In season, atmospheric conditions can drive disease

When winter comes, it usually brings more than just snow. The frigid temperatures coincide with a predictable uptick in colds and influenza. Lately, though, researchers are finding some seasonal patterns in conditions one wouldn't necessarily expect to be tied to the calendar.

In August, scientists reported new insights into the seasonable variability of multiple sclerosis. They had examined 939 brain scans taken from 44 individuals with multiple sclerosis over a period of three years. The scans used magnetic resonance imaging to measure edema as an indicator of new lesions in the brain. The researchers discovered that between March and August, the subjects suffered brain lesions at a rate that was, on average, two to three times higher than during the rest of the year (*Neurology* **75**, 799–806, 2010).

"It peaks in spring and then summer, and then falls off very rapidly, with much less activity in fall and winter," says Dominik Meier, the lead author of the paper and a radiologist at Brigham and Women's Hospital in Boston.

Meier says there's a lot of speculation as to what environmental factors could contribute to the seasonal pattern. It's thought that stores of vitamin D from summer sun exposure may be depleted by the time spring rolls around. Vitamin D affects the immune system and may dampen the autoimmune response thought to drive neurodegeneration in multiple sclerosis.

'Tis the season: Colder temps hurt hearts.

It's not just disease symptoms that vary seasonally; responses to treatment have been shown to vary throughout the year as well. A clinical trial of more than 1,200 patients given chemotherapy treatments for breast cancer, conducted across several regions of Spain, reported in August that adverse reactions to the treatment—such as weaknesses and elevated levels of transaminases, which can be a sign of liver damage—occurred more frequently in spring and summer and in warmer climates overall (*Breast Cancer Res. Treat.* doi:10.1007/s10549-010-1136-0, 2010).

Sometimes it is variability within the climate, irrespective of the absolute temperatures, that's the deciding factor. Such is the case with heart attacks, according to a recent study from researchers at the London School of Hygiene and Tropical Medicine (*BMJ* **341**, c3823, 2010). They obtained the records for more than 84,000 hospital admissions for heart attacks across England and Wales and compared the data to local weather reports. They found that a drop in temperature by just 1 degree Celsius increased the overall risk of heart attack by 2%, or about 200 extra heart attacks on that day.

"People were unsure whether it was the cold itself or the reduction in temperature," says Liam Smeethe, the study's senior author. "But it didn't matter what temperature you started at. The increase in heart attacks was consistent." Smeethe says these results could help hospitals to prepare for an influx of patients by simply paying attention to the weather forecast.

Roxanne Palmer

Call for renewed focus on rare mutations grows more common

In the past five years, scientists have identified more than 3,000 common genetic mutations associated with diseases including cancer, Alzheimer's and diabetes, thanks to insights gleaned from genome-wide association studies (GWASs). But the inherent value of these studies has come under scrutiny, in part because they largely ignore rare mutations. Given this flaw, researchers have called for renewed focus on the rare mutations that might be more likely than common ones to cause illness.

The GWAS approach involves comparing the genomes of healthy people with those suffering from illness to pinpoint disease-associated single nucleotide polymorphisms (SNPs) typically present in at least 5% of the population. "A GWAS study is meant to capture most of the common variation in the genome, and that's something it does very well," says Jonathan Sebat, a geneticist at the University of California–San Diego.

So far, though, the common variants that have been identified by GWASs confer relatively small increases in risk and explain only a fraction of the heredity that clearly exists in many common diseases.

In an analysis published last month in the journal *Clinical Genetics* (doi:10.1111/j.1399-0004.2010.01535.x, 2010), medical geneticist Ivan Gorlov and his colleagues from the MD Anderson Cancer Center in Houston argued that scientists should speed the search for rare mutations that slip under the radar. "Until now, we've studied two tales of the distributions of polymorphisms: extremely rare mutations with strong effects, or monogenic diseases, and common polymorphisms with small effects on disease risk," explains Gorlov. "Common sense tells us that the most cases should be in the middle."

According to the new study, more than half of all SNPs are probably rare in terms of their prevalence in the population, and these are the ones that are most likely to cause disease. "They are likely to be slightly deleterious," Gorlov says, "and because of this, they will be under the pressure of negative selection that will drive their frequencies down."

As a result, Gorlov contends, scientists conducting GWASs need to maximize their sample sizes so that rarer mutations can be assessed. Others agree. "The bigger your sample size is, the more things you find," says John Witte, a genetic epidemiologist at the University of California–San Francisco.

Others, such as Sebat, believe that more drastic measures will ultimately be necessary. "If you really want to understand how much rare variation contributes to disease, what you need are complete genome sequences," Sebat says.

Melinda Wenner Moyer