell us

To every thing there is a season...A time to be born, a time to die, a time to plant, a time to reap. A time to kill, a time to heal. A time to laugh, a time to weep. A time to build up, a time to break down...A time to dance, a time to mourn. A time to cast away stones. A time to gather stones together.

So goes a <u>catchy song</u> by the 1960s rock band The Byrds, a passage rearranged brilliantly from the biblical book of *Ecclesiastes*. We can add to this list: a time to get sick. For many years, various diseases have been observed to occur more frequently in certain seasons. Why is that?

Proposed explanations range from scientifically valid rationales backed by published data and statistics to hyped speculation. The most exotic speculation with no evidence is an hypothesis that certain infectious diseases, like the flu, come from "space". The seasonality, according to proponents of the idea, is because of the Earth moving through different regions of space, thereby exposing our planet, along with humans, to <u>infectious agents of extraterrestrial origin</u>. The hypothesis is based on calculations by astrophysicists showing associations between disease outbreaks, the Earth's position, and various atmospheric conditions.

However, while the math is correct, the biology is all wrong. Because of genomic comparison analysis, we know the connections, and can track the evolutionary origin of the genes in various influenza viruses. This is not to say that life on Earth might not have extraterrestrial origins billions of years back in time. It's possible that Earth was seeded with some kind of early microbes from Mars, or elsewhere, leading to the life we know today. But the gene sequences of viruses like influenza suggest that they've been evolving right here on this planet, just like all other organisms we see around us. Additionally, it's because they coevolved along with us that disease-causing viruses are able to infect us. A microbe coming from a distant location in space probably would not be able to do that.

But the seasonality of a variety of diseases, not just flu, can be explained with more down-to-Earth ideas.

Allergies, asthma and upper respiratory infections

For most people, this category of medical conditions is most obviously seasonal. Allergic rhinitis—sneezing and runny nose and other upper respiratory tract symptoms—can be stimulated by pollen, and certain types of asthma are triggered by allergens. Pollen and various other allergens are released into the air in connection with plant life cycles. When it comes to upper respiratory infections, notably the flu and the common cold, it might be fun to think that the causative viruses come from space, but, as noted above, they evolved alongside us on Earth. Cold viruses and influenza are around us all the time, but in winter people tend to stay inside and with the windows closed. This concentrates the viruses, leading to outbreaks and the problem is exacerbated in poorly ventilated buildings that are overheated.

Whatever your grandmother told you about the cold air making you sick, it's an urban myth. Hot, dry air

dries out mucous membranes making it harder for the immune system to fight off cold viruses in the nose and mouth. With multiple people gathering inside with the windows shut, the viruses are concentrated. And so, the best health policy in winter is to keep rooms ventilated and avoid overheating.

Winter blues

For certain types of disease, mood disorders in particular, seasonal influences are connected with light. The pineal gland in our brain sends the hormone melatonin through the blood stream at night, or at other times when it's dark. Melatonin production turns off when the lights come on, but the turn-off is sluggish unless it's bright, morning sunlight, or a good simulation of morning sunlight. Melatonin makes us feel sleepy and the pineal gland makes more of it in winter than summer, and too much melatonin in the morning is associated with depression. For this reason, the incidence of depression is higher in winter in high latitude locations, like Alaska. Known as seasonal affective disorder, the phenomenon afflicts roughly 10 percent of Alaskans, and the problem is just as bad in northern cities of the continental United States, like Seattle.

In such northern places, the suicide rate jumps in early spring, as the amount of sunlight starts to increase. Why not in the dead of winter? According to Suzanne Womack Strisik, a psychologist in Anchorage, the reason may parallel an hypothesis that's been proposed to explain why the suicide risk sometimes actually worsens soon after a depressed patient starts using a powerful antidepressant drug.

"You don't have enough energy to make a [suicide] plan before then," Strisik noted. "Once the light starts coming back, there's more energy, but reasoning is still off."

It sounds gloomy, but here's the good news: Around the turn of the century, researchers in Seattle figured out that light therapy in the morning—bright light from a visor or other device that sends it directly to the eyes—works well to mitigate depression or prevent it outright. At first, plain old white light was used, but, integrating discoveries from aerospace medicine researchers working with pilots in recent years, science has since honed in on the optimal wake up color. It's now known that if you expose people to bright light in the transition between blue and green—in other words, the aqua range—the trigger to have the pineal gland turn off melatonin production is most efficient.

Melatonin is good, because it helps make you tired to go to sleep and may prevent certain cancers. But it also causes depression, if it lingers in the bloodstream while you're awake, and that's the connection between depression, light, and the latitude where a person lives. How does light, and the lack of it, turn the production of melatonin off an on? It turns out that it works through an on/off switch for the melatonin gene. That's an important concept, because very recent research shows that the seasons are a major factor when it comes to a multitude of diseases, far beyond the realm of mood disorders and psychiatry.

Chronic diseases

"Certain chronic diseases are very seasonal..," explained University of Cambridge geneticist John Todd. In a <u>study</u> published in the prestigious journal *Nature Communications*, Todd and several colleagues recently analyzed genetic data from more than 16,000 volunteers. The results showed that seasons have

a major impact on the activity of approximately 4,000 different human genes.

Many of the genes found to be turned on or off based on season play an intimate role in the development of various common, chronic diseases, such as diabetes Type 1, cardiovascular disease, rheumatoid arthritis, multiple sclerosis, and, as expected, seasonal affective disorder. In the latter case, the genetic connection was found to go beyond the gene that turns on melatonin. Furthermore, considering a range of diseases, Todd added that "[in the study] genes promoting inflammation were increased in winter, whereas genes suppressing inflammation were decreased in the winter."

Inflammation is one of the main mechanisms leading to chronic diseases—not just those listed above, but also many others. Therefore, winter, in general, promotes the development of disease, and it may have other negative effects too.

"Your cognitive performance...might be influenced subtly by the time of year at which you're assessed," according to Akhilesh Reddy, another University of Cambridge researcher and specialist in circadian rhythms. "There's never been a marker before that you can look at in the blood, or whatever, to say, 'You're looking like you're a winter person now versus a summer person.'"

Reading all of this during winter, complete with the lyrics from the famous song by The Byrds, may have been depressing, but—at least in Earth's northern hemisphere—we're a few days from the onset of spring and the days are getting longer. And so, it's probably better to end with another famous song by another 1960s band, the Beatles, and the name of that song: *Here Comes the Sun*.

Here comes the sun, here comes the sun And I say it's all right

Little darling, it's been a long cold lonely winter Little darling, it feels like years since it's been here

Here comes the sun, here comes the sun And I say it's all right

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